

StartUP⁷ Stories

StartUp Stories: Dr. Brigitte Zrenner and Dr. Christoph Zrenner, founders of sync2brain GmbH

A perfectly timed brainwave

(Stuttgart/Tübingen) – Psychiatrist Dr. Brigitte Zrenner and neurologist Dr. Christoph Zrenner have found a way to personalise transcranial magnetic stimulation for patients and boost its effectiveness. This technology, which has been in use for decades, utilises strong magnetic fields to stimulate specific areas of the brain. The researchers have now invented “bossdevice”, an instrument that ensures this stimulation is applied at precisely the right time. To get their invention onto the market, they founded sync2brain GmbH. Along with the company’s CEO, Dr. Ramona Samba, they hope that both stroke patients and people suffering from depression and obsessive-compulsive disorder will soon benefit from this new technology. The story of sync2brain is just one of many successful StartUp Stories in the STERN BioRegion.

Everything seemed to fall into place at just the right time when, some years ago now, two students happened to meet in a laboratory at the University of Tübingen. Together, they would go on to change the potential of brain stimulation for the long-term. Both were studying medicine and both were working intensively on real-time electroencephalograms (EEGs) and transcranial magnetic stimulation (TMS). Today, husband-and-wife team Dr. Brigitte Zrenner and Dr. Christoph Zrenner are not just parents to four children, they are also scientists who have launched another great project – their company sync2brain GmbH.

The idea – how did the product and company come to be?

The Zrenners had been working on an idea for a number of years. Dr. Brigitte Zrenner, a specialist in neurology and psychiatry, conducts research on the translational development of individualised brain stimulation protocols and on the

mechanisms of pathophysiology in major depressive disorders and obsessive-compulsive disorder (OCD). Neurologist Dr. Christoph Zrenner researches brain-state-dependent brain stimulation and uses real-time electroencephalograms (EEGs) to investigate oscillatory brain-states with the goal of identifying “temporal targets” for neuromodulatory interventions. In brain stimulation, the aim is to find the perfect point in time that will determine how effective the planned treatment will be. Together, the researchers struck on the idea of developing special hardware and software and then marketing it as a product. sync2brain was born.

The Zrenners are actually following in something of a family tradition. The Medical Innovations Incubator, which is part of the Tübingen-based Stiftung für Medizininnovationen (Foundation for Medical Innovations) and helps start-ups in the medical technology sector on their journey to success, was established by Prof. Eberhart Zrenner. Evidently, Prof. Zrenner, who is a former member of the German Science and Humanities Council, Senior Professor of ophthalmology at the University of Tübingen and himself a company founder, has passed on his entrepreneurial genes to his son Christoph. As the father and son see it, carrying out basic research and then developing your results into products are two activities that go hand in hand. Brigitte and Christoph Zrenner don't see their personal relationship as an obstacle. In fact, it is a bonus – being a team at work and at home and pursuing the same goals means that these parents can support each other perfectly as they raise their four young children.

The first step – setting up a company on the basis of an inspired idea – was taken in 2019. The newly formed company now needed to be nurtured and a product placed on the market. Fortunately, the team at sync2brain crossed paths with Dr. Ramona Samba at just the right time. Holding a doctorate in chemistry, Dr. Samba had been researching microelectrode arrays that are used to record and stimulate nerve cells and measure neurotransmitters. Alongside her scientific career, she also studied management at Steinbeis School of Management and Technology and St. Gallen Business School and was head of a division at NMI Technologietransfer GmbH in Reutlingen. The specialist expertise and business acumen she brought to the table were precisely what the young company needed for its next steps. In 2020, she

helped the company submit a successful application to the German government's EXIST funding programme, which financed her appointment as CEO.

The fact that Dr. Samba was able to take over the running of the company proved to be a stroke of luck for the two founders, as she is now “on her own” with the growing team at its home in Tübingen. Shortly after founding their business, Brigitte and Christoph Zrenner took up an offer to work at the Centre for Addiction and Mental Health (CAMH) in Toronto, Canada. The Zrenners are now expanding their studies on brain interventions using TMS at one of the biggest research centres for clinical studies in psychiatry. However, the physical distance between Tübingen and Toronto has had no impact on the development of their business back home. Ultimately, business partners no longer need to be in the same building to run a company together. They are also shattering all the usual stereotypes associated with working in a start-up – never being at home, living in the lab, having no children or relationships, being totally devoted to “the cause”. Dr. Samba, who herself has three children, strikes the right balance and sees “being the boss” as only a good thing. She decides how important her parental commitments are and doesn't need to ask permission to take time off. She is also happy to clear up misconceptions about the mythical “genius loner”, so often pictured working tirelessly in their garage on their idea for global success. The right mix for a successful start-up consists of scientists who have visionary ideas paired with practical people who can get things done and take care of organisation and management.

The need – who benefits from the idea?

At least 350 million people around the world suffer from depression. Many forms of this disorder are incurable, and conventional psychotherapeutic drugs sometimes have severe side-effects. In a patient with depression, the left forebrain “locks” into a state of hypoexcitability, which means that a pulse at this area of reduced activity – when initiated at the right time – can optimally stimulate the nerve cells. This stimulation can be provided without any need for anaesthetic or surgical intervention. Patients, who wear an EEG cap fitted with electrodes during the treatment, feel nothing. Transcranial magnetic stimulation (TMS) can help in virtually all cases where there is an imbalance in the brain. If a patient has suffered brain damage due to a

stroke, for example, they will have to carry out repeated exercises – usually during physiotherapy – so that their brain can learn to reorganise itself. TMS can help activate the patient’s brain and put it in a state that is more conducive to building new networks, thus making it easier for the patient to complete the programme of exercises. TMS has actually been used as a treatment for years and is listed as an approved method in guidelines for treating psychological disorders. The team at sync2brain believes that an optimised mix of drugs, rehabilitation, talking therapies and TMS offers a genuine solution for many patients.

The USP – what is the innovation?

TMS involves stimulating key areas of the brain by using an external magnetic coil to apply an electrical current for fractions of a second. However, because the brain is highly dynamic and constantly changing, it has not previously been possible to respond in real time to the activity and connections in the different parts of the brain. Although an EEG measures excitability states in the brain and records them in oscillating curves, these oscillations last mere milliseconds, and scientists haven’t had the computing power and algorithms they need to get the timing exactly right. Previously, stimulation has been applied at a set rate that does not necessarily “catch” the right point of oscillation. Studies have, however, shown that there is a specific point at which this stimulation is particularly effective. It is similar to a swing – it only achieves the pinnacle of oscillation when it reaches its highest point. sync2brain GmbH has developed the “bossdevice” tool so that scientists can target this point with precision. Switzerland-based Speedgoat GmbH manufactures the real-time computer that provides the computing power. US company MathWorks, meanwhile, supplies the all-important software platform. “bossdevice” is thus able to analyse the real-time raw data feed from the EEG in less than three thousandths of a second during treatment and identify the patient’s personal pattern. It synchronises the stimulation with the precise state of the brain and makes the TMS much more effective. The development by sync2brain therefore represents a genuine revolution in brain stimulation therapy.

Milestones – what next?

bossdevice RESEARCH is already available on the market, although the device is only licensed for use in research. bossdevice MEDICAL is to be certified in the coming months, meaning that hospitals and clinics will then be permitted to use it. As is the case for so many other medical devices, the certification process represents a bottleneck. sync2brain has already found the relevant “notified body” that will carry out the necessary assessment as stipulated by the Medical Device Regulation (MDR). The MDR is the EU regulation that manufacturers must abide by if they wish to market medical devices in the EU.

A major multi-centre stroke study involving 130 patients has also been initiated and is being led by the Department of Neurology at University Hospital Tübingen. What’s more, CAMH is involved in a major Canadian study on the psychiatric application of TMS in the treatment of OCD (obsessive-compulsive disorder). It is only a question of time before bossdevice secures its MDR certification for Europe and is certified by the FDA in the USA. However, certification is not the only obstacle that sync2brain has to overcome. Doctors and health insurance companies also need to be persuaded that it is worthwhile trying something new. CEO Dr. Samba expects to see the first positive results from the studies before the end of the year. The long-term goal is to establish the bossTMS therapy as a standard treatment for strokes, depression and other neuropsychiatric conditions. It is a brainwave that many patients will ultimately benefit from.

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Stories

Link to technology transfer page

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BioRegio STERN Management GmbH promotes economic development in the life sciences industry, helping to strengthen the region as a business location by supporting innovations and start-up companies in the public interest. It is the main point of contact for company founders and entrepreneurs in the Stuttgart and Neckar-Alb regions, including the cities of Tübingen and Reutlingen.

The STERN BioRegion is one of the largest and most successful bioregions in Germany. Its unique selling points include a mix of biotech and medtech companies that is outstanding in Germany and regional clusters in the fields of automation technology and mechanical and plant engineering.

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