Neurobiology

Supporting the damaged brain

A new study in 'Nature' shows that embryonic nerve cells can functionally integrate into local neural networks when transplanted into damaged areas of the visual cortex. The work was published by scientists based at Helmholtz Zentrum München with colleagues from LMU Munich and the Max Planck Institute of Neurobiology in Martinsried.

When it comes to recovering from insult, the adult human brain has very little ability to compensate for nerve-cell loss. Biomedical researchers and clinicians are therefore exploring the possibility of using transplanted nerve cells to replace neurons that have been irreparably damaged as a result of trauma or disease. Previous studies have suggested there is potential to remedy at least some of the clinical symptoms resulting from acquired brain disease through the transplantation of fetal nerve cells into damaged neuronal networks. However, it is not clear whether transplanted intact neurons can be sufficiently integrated to result in restored function of the lesioned network.

Now researchers based at Helmholtz Zentrum München, LMU Munich and the Max Planck Institute for Neurobiology in Martinsried have demonstrated that, in mice, transplanted embryonic nerve cells can indeed be incorporated into an existing network in such a way that they correctly carry out the tasks performed by the damaged cells originally found in that position.

The researchers specifically asked whether transplanted embryonic nerve cells can functionally integrate into the visual cortex of adult mice. "This region of the brain is ideal for such experiments," says Magdalena Götz, Director of the Institute of Stem Cell Research and joint leader of the study together with Mark Hübener. Hübener is a specialist in the structure and function of the mouse visual cortex in Professor Tobias Bonhoeffer's Department (Synapses – Circuits – Plasticity) at the MPI for Neurobiology. As Hübener explains, "we know so much about the functions of the nerve cells in this region and the connections between them that we can readily assess whether the implanted nerve cells actually perform the tasks normally carried out by the network." In their experiments, the team transplanted embryonic nerve cells from the cerebral cortex into lesioned areas of the visual cortex of adult mice. Over the course of the following weeks and months, they monitored the behavior of the implanted, immature neurons by means of two-photon microscopy to ascertain whether they differentiated into so-called pyramidal cells, a cell type normally found in the area of interest.

"The very fact that the cells survived and continued to develop was very encouraging," Hübener remarks. "But things got really exciting when we took a closer look at the electrical activity of the transplanted cells." In their joint study, PhD student Susanne Falkner and Postdoc Sofia Grade were able to show that the new cells formed the synaptic connections that neurons in their position in the network would normally make, and that they responded to visual stimuli.

The team then went on to characterize, for the first time, the broader pattern of connections made by the transplanted neurons. Astonishingly, they found that pyramidal cells derived from the transplanted immature neurons formed functional connections with the appropriate nerve cells all over the brain. In other words, they received precisely the same inputs as their predecessors in the network. In addition, they were able to process that information and pass it on to the downstream neurons which had also differentiated in the correct manner.

“These findings demonstrate that the implanted nerve cells have integrated with high precision into a neuronal network into which, under normal conditions, new nerve cells would never have been incorporated,” explains Götz. The new study reveals that immature neurons are capable of correctly responding to differentiation signals in the adult mammalian brain and can close functional gaps in an existing neural network.

Further information

Background: Such work is of importance in the potential treatment of all acquired brain disease including neurodegenerative illnesses such as Alzheimer‘s or Parkinson’s disease, as well as strokes and trauma, given each disease state leads to the large-scale, irreversible loss of nerve cells and the acquisition of a what is usually a lifelong neurological deficit for the affected person. The study was supported by funding from the DFG for SFB 870 “Assembly and Function of Neuronal Circuits”

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The Helmholtz Zentrum München, the German Research Center for Environmental Health, pursues the goal of developing personalized medical approaches for the prevention and therapy of major common diseases such as diabetes and lung diseases. To achieve this, it investigates the interaction of genetics, environmental factors and lifestyle. The Helmholtz Zentrum München is headquartered in Neuherberg in the north of Munich and has about 2,300 staff members. It is a member of the Helmholtz Association, a community of 18 scientific-technical and medical-biological research centers with a total of about 37,000 staff members. www.helmholtz-muenchen.de/en

The Institute of Stem Cell Research (ISF) investigates the basic molecular and cellular mechanisms of stem cell maintenance and differentiation. From that, the ISF then develops approaches in order to replace defect cell types, either by activating resting stem cells or by re-programming other existing cell types to repair themselves. The aim of these approaches is to stimulate the regrowth of damaged, pathologically changed or destroyed tissue. www.helmholtz-muenchen.de/en/isf

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The Max Planck Institute of Neurobiology is one of currently 83 independent research institutes within the Max Planck Society. The Institute's research takes place at the very boundaries of human knowledge with the aim to understand the basic functions, structure and development of the brain and the nervous system. The scientists employ and enhance the latest techniques from the areas of genetics, molecular biology, computer simulations and microscopy. The Max Planck Institute of Neurobiology is found at the Life Science Campus Martinsried, at the southwest border of Munich. www.neuro.mpg.de/home

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