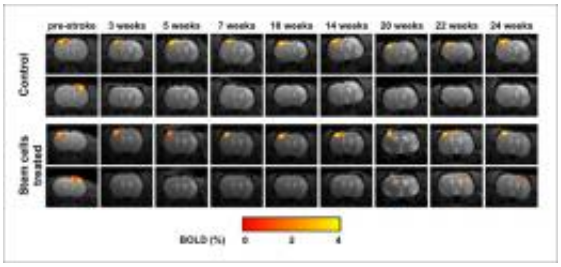
Rescue services at the cellular level: How stem cells help brain to regain its functions after stroke

September 28 2010



Functional recovery of the brain six months after a stroke: the images show brain activation in the healthy and ischaemic brain hemispheres (ischaemia - deprivation of blood supply) over the course of the study. Without stem cell implantation (top two rows of images), there is no recovery in the hemisphere affected by the stroke (second row of images). Following implantation of neural stem cells (bottom two rows of images), the brain regenerates after 14 weeks (fourth row of images). Image: Max Planck Institute for Neurological Research

(PhysOrg.com) -- The aim of regenerative medicine is to repair or replace malfunctioning cells, tissues, and even organs. Stem cells, the multi-taskers and jacks-of-all-trades that can regenerate themselves indefinitely and transform themselves into various cell types, are seen as offering a promising solution in this context. Researchers have reported numerous cases of the successful use of stem cells to heal damaged tissue; however, the underlying physiological mechanisms at work here are still largely unknown.

A study carried out by the In-vivo NMR Research Group headed by Mathias Hoehn at the Max Planck Institute for Neurological Research in Cologne has now demonstrated, in a long-term animal study on rats, that the positive effect of stem cell injection after a stroke is mainly based on a stimulative effect in the surrounding cell region (*PLoS One*, September 22, 2010).

Before the routine therapeutic use of stem cells in stroke patients can be considered, however, the mechanism behind this tissue regeneration must first be understood. Stem cells could conceivable repair damaged tissue, being integrated into defective neuronal networks, or that they support regenerative processes through their proximity to the damaged cells ("paracrine effect"). To enable the differentiation between these alternative explanations, the possibility of spontaneous recovery must be excluded and, second, the administered stem cells must be made visible.

The study that has just been published fulfils both of these criteria: three weeks after an experimentally induced stroke, MRI scans of all of the rats (n = 8) involved in the study revealed no activity in the somatosensory cortex during stimulation of the forepaw, indicating that the malfunction was permanent. Four rats were injected close to the site of the stroke with half a million neural stem cells (C17.2), of which approximately ten percent had been marked using a ferrous contrast agent so that they could be visualized in the scanner. All of the rats were repeatedly tested over a period of 24 weeks.

The untreated rats (n = 4) displayed no changes in behaviour or brain activation during the observation period. In two of the four treated rats, the stimulation of the forepaw triggered a signal on the side of the brain contralateral to the stroke, seven and ten weeks after the injection of the stem cells. This signal was indicative of brain activation in the corresponding defective zone, to which no stem cells had migrated. The brain activation was accompanied on the behavioural level by a

reduction in the latency time in which the rats began to remove a disturbing adhesive band on the affected forepaw. No stem cells were detectable after 24 weeks.

The results of this long-term study clearly suggest that the observed functional improvement was achieved through the mediating influence of the implanted stem cells ("paracrine effect"): the cellular rescue service appears to trigger the regenerative process through its proximity to the damaged cells. Mathias Hoehn and his team are now working on the further optimisation of the processes. This work also involves the use of human stem cells.

More information: Pedro Ramos-Caberer, Carles Justicia, Dirk Wiedermann, Mathias Hoehn, Stem Cell Mediation of Functional Recovery after Stroke in the Rat, *PLoS One*, DOI:10.1371/journal.pone.0012779 September 22, 2010

Provided by Max-Planck-Gesellschaft