

# A Way Out of the Inner Prison

The paralysis starts gradually, but in the course of time, it affects the entire body. People with amyotrophic lateral sclerosis eventually reach a point where they are no longer able to move any muscles or communicate with the outside world. A research group headed by **Moritz Grosse-Wentrup** at the **Max Planck Institute for Intelligent Systems** in Tübingen is looking for ways to help ALS patients break out of their isolation by teaching computers to read their minds.

TEXT **TIM SCHRÖDER**

**W**ilfried Leusing noticed something was amiss after doctors had inserted implants in his jaw for a dental prosthesis. His tongue felt numb, his speech was slurred. His doctor said that his tongue needed to recover from the operation. But it didn't get any better. A neurologist referred him to Tübingen Hospital. The diagnosis was sobering: "suspected motor neuron disease." Motor neurons are nerve cells that control muscles – in the fingers, in the chest cavity, in the tongue.

The control center for these neurons is located in the middle upper section of the brain, in the cortex: A dense meshwork of nerve cells forms what is known as the motor cortex. If the nerve cells in the motor cortex fail, it becomes impossible to voluntarily move muscles, despite the fact that they are still intact. Wilfried Leusing accepts his fate stoically: "It wasn't a shock for me, but it was for my wife," he says. At the time, in the spring of 2010, he consulted other specialists at hospitals in Munich and Ulm, but the findings were the same everywhere.

Wilfried Leusing has ALS, short for amyotrophic lateral sclerosis, a disease

in which the cells of the motor cortex slowly die. The speed at which the neurons fail varies from one patient to the next. Some are unable to move their arms and legs two years after diagnosis. In Wilfried Leusing's case, the disease has progressed more slowly.

## MANY PATIENTS WANTED TO TAKE PART IN THE STUDY

Today, four years after being diagnosed, he is barely able to speak. He also has difficulty swallowing. Since his tongue became semi-paralyzed, he has realized just how complex the acts of chewing and swallowing are, he remarks on his website, "*Das Alternativ*." "Your tongue pushes mashed food between your teeth and then toward the back of your mouth." Because of his paralysis, that's no longer possible for Wilfried Leusing. He now squeezes liquid food into his stomach through a tube. He types what he wants to say into a tablet computer. A program then reads the words aloud.

"As a result of the disease, I've rediscovered the art of writing," he says through his computer. Although he's no longer able to communicate by speaking, there are other ways to convey words and emotions. "I've had whole

new experiences, not despite but precisely because of my disease." In the past few months, Wilfried Leusing has been participating in a study by the Max Planck Institute for Intelligent Systems in Tübingen. That, too, is a new experience. The project is headed by Moritz Grosse-Wentrup who, as an electrical engineer, is responsible for the Brain-Computer Interfaces research group.

Last year, Moritz Grosse-Wentrup advertised for subjects on the Internet. There are around 15,000 ALS patients

A direct path from brain to computer: The electrodes attached to the head of student Sebastian Weichwald measure activity in various areas of the brain. By switching between two concentration states that produce characteristic electrical wave patterns, Weichwald tries to control a ball on a monitor that isn't visible in the photo.





Paving the way out of isolation: Moritz Grosse-Wentrup (left) has found a cognitive process that may help ALS patients communicate with the outside world if their motor cortex is severely damaged. It is hoped that patients will be able to control a ball on a screen through activity in the default-mode network, which comprises several areas of the brain that are particularly active during emotional states. The software is currently being tested in a study with ALS patients and healthy subjects like Sebastian Weichwald, who is a member of the Max Planck team.

in Germany, and a lot of them responded. For now he has selected four people for the study. One of them is Wilfried Leusing, who also lives in Tübingen, and who impressed Moritz Grosse-Wentrup with his life-affirming attitude.

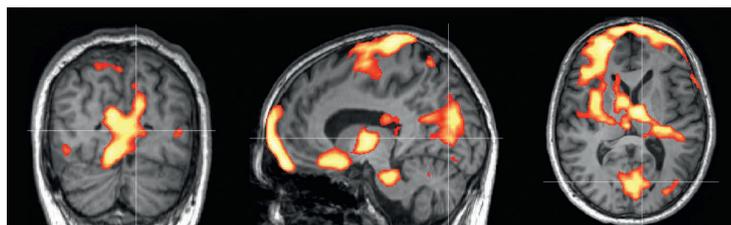
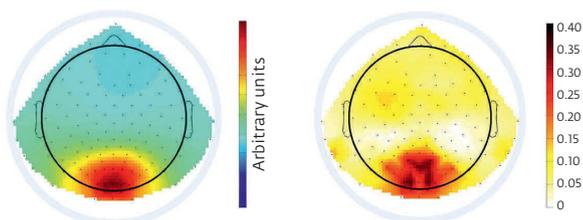
### SOME PATIENTS ARE TRAPPED IN THEIR BODIES

The tragedy of ALS is that all of the body's functions for which muscles are used are gradually lost. It starts with small areas of paralysis. Then the limbs fail. The tongue and larynx stop work-

ing, which makes swallowing impossible. Eventually, the patient lies immobile and unable to communicate because he can no longer speak. In some cases, the eye muscles stop working. The patient is then no longer able to focus on others. "Specialists refer to this as the locked-in state," says Grosse-Wentrup. "The patient is completely trapped in his body." Late-stage patients even lose the ability to indicate when something ails them. "We know of patients whose pneumonia was picked up too late because they could no longer communicate."

Some researchers, like neurobiologist Niels Birbaumer of Tübingen University, believe that ALS patients gradually slip into a dreamlike state. Their theory is that a person can normally interact with their environment by communicating through touch, gestures, language or facial expressions. If a person loses the ability to interact, their consciousness withdraws. There is no longer any contact with the outside world.

Moritz Grosse-Wentrup hopes to restore at least a small link to the outside world. His approach sounds bold: in the late stage of the disease, when noth-



Nearly ideal: To enable ALS patients to communicate with the outside world via their brain activity, Max Planck researchers record an EEG activity pattern in the posterior region of the brain, as shown in the photo on the left. In the recording from an ALS patient, they observed the brain activity pattern shown in the middle photo, which matches the desired pattern very well. This is consistent with functional MRI scans, in which the main activity is also observed in the posterior region of the brain, marked by the crosshairs.

ing else works, patients may be able to communicate via their thoughts, or rather, their brain activity. “This should enable patients to respond to simple yes or no questions,” says Grosse-Wentrup. Are you in pain? Would you like to listen to the radio?

To open a way out of this inner prison in which ALS patients are trapped, Grosse-Wentrup and his team first have to learn how to interpret cognitive activity correctly. They aren’t the only ones seeking to create a direct link between the brain and the outside world, without help from any muscles. For instance, researchers at Brown University in Providence, USA, are working with experts from the German Aerospace Center (DLR) in an attempt to read and process signals from the brain. They have developed a method that enables paraplegics, for example, to move a robotic hand. Their videos on the Internet show a subject guiding the robotic hand to a plastic bottle with the power of her mind. The woman beams happily as she sucks on a drinking straw for the first time without assistance.

For their experiments, the US researchers use small electrodes that they implant directly into the motor cortex below the cranium. The electrodes sense neural activity. The trick is that even imagined movements stimulate neurons in the motor cortex. In many paralyzed people, the motor cortex remains active even though the body is unable to execute movements. The electrodes pick up signals from the neurons and relay them to a computer that converts the pulses into control commands for the robotic arm. Of course the patient has to undergo lengthy training. The payoff, however, is that patients can learn to control the robot by imagining movements in their mind. The advances the US researchers have achieved are impressive.

However, this approach doesn’t work for ALS patients, because in their

case, it is precisely the motor cortex that is damaged. “So we have to find other regions of the brain, other signals, that will enable ALS patients to communicate,” says Grosse-Wentrup. It looks like he has found a way. For some years now, neurologists have known that a number of areas in the brain are active simultaneously while various tasks are being performed. Thought isn’t constrained to a single area of the brain. During some thought processes, specific areas engage in a kind of finely tuned polyphony.

Moritz Grosse-Wentrup is particularly interested in an activity pattern that occurs when people concentrate on themselves, focusing their thoughts inward through meditation. During this state, an area behind the brow and a second area deeper in the brain, known collectively as the default-mode network, are simultaneously active. By contrast, when a person concentrates on an activity, like reading or doing calculations, the default-mode network is less active.

### THE DEFAULT-MODE NETWORK IS LESS AFFECTED BY ALS

Grosse-Wentrup believes that by switching between two different states of concentration in this way, even late-stage ALS patients can communicate and give yes or no responses to questions because the default-mode network is less affected by ALS than the motor cortex.

In the Tübingen scientists’ experiment, patients try to move a ball up or down on a computer screen. Up means “yes,” down means “no.” The height of the ball corresponds to the strength of activity in the default-mode network, so any changes in the activity state cause the ball to move. At present, it isn’t possible to move the ball sideways.

Unlike the US researchers, Grosse-Wentrup doesn’t use electrodes im-



Wilfried Leusing, who has ALS, wants to help make life easier for other patients. That is why he is participating in the Max Planck study.

planted directly in the cortex. The risk of infection is too great, he says. Moreover, the body’s rejection reactions often cause the electrodes to become coated with a deposit, interfering with signal transmission to the computer. He thus prefers to use a conventional electroencephalogram (EEG). The subject wears a helmet fitted with scores of small electrodes that detect the electrical signals of neurons through the cranium. Of course such a signal is less precise than signals from electrodes implanted directly in the brain. But it’s sufficient for the time being, says Grosse-Wentrup.

“I give as few instructions to the subjects as possible,” he says. “Each patient must personally find a way to influence his or her brain activity in the default-mode network to move the ball up or down.” Turning one’s thoughts inward through meditation is only one way to activate the default-mode network. Some subjects manage to move the ball by calling up various emotional states, as different feelings also lead to variations in the activity of the default-mode network. >



Ultimately, it's about the subject and computer understanding each other quickly. In the future, the computer will have to be able to rapidly convert the subject's thought commands into a response. The patient has to learn to control the ball on the screen; the computer has to learn how the corresponding activity patterns look so that it can reliably and rapidly change the height of the ball. "We can already see that we receive a correct answer to questions all the more quickly the better the computer learns the frequency patterns," says Grosse-Wentrup. That will later be essential in the everyday lives of ALS patients because, naturally, simple questions like "are you in pain?" should be followed by a quick answer.

Together with Niels Birbaumer of Tübingen University, Schölkopf's department has been working for a decade on communicating with ALS patients via thought commands. However, they initially selected thought processes and concepts that were ultimately unsuitable. They found that the thought processes and neuronal voltage patterns depended too strongly on the patient's form on the day, and the computer wasn't sufficiently adept at interpreting the patient's thoughts. As the disease progressed, these methods eventually failed completely. "Moritz appears to have found another paradigm, another thought process, that is more robust," says Schölkopf.

To obtain a large volume of training data with which to feed the computer, Grosse-Wentrup is also testing his method on healthy subjects. Over the past five years, he and his colleagues have taken EEG recordings from around a hundred students. It looks as if Grosse-Wentrup's method really is robust. Although the computer learning machine takes some time to adjust to the subject's thought patterns each time, the subject is able to move the ball very soon. So evidently thought patterns exist that are similar enough in everyone for machine-learning methods to recognize them. The details of the thought processes are somewhat different in every patient and vary with the subject's daily condition.

Because Moritz Grosse-Wentrup has been working with Wilfried Leusing and the other ALS patients for only around six months, it is still uncertain whether his method will still work in the late stage of the disease. But the fact that it is already very robust gives him cause for hope. In one of his patients, the disease is progressing rapidly. The patient already has difficulty moving his limbs. He could be the first person to show that the new method provides a reliable communication channel to the outside world as the body gradually shuts down.

### MORE DATA REQUIRED

Moritz Grosse-Wentrup originally decided to study electrical engineering and later became involved in robotics. He then heard about the work on ALS patients. Today he says work that helps people is much more rewarding than robotics. If his method, his thought-pattern paradigm, turns out to work in the

late stage of the disease, he could imagine switching from EEG to implanted electrodes that aren't attached to a computer via a cable, but instead transmit data wirelessly. Suitable electrodes are currently being developed. They would be ideal for everyday use and would also provide clearer frequency signals.

But first Grosse-Wentrup needs more data from his ALS patients. Wilfried Leusing intends to do his part and will continue to meet with the researchers once a week. Grosse-Wentrup or his fellow scientists arrive each time with a basket full of cables and electrodes. "It's important for everyone to realize what role he or she plays in life," says Wilfried Leusing through his computer. One of his roles is that of a subject who is helping to make life a bit easier for ALS patients in the future – even if he will no longer be able to benefit from it himself. ◀

 [www.mpg.de/brain\\_computer\\_interface](http://www.mpg.de/brain_computer_interface)

### TO THE POINT

- Patients with amyotrophic lateral sclerosis (ALS) suffer from progressive paralysis. Eventually they lose the ability to speak and, in some cases, even move their eyes, depriving them of any possibility of communicating with the outside world.
- The members of Moritz Grosse-Wentrup's research team at the Max Planck Institute for Intelligent Systems in Tübingen hope to enable ALS patients to break out of their isolation. They are teaching ALS patients to control a ball on a computer screen through activity in the default-mode network, allowing the patients to answer yes or no questions.
- The scientists record activity in the default-mode network by means of EEG electrodes that are attached to the head. Using machine-learning methods, they are teaching a computer how to interpret the activity pattern in the brain and convert it into control signals.
- The researchers are currently refining the methods for analyzing brain activity with the help of four ALS patients and around a hundred healthy subjects.

### GLOSSARY

**Amyotrophic lateral sclerosis (ALS):** In this neurodegenerative disease, the nerve cells in the motor cortex slowly die, causing the affected person to ultimately no longer be able to carry out any movements.

**Default-mode network:** The default-mode network consists of areas in the anterior and posterior parts of the brain that are especially active in the resting state, as well as in emotional states.

**Machine learning:** Computers learn to detect patterns in data by analyzing examples and deriving general rules. In this way, they can recognize handwriting, for example, or interpret activity patterns in the brain.