

Healthcare industry BW

The brain, its function and its architecture

Does tactile sensation also depend on structure and order? The research group led by Prof. Dr. Jürgen Hennig from the University Hospital of Freiburg is investigating the functional composition of a highly structured sensory brain area in mice which receives information from the important tactile sensors that are the animals' whiskers. Using modern imaging methods such as functional magnetic resonance imaging (fMRI) or diffusion tensor imaging (DTI), the scientists hope to find out whether mice with disturbed brain organisation are able to process tactile stimuli normally. DTI already provides spectacular insights.

Just a few weeks ago, Professor Dr. Jürgen Hennig, Scientific Director of the Department of Diagnostic Radiology – Medical Physics at the University Hospital of Freiburg, received a highly prestigious grant from the European Research Council. Hennig will use the 2.5 million euros of funding for his investigations into magnetic resonance imaging. MRI opens up new possibilities in the field of neurology, the neurosciences and oncology. The know-how of the researchers in Hennig's group allows deep insights into the body without causing any damage to the tissue. The knowledge generated by Hennig's group benefits doctors who use it for human diagnostics. Hennig and his colleagues, Dr. Dominik von Elverfeldt and Dr. Laura Harsan, have recently started to look into areas other than human application. Working with Prof. Dr. Jochen Staiger's group at the Freiburg Centre of Neurosciences and the Department of Neuroanatomy at the University of Freiburg, the researchers are taking a closer look at the mouse in the collaborative research centre "Synapses and networks" (SFB 780). "The experimental work with animals enables us to optimise our methods," said Hennig. "In addition, the scientific side of the project is very exciting."

Barrels stacked side by side

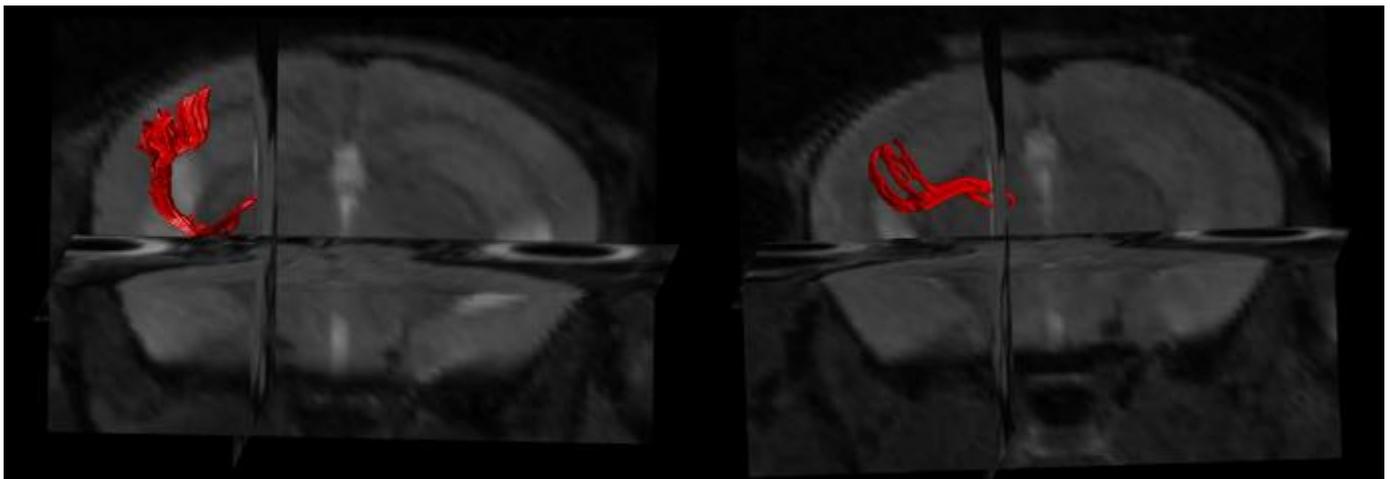
Hennig and his colleagues are interested in the functional architectonics and plasticity in an area of the mouse's brain that is responsible for certain aspects of the animal's tactile sense. This area, which is referred to as the barrel cortex, is normally strictly organised: it consists of parallel barrel columns that are separated by septa. When stained with specific dyes, a cross section of the area looks like a chessboard. This spatial order also reflects a functional organisation, because the area is virtually a mirror image of a mouse's whiskers. The whiskers are specialised hairs with a tactile function. Each individual hair is connected to a specific barrel column in the barrel cortex. All the columns taken together form a map which reflects the spatial distribution of the hairs and the connected tactile receptors.

The functional organisation in the mouse's brain is a model for similar neural networks in the

human brain, for example in the visual cortex which is responsible for higher-level processing of the visual image. But is the anatomical organisation necessary for mice to be able to effectively use their whiskers? Insights can be obtained with experiments involving so-called reeler mouse mutants in which the cortical neurones are abnormally placed, and hence no longer have the same organisation. Reeler mice lack reelin which is a key extracellular matrix protein and is important for brain development.

Reelin-deficient mice do not therefore have normally arranged barrel columns. It is still unknown what this disorganisation actually looks like. In order to gain further insights, the medical physicists in Hennig's group have adapted the diffusion tensor imaging method in such a way that it also produces an excellent resolution of small mouse brains (100 micrometres). The technology measures the restricted diffusion of water molecules in tissue using magnetic fields that have been combined with each other in a complex way. Normally, the water molecules in the axons of neurones diffuse parallel to the cellular projections. They are hindered by the cell membrane when trying to diffuse in other directions.

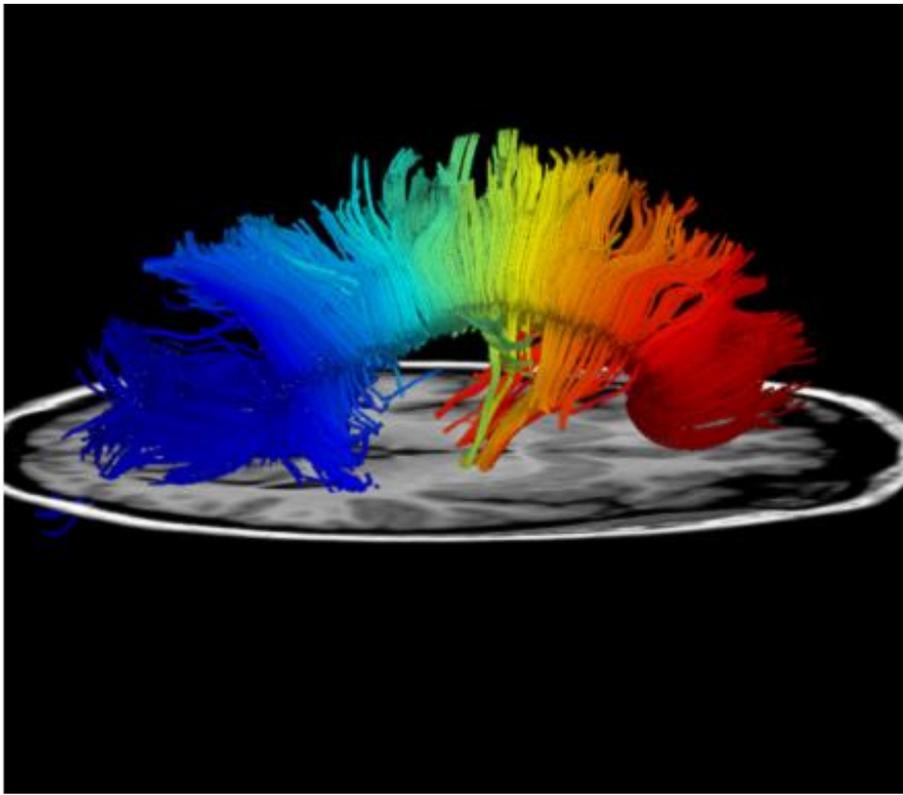
The medical physicists from Freiburg are able to visualise this directional tendency using magnetic resonance imagers and hence they are able to show the course of nerve fibres and nerve bundles from the barrel cortex to the whiskers.



The picture shows a cross section of the brain of mice from the front. Left: In normal mice, the connections coming from the whiskers in a deeper brain area project into the barrel cortex at the surface where they take on a fan-like structure (red). Right: This fan-like structure is more disorderly in reeler mice. (Figure: L. Harsan, D. Elverfeldt, J. Hennig, J. Staiger)

An architectonic clutter

“In normal mice, DTI reveals a textbook image of the barrel cortex,” said Hennig. “The parallel barrels send parallel connections up to the whiskers.” The confirmation of what is already shown in textbooks is remarkable by itself, because such images have never before been taken from living animals. But the architectonic situation in the brains of reeler mice is even more interesting because Hennig and his colleagues clearly see that the nerve fibre bundles are totally disarranged and do not seem to follow a specific order. These pictures reveal the clear spatial orientation of the barrels, thereby enabling the scientists to investigate the functional importance of normal barrel orientation. “Is the correct function of the whiskers impaired when the nerve fibre bundles are disarranged,” asks Hennig. “Or are the reeler mice able to process tactile stimuli as well as normal mice?”



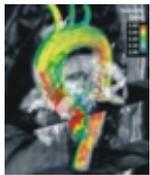
In the human brain, diffusion tensor imaging (DTI) can for example reveal nerve fibre bundles coming from deeper brain areas into the cortex. (Figure: Prof. Dr. Jürgen Hennig)

This question is the basis of future experiments. Hennig and his colleagues hope to mechanically stimulate individual whiskers of reeler mice and measure which areas of the barrel cortex become active. This helps them to test whether the map in the brain area is just distorted or whether something is actually missing. Their knowledge will be of great use in functional magnetic resonance imaging, which is able to present the metabolic rates in the brain and which allows conclusions to be drawn on the electrical activity. Over the last few months, the researchers at the Advanced Molecular Imaging Research Centre (AMIR) have spent a lot of time setting up a piece of equipment that allows them to carry out automated and computer-assisted experiments on mice. Perhaps they will soon know how much disorganisation the barrel cortex of rodents can tolerate.

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