Abo **Important study with paraplegics**

Antibody therapy helps paralyzed patients to become more independent

An international study reveals positive results. A drug could be ready for the market in three years. Zurich researchers are behind it.

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Basketball players in wheelchairs: Swiss anti-nogo therapy is able to improve the quality of life of some paraplegics.

Photo: Getty Images

In brief:

- An international team investigated the promising anti-Nogo therapy from Switzerland.
- Almost 130 paraplegics were examined in a placebo-controlled study.
- Significant progress has been observed, particularly in patients with incomplete paralysis.

The media often likes to celebrate them: supposed breakthroughs and milestones in the treatment of paraplegics. However, these are usually small studies with few or even only one patient, which are far removed from any possible application.
The current publication in the specialist journal "Lancet Neurology" is different. An international research team reports on an important intermediate step in a therapy that could make life easier for many paraplegics in the not too distant future. It involves treatment with an antibody that blocks a protein in the spinal cord called Nogo (English for "can't") and thus enables the regeneration of nerve fibers. It is based on decades of detailed work by researchers led by Swiss neuroscientist Martin Schwab and is now the most advanced therapeutic approach for paraplegics.

The placebo-controlled study with almost 130 patients was conducted at 13 clinics in Switzerland, Germany, the Czech Republic and Spain. "It is the largest study to date that shows that the spinal cord of paraplegics can regenerate," says Armin Curt from the Balgrist University Hospital in Zurich, who co-initiated and organized the study. A preliminary clinical study has already shown that the antibody enables regeneration in some paraplegics.

Improvement in independence in everyday life

The study participants, who were paralyzed due to a spinal cord injury in the neck area, were injected with the antibody directly into the spinal fluid one month after the accident. Not quite half were injected with a placebo. After six months of rehabilitation training, the researchers tested the strength in the arms and hands as well as the ability to independently perform everyday tasks such as taking off clothes, washing, eating or going to the toilet.

The study showed significant improvements: 60 percent of participants who received the full treatment achieved the maximum level of self-care - twice as many as with placebo. "We are very pleased with the result, because these improvements make a big difference for those affected," says Martin Schwab. It means that people with spinal cord injuries can manage their everyday lives without help or with limited Spitex care. Mobility and strength in the arm or hand also improved compared to the control group. The data also indicates that there was also progress in the control of the legs.
However, the improvements only occurred in patients with incomplete paralysis. In these patients, the spinal cord is only partially severed, which means that certain sensations and movements below the affected area are still possible. However, regeneration does not appear to be possible in complete paraplegics. "They make up just under half of all those affected," says Curt.

Hoping for easier approval

The study authors were also pleased to note that complications such as infections or pulmonary embolisms did occur during treatment, but not more frequently than in the placebo group. There was also no increase in pain or muscle cramps (spasms). "With a therapy that increases neuroplasticity, such negative side effects would have been conceivable," says Curt.

Despite the positive assessment, the authors concede that the overall results of the study are mixed. Because the completely paraplegic patients have not yet responded demonstrably to the treatment, no effect could be demonstrated across all study participants. "The good result in the incompletely paralyzed patients was diluted as a result," says Martin Schwab.

A follow-up study, which has just started, now aims to correct this. In addition, a new, improved antibody is to be tested and, if possible, administered in higher doses. "We have

We have seen that we have probably used too low a concentration," says Schwab. He believes that sufficient data will be available in three years' time to negotiate with the relevant authorities. "Then it will become clear whether another large, so-called phase 3 trial is necessary or whether we will receive a simplified approval for rare diseases."

Non-involved experts who are researching the same topic particularly praise the quality of the publication and confirm that further studies are needed. For example, James David Guest from the University of Miami Miller School of Medicine (USA) tells the German Science Media Center: "As for the future of anti-nogo therapy, these results are encouraging." Further studies should focus on people with incomplete injuries and could show which patients benefit from the treatment.

Winfried Mayr, Professor Emeritus at the Medical University of Vienna, writes on request: "Whether Nogo antibodies can make a significant contribution to the overall outcome of rehabilitation efforts still needs to be verified in further studies." He emphasizes that sensational breakthroughs in the field of cross-sectional rehabilitation are not realistically to be expected. "Unfortunately, misleading promises of success from individual research initiatives continue to emerge, which unfairly lead to false hopes on the part of patients." The authors around Schwab and Curt set a positive example in this respect and describe what has been achieved in all objectivity, without making exaggerated promises for the patients' living conditions.

Setback due to Novartis exit

The now 75-year-old neuroscientist Martin Schwab has been researching molecules that stimulate nerve growth since the 1970s. In 1990, he succeeded for the first time ever in making injured nerve fibres of the central nervous system of a mammal grow by blocking a then uncharacterized molecule with an antibody.

It was eight years before he and his team isolated this growth factor in its pure form and named it Nogo. Schwab decoded the gene sequence in 2000 and started the first human trials in 2006.

Eventually, Novartis was brought on board and a large patient study was initiated. However, the company then withdrew from all neuroresearch in 2013, setting back the Nogo efforts by many years. Martin Schwab and Armin Curt decided to push ahead with the therapy on their own without pharmaceutical support. The two finally launched the study that has now been published, which was funded by the EU and foundations.

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