Embryonic progenitor cell grafts improve functional recovery in the spinal cord in vitro

Functional recovery after spinal cord injury is limited, mainly due to a hostile environment provided by central nervous system myelin and reactive astrocytes. Recent results indicate that intraspinal connections are a promising target for intervention to improve functional regeneration. To study these fibers, we developed an in vitro model consisting of the following experimental design: Two organotypic spinal cord slices of embryonic rats (E14) are placed adjacently on a multi-electrode array. The electrodes allow us to record the spontaneously occurring neuronal activity, which is often organized in network bursts. Within a few days in vitro (DIV), these bursts become synchronized between the two slices due to the formation of axonal fibers, representing intraspinal connections. Next, we cut these formed connections with a scalpel at different time points in vitro and record the neuronal activity three weeks later. The functional recovery potential is assessed by calculating the percentage of synchronized bursts between the two slices. We found that cultures lesioned at a young age (8-12 DIV) retained the high regeneration ability of embryonic tissue (mean % of synchronized bursts ± SEM; e.g. lesion at 8 DIV: 97.5% ± 1.7%). However, cultures lesioned at older ages (>19 DIV) showed a distinct reduction of synchronized activity (e.g. lesion at 21 DIV: 10.5% ± 3.2%).

To study the effect of embryonic spinal cord progenitor cell grafts on functional recovery, we inserted these cells into the lesion site of old cultures (lesion at 21 DIV). We found a remarkably increased percentage of synchronized bursts in cultures with grafts (75.9% ± 5.3%) compared to control groups. With patch clamp experiments we identified mature neurons in the grafted cell population. These results suggest that embryonic spinal cord progenitors can differentiate in the damaged spinal cord environment, bridge lesions and thereby improve functional recovery.