Diplom-Biologin Prilloff, Sylvia

"The role of activating residual neurons in recovery of vision after partial optic nerve damage: *in vivo* observations in rats"

ABSTRACT

Traumatic brain injury is one of the main causes of functional loss in the central nervous system after injury. These functional deficits are often not permanent but can be partially regained from the brain often surprisingly and partly spontaneously in the first few weeks after the lesion. A small number of retinal ganglion cells (10-20 %) are sufficient to spontaneously recover lost functions. It is now necessary to acquire more knowledge about the role of activating residual neurons in the recovery of vision after partial optic nerve damage as this is of high clinical relevance. To learn more about this issue, a defined ONC in adult rats was used to analyse the functional recovery by using behaviour and cell biological methods. First, the *in vivo* confocal neuroimaging (ICON) was used for the non-invasive visualization of individual retinal ganglion cells (RGCs), and second an automated test system to study the psychophysics of rat vision (VIST). By applying these two procedures significant new insights have been gained regarding neurobiological mechanisms of functional recovery after partial injury of the visual system:

- It is possible to use two different fluorescent markers under *in vivo* conditions in order to observe retrograde axonal transport in RGCs in living rats. With this design an effective protocol is in place to observe the temporal pattern of recovery of retrograde axonal transport in injured RGCs.
- By ONC the axons of the RGCs are damaged which results in a temporary loss of axonal transport. The results from the double-labelling studies described here show that there is an intrinsic repair of damaged axons. The axonal transport in the injured optic nerve recovered within 2-3 weeks and consequently the visual function, too. As expected, axotomy did not allow such recovery.
- The *in vivo* imaging of calcium dynamics in individual RGCs is an important indication of the function or injury of these cells. Surviving RGCs show a delayed moderate ("compensatory") calcium activation, which is significantly different from cell death-associated massive calcium influx, which occurs immediately after the injury.
- The repeated stimulation of the visual system following ONC has a positive effect on the recovery of vision. It could be observed, that "visual enrichment" produced a faster recovery of vision in rats compared to rats kept under normal dark/light conditions or rats held in total darkness.

These results show that activating residual neurons is a very important mechanism in recovery of vision. Through these new findings it is possible to understand the role of residual neurons much better and it allows new approaches for the development of potential therapies.