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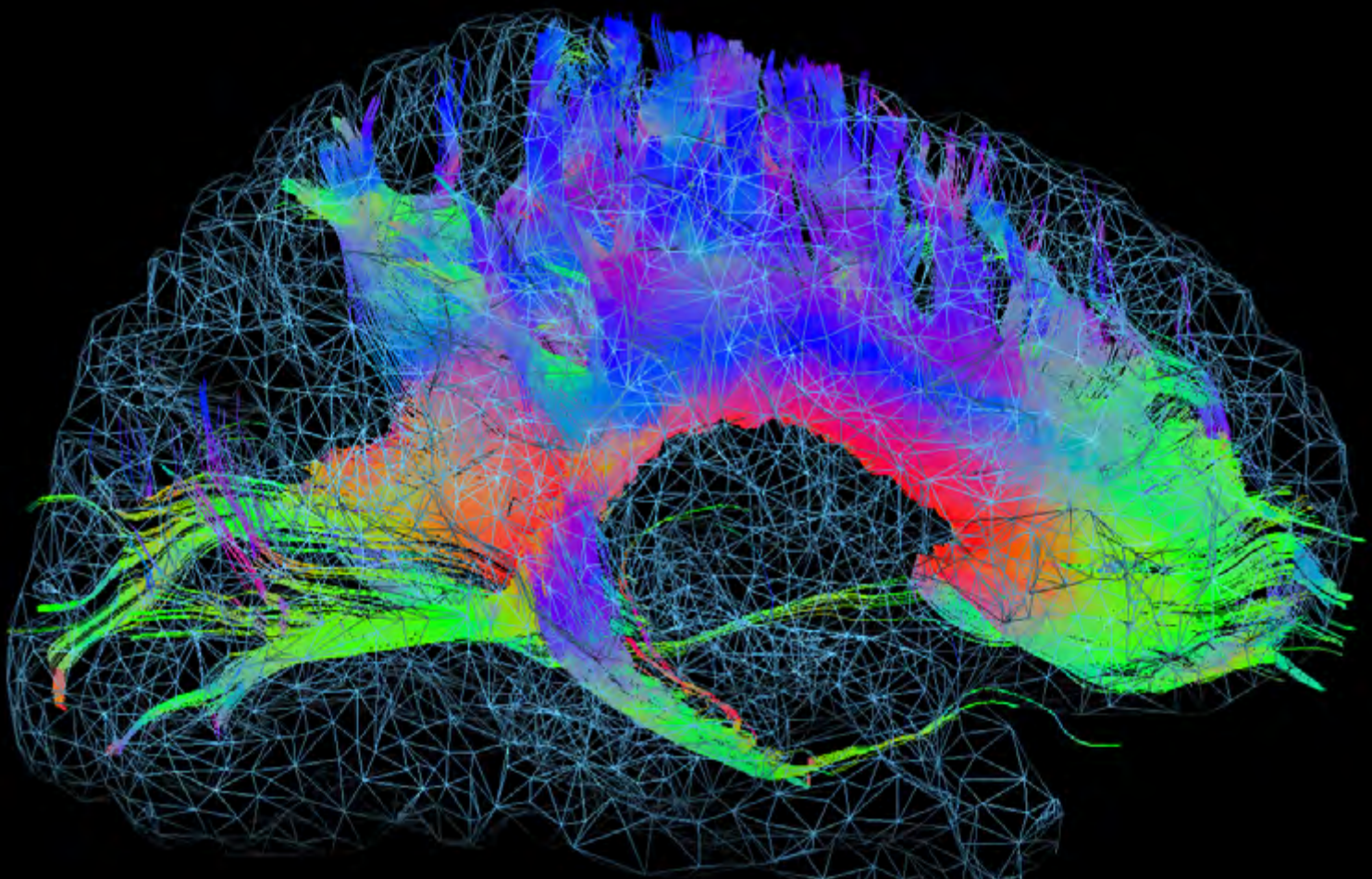

EXTINCTION LEARNING

What happens in the brain during learning

Why the context of an experience is crucial in this process

And how research into extinction learning helps patients overcome pain and anxiety

#35

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Extinction Learning

Pain is learned faster and in a more lasting way than other things. Although that makes sense from an evolutionary perspective, for people with chronic pain, it's a problem.

„Since my lower back pain last year, I tense up just doing the vacuuming," reports Jürgen W. "I haven't dared to get into my car since then because it's lower down, only my son drives it now." There are many people like him. "Every day, we see patients who have experiences like this. They have learned to expect and fear pain," says Professor Ulrike Bingel. The professor of Clinical Neuroscience heads the University Center for Pain Medicine at Essen University Hospital. In various experimental studies, she and her team are investigating the connection between pain and learning processes. "Studies have been conducted on this topic for the last 20 years," she says. "But never as broadly and extensively as is possible in the Collaborative Research Center 'Extinction Learning'."

The experiments conducted concern how and which people, in particular, learn to associate a neutral stimulus with a subsequent pain stimulus, or learn that this stimulus will no longer be followed by pain. To administer experimental pain stimuli, the researchers use what is known as a thermode: a metal plate attached to the skin of the forearm that can be heated and cooled. Before each experiment, the research team determines the individual pain threshold of the participants.

The team used this approach to investigate, for example, whether the learning of pain fundamentally differs from the learning of other unpleasant stimuli. "After all, pain is a warning stimulus that tells us there may be damage to our body's tissue, or there is the risk of damage occurring that could even cost us our lives," clarifies Ulrike Bingel.

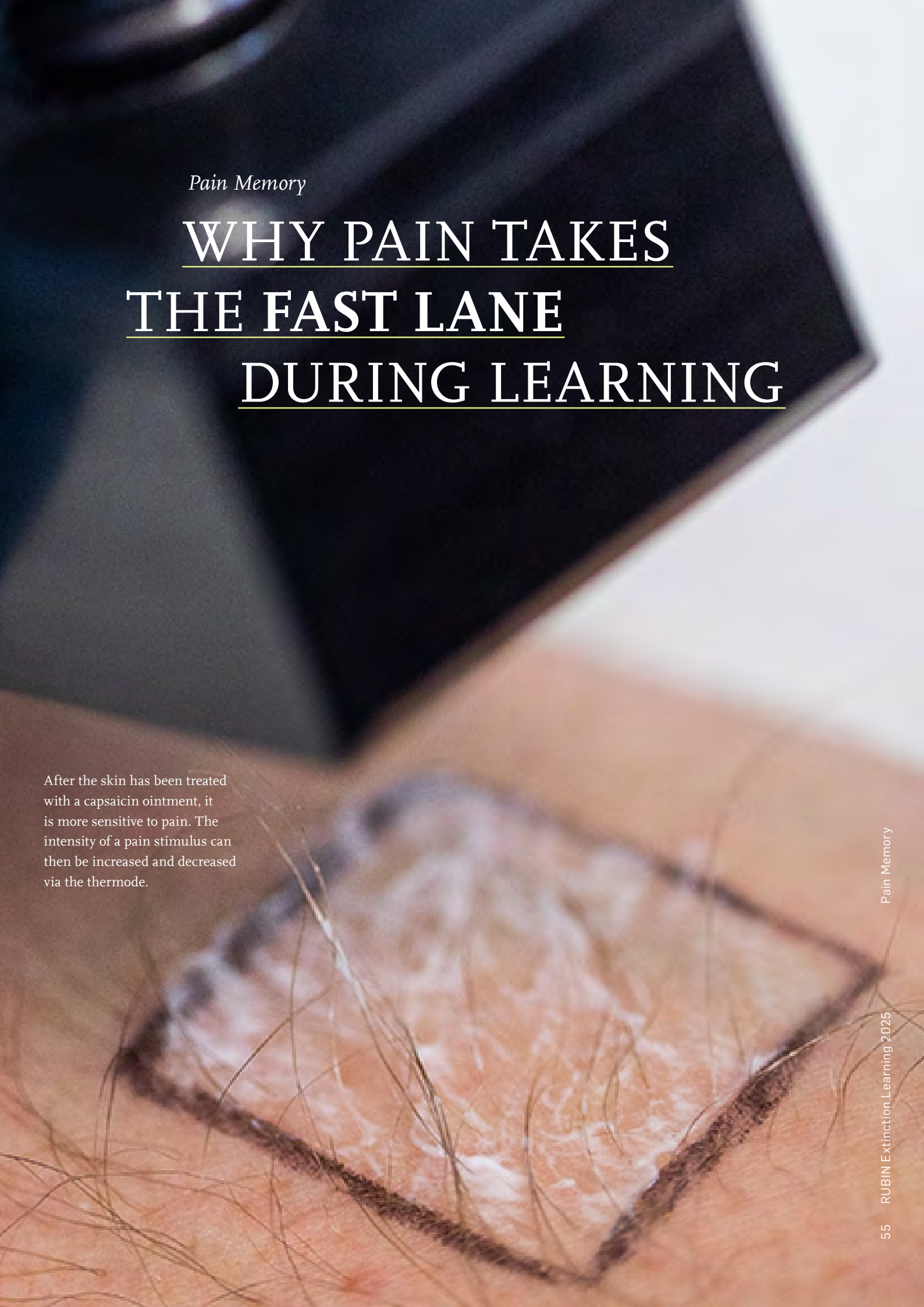
The researchers chose an unpleasant tone as a counterpart to the heat pain stimulus. They coupled the pain stimulus and the tone with neutral visual stimuli: They initially presented the participants with different geometric shapes, which were then followed with a certain likelihood by one of the unpleasant stimuli. The participants thus learned to link a shape with either pain or the tone. This link was broken again in a subsequent experimental phase, during which only the shapes were presented without the unpleasant stimuli. An established link between the geometric shape and the pain or tone was measured by the researchers using the assessed unpleasantness of the geometric shape. The researchers also measured physiological reactions such as skin conductance as a sign of stress.

Alongside the physiological measurements and surveys, the team used functional magnetic resonance imaging in ▸

Katharina Schmidt is co-project leader in the Collaborative Research Center Extinction Learning.

Pain Memory

WHY PAIN TAKES THE **FAST LANE** DURING LEARNING



After the skin has been treated with a capsaicin ointment, it is more sensitive to pain. The intensity of a pain stimulus can then be increased and decreased via the thermode.

Ulrike Bingel uses a thermode to induce experimental pain and investigates how quickly people learn the connection between a neutral stimulus and a pain stimulus.

> EVERY DAY, WE SEE PATIENTS WHO HAVE LEARNED TO EXPECT AND FEAR PAIN.

Ulrike Bingel

this study. This imaging method makes it possible to observe which areas of the brain are particularly active during a task or experiment.

"This allowed us to show that the link between the image and pain was learned more quickly and strongly than the link between the image and tone," reports Dr. Katharina Schmidt, co-project manager together with Ulrike Bingel. "The insula and amygdala areas of the brain, which are relevant for the processing of threatening stimuli, were activated more strongly during the learning of pain than of tone."

"From an evolutionary perspective, it absolutely makes sense that the learning of pain takes the fast lane, so to speak," says Ulrike Bingel. "This 'better safe than sorry' account, presumably enabled our ancestors to best protect themselves from life-threatening situations."

The group designed another experimental scenario for patients with chronic back pain and healthy control participants, this time with the possibility of changing the intensity of the pain, and once again accompanied by imaging. "Such data collections are very labor-intensive and can sometimes take several years," clarifies Katharina Schmidt. "Fortunately, our patients are very open to research and are often willing to take part in studies," says Ulrike Bingel.

In the study with over 60 healthy people and 60 patients with chronic back pain, an ointment containing the chili pepper extract capsaicin was applied to the participants' skin for a short time. Capsaicin causes the skin to be more sensitive to pain for a while. Once the ointment had been removed again, the researchers attached the thermode to this area. It was possible to slightly heat and cool the thermode to increase or decrease the pain, which was moderate at the beginning.

Does the appearance of the rhombus suggest a pain stimulus or not? The participants learn the connection between geometric figures and pain stimuli.

Using functional magnetic resonance imaging, the researchers can observe which areas of the brain are particularly active during a task.

This process was then once again linked to various geometric shapes. In this experiment, too, the participants first learned to link the increasing and decreasing of the pain stimulus to the shapes, and later to give up the link again. “This learning is very important in the context of pain,” explains Ulrike Bingel. “We learn what movements, actions or times of the day are associated with an increase in pain. However, it is also just as important to learn how we can find relief and which medications may help us.”

The researchers were able to observe that the linking of a stimulus with an increase in pain was learned much faster than with a decrease in pain. “This memory trace can also be seen for longer in the person’s behavior – a remnant of it remains,” reports Katharina Schmidt.

In a further study, the researchers investigated whether the learning of the link between the stimulus and pain differed between the healthy people and people suffering from chronic, non-specific back pain. “Chronic pain persists over at least three months,” explains Ulrike Bingel. “When we talk about non-specific pain, no specific organic cause can be found for these symptoms. They are not based on tissue being continually damaged, as would be the case, for example, with osteoarthritis.”

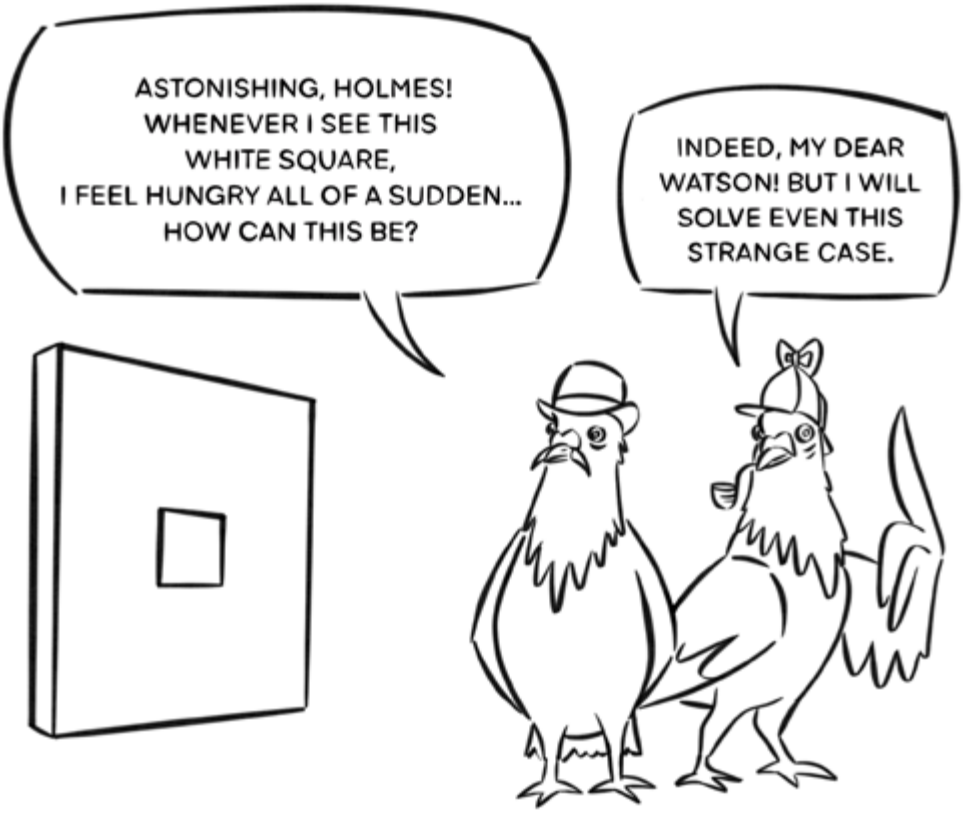
The researchers showed both groups of participants – each more than 60 patients with chronic back pain and healthy control people – different geometric shapes, which were sometimes followed by a pain stimulus. The link between the neutral stimulus and pain was learned first, followed by an experimental phase of breaking this link.

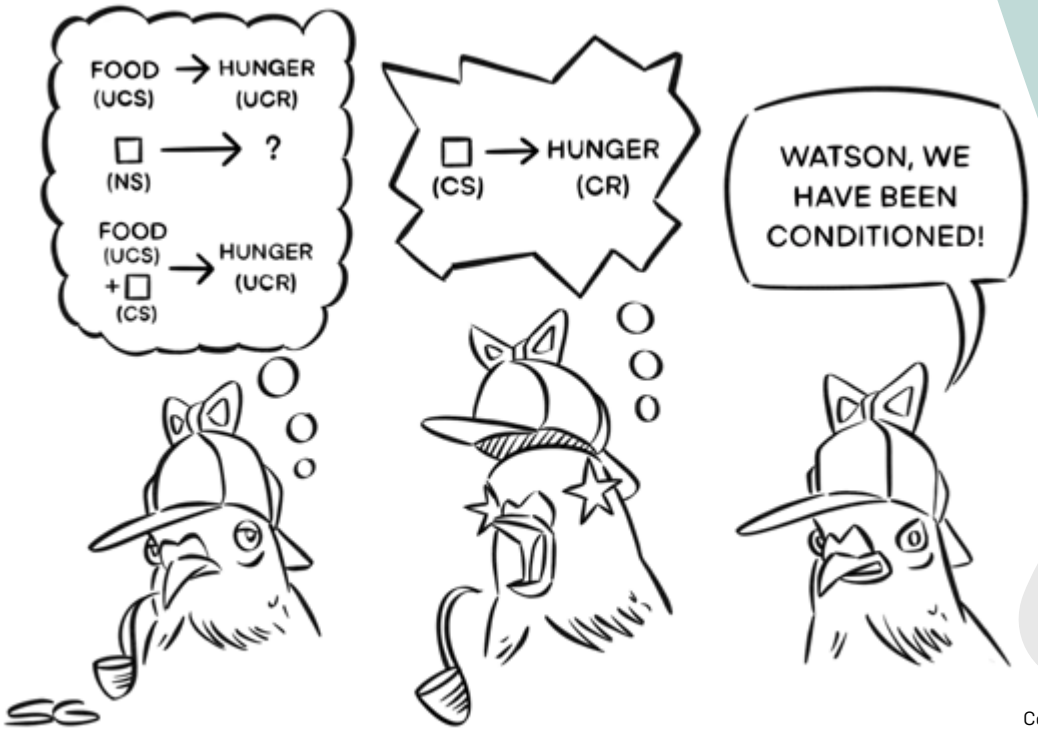
“The study showed that patients with chronic back pain distinguished less between the shapes shown than pain-free people,” reports Katharina Schmidt. “We can conclude from this that chronic pain is associated with altered threat and safety learning.”

The more the researchers find out about the mechanisms underlying the learning of pain, the better they hope to be able to help patients with chronic pain that significantly restricts their lives. “In the collaborative research center, we have the opportunity to work with colleagues who are dedicated to various aspects and disease patterns, such as visceral pain, in addition to back pain, which is our main focus,” says Ulrike Bingel. “There may be a general phenomenon underlying chronic pain, despite its different forms. That’s what we want to understand.”

text: md, photos: Essen University Hospital

EDITOR'S DEADLINE





Comic: Simon Gies

UCS: unconditioned stimulus
NS: neutral stimulus
CS: conditioned stimulus
CR: conditioned response
UCR: unconditioned response

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