Professor Dr Andreas Luft is helping patients recover from neurovascular accidents. In this enlightening interview, he discusses his translational approach to neurorehabilitation and an ongoing project to improve robotic gait training.

Could you provide an overview of your work in neurorehabilitation and your main objectives?

We work on a translational approach to neurorehabilitation, moving from animal models to human therapies. Our focus is the physiology of reward and motivation in the context of learning and recovery after stroke. We investigate the factors that negatively or positively influence motivation and reward appreciation after stroke, and develop novel treatment approaches to circumvent negative influences while enhancing positive ones.

The study also explores the influence of motivation and reward on recovery after stroke in conjunction with standardised training regimes, partly based on robotic training devices and instruments. We study the effects of training therapies on the brain using neurophysiological techniques, including functional imaging and transcranial magnetic stimulation.

Why is neurorehabilitation crucial to patient recovery post-stroke?

Neurorehabilitation has been an integral part of stroke care for around 50 years. Previously, the field was primarily based on experience rather than scientific evidence. Due to advances in the neuroscience of learning, plasticity and recovery, neurorehabilitation has become a focus for clinical scientists. However, scientific results are still scarcely implemented in routine rehabilitation.

Early rehabilitation is particularly important, because the brain has a special capacity to undergo plastic reorganisation shortly after stroke, likely due to the expression of specific genes induced by the stroke lesion (see studies by S Thomas Carmichael and collaborators). Although therapy can still have positive effects even years after stroke, gains are greatest in the acute and subacute phases (the initial two to four months).

The recuperation of functional movements following central nervous system (CNS) injury is complex and multifaceted. By what means do you intend to identify the mechanisms of cortical plasticity during recovery after brain lesions? How could predictive biomarkers of successful recovery and outcome be established?

Neurophysiological techniques have the potential to visualise brain plasticity and can provide important surrogate markers for recovery and therapy responsiveness.

Biomarkers could be established by correlating the measurements with treatment effects and outcomes and then measuring the sensitivity, specificity and predictive value of such measurements. In the future, biomarkers could be crucial in deciding which patients receive which therapy and for how long.

How important is the input of collaborators and partners to advancing your studies? What is the Rehabilitation Initiative and Technology Center Zurich (RITZ)?

Partners have a major influence on our work. This is especially true for our partners in Zurich who form RITZ, which brings together basic scientists, engineers and clinical scientists.

Could you briefly outline your project on advanced robotic gait training with additional degrees of freedom?

Clinical trials suggest that patients after spinal cord injuries with severe gait impairment benefit from gait training using a robotic gait orthosis (Lokomat, Hocoma AG, Volketswil). However, chronic stroke patients with mild to moderate locomotor deficits require a training setup that challenges locomotor movement with more degrees of freedom and asymmetrical training, ie. training the impaired limb differently than the intact limb, than the current Lokomat system allows for. Pelvis and trunk movements must be enabled to train weight shifting and balance.

Therefore, the Lokomat system has been augmented with additional degrees of freedom, enabling training of advanced gait patterns, balance and asymmetrical training. The efficacy of the two integrated modules will be evaluated in a single-centre clinical study.

RESEARCH INTERESTS

- Investigating the role of motivation and reward mechanisms in recovery (key focus area)
- Improving acute care of stroke through methods of early rehabilitation
- Understanding the processes that lead to cognitive and psychological deficits following a stroke
- Understanding motor system recovery following stroke
- Testing novel neurorehabilitative therapies based on robots and computer games
STROKE CAUSES FUNCTIONAL movement deficits that impede independent living and reduce quality of life. Over 16,000 people suffer a stroke every year in Switzerland, a number which looks set to grow as the population ages. Despite effective acute stroke therapies, 80 per cent of these people are left disabled, due to motor, speech, visual or cognitive deficits.

In the past few decades a better understanding of recovery processes and advances in biomedical engineering have fuelled the rapid growth of neurorehabilitation, which aims to minimise impairment and disability and facilitate return to independence. However, despite such progress, the field still lacks clear scientific evidence and has many inconsistencies.

Professor Dr Andreas Luft is working to address the pressing need for more informed neurorehabilitation. Luft heads the Stroke Service in the Department of Neurology, University Hospital of Zurich and the cereneo Center for Neurology and Rehabilitation, Vitznau, Switzerland. He is passionate about translating findings in neuroscience to the clinical arena.

RITZ

The Rehabilitation Initiative and Technology Center Zurich (RITZ) is an interdisciplinary platform aiming to close the existing knowledge gaps and advance the field of neurorehabilitation. The Zurich-wide network encourages collaboration and knowledge transfer between basic neuroscience, clinical science and engineering. Luft leads the clinical neurorehabilitation laboratory as part of RITZ, which investigates the brain’s capacity for recovery and plasticity in both animal models and human patients. By studying the mechanisms involved in healthy motor learning and the recovery of motor function after stroke, the researchers are seeking to gain a more comprehensive understanding of the way movements are learned and performed and ultimately improve treatment for brain damage.

DIVERSITY OF RESEARCH

Amongst a wide range of different projects, Luft’s team is working to characterise motor skill learning in healthy and brain-lesioned rats. In conventional reaching tasks, if the rat succeeds in carrying out a reach and grasp movement, it is recorded as a success. If, however, the rat is unable to reach, it is recorded as a failure. But this binary method of evaluating motor skills does not take into account all the changes in movement that occur during a learning period. Animals with brain lesions may continue to display abnormal movements even if the success rate indicates full recovery. Therefore, in collaboration with the laboratory of Professor Roger Gassert from the Swiss Federal Institute of Technology (ETH), Luft’s group has helped to develop the ‘ETH Pattus’, a robotic device that records, guides and perturbs the rat’s forepaw movement to fully elucidate the dynamics of motor learning and recovery.

Also in rats, Luft is leading investigations into post-stroke recovery mechanisms using a photothrombosis stroke model. The researchers are studying the effects of different types of medication and rehabilitation therapies on functional deficits in the hope of improving existing rehabilitation therapies, and even developing novel ones.

PROGNOSIS PROFILES

Although the vast majority of stroke victims suffer a permanent motor, verbal or cognitive deficit, the long-term development of these deficits is largely unknown. To better understand this, Luft is involved in a clinical project called ‘Zurich Observational Registry or Rehabilitation Outcomes’ (ZORRO). This registry is tracking stroke patients for five years in the hope of identifying which factors affect recovery and to what extent. In the long-term, the aim is to create prognosis profiles that could predict outcome for individual patients. In collaboration with Johns Hopkins University, Baltimore, USA, and Columbia University, New York, USA, a multi-centre study is underway investigating the neurophysiology or recovery during the first year after stroke.

Another major area under study is the mechanisms of motivation and reward, both...
of which have a significant role in facilitating recovery, as Luft explains: “Motivation has a major influence on real-world patient recovery. Without the will to get better, recovery remains incomplete”. The team has already established a link between the reward circuitry of the brain and plasticity in the motor cortex, and they are presently exploring the influence of reward on recovery.

**RECIPROCAL KNOWLEDGE FLOW**

Luft believes neurorehabilitation patients require continuous and empathetic care, backed by the latest science, in order to achieve maximum recovery. This concept is one of the drivers underpinning the ethos of the Center for Neurology and Rehabilitation (cereneo) of which he is Medical Director – a hospital which is connected to a clinical research centre, thereby enabling knowledge translation from the bench to bedside, and back again. As a collaborator of RITZ, cereneo has access to leading-edge treatment methods and technology found in only a few laboratories worldwide.

By working at the interface of science and therapy, Luft has created a novel and extremely effective approach to neurorehabilitation

The hospital cereneo combines expert medical care with a motivating environment and science-based neurorehabilitation therapies, spanning physical therapy to neuropsychology. cereneo’s scientists investigate the neural mechanisms underlying the brain’s response to injury, while patients directly benefit from this approach through novel therapeutics for faster and more effective recovery. This affords them a unique opportunity; in most healthcare systems, research is not accessible to these kinds of patients, who are disabled and hospitalised in institutions or nursing homes without access to research.

cereneo is working at the forefront of the healthcare field. It provides a customised, intense rehabilitation programme which aims to achieve a sustained improvement in quality of life. Each patient is offered a unique therapy concept, based on a thorough medical investigation and their individual impairment profile.

ROBOTICS: THE FUTURE OF NEUROREHABILITATION?

Rapid advances in neuroscience and engineering are making leading-edge central nervous system (CNS) technologies more commonplace in neurorehabilitation. Virtual reality simulations allow patients to re-learn aspects of their lives, as well as how to navigate the environment around them, and all whilst in the safety of a clinical environment. In addition, robotics is able to provide patients with the opportunity to train, both physically and mentally, much sooner than would otherwise be possible – potentially shortening the recovery period. Robots enable patients to carry out highly repetitive and precise movements; the therapist has to define and continually adjust the robot training parameters.

Implementing robotic training within a computer game may increase success by introducing an element of reward or competition, as Luft elucidates: “This therapeutic approach could enhance neuroplasticity by increasing the intensity (time, complexity, repetitions) and the motivation for training”. His group is currently exploring the value of this combined approach in improving movement.

Looking ahead, Luft has developed a new version of the Lokomat robot optimised for stroke patients as part of an exciting collaborative project between the University of Zurich, ETH (Professor Robert Riener) and Hocoma, a medical technology company who manufactured the original model. Lokomat helps people improve their ability to walk following neurological injury. The existing version of the robot automates locomotion therapy on a treadmill to enhance the efficiency of training. This innovative project aims to increase the degrees of freedom afforded by Lokomat; the modification will soon be evaluated by clinical trial.

**PERSONALISED THERAPY**

By working at the interface of science and therapy, Luft has created a novel and extremely promising approach to neurorehabilitation. His lab has applied a pioneering translational approach to investigate the role of motivation and reward in recovery, translating neurophysiology and neuropathology in animal models to clinical trials in human stroke patients that are currently ongoing. Clinically, his emphasis on a patient-centred approach has helped improve quality of life for many.

Neurorehabilitation treatment response varies between individuals and, given the heterogeneity of clinical deficits seen in patients, it seems likely that a diverse range of therapies is therefore required. The current lack of evidence in this regard acts as a barrier to sophisticated, tailored therapies. However, Luft’s work to better understand the neuroscience of recovery may pave the way for individualised rehabilitation programmes – therapeutic concepts which are becoming a clinical reality at cereneo.