

ALTERATIONS OF GLUTAMATERGIC TRANSMISSION IN A MURINE MODEL OF MULTIPLE SCLEROSIS: PRELIMINARY RESULTS

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Glutamic acid (GLU) is the major excitatory transmitter of the central nervous system that, however, at high concentration is known to be responsible of excitotoxic phenomena characterizing several neurodegenerative pathologies. The recent findings that antagonists of GLU receptors of the AMPA type are neuroprotective and ameliorates symptoms in a murine model of multiple sclerosis (MS), the experimental autoimmune encephalomyelitis (EAE), suggest that GLU could be involved in demyelination/axonal damage of spinal cord neurons. However, the precise role of GLU in this pathology is unclear. Therefore, we decided to investigate possible alterations of GLU transmission in MS by directly measuring its in vitro release from mice spinal cord slices at different time points (13, 21 and 52 days) following the in vivo induction of EAE by immunization with MOG. Briefly, fresh slices have been labelled with [³H]-D-aspartate ([³H]-D-asp), a well known non metabolizable marker of glutamatergic transmission, and then subjected to superfusion using a modified Krebs-Ringers solution. We have evaluated both the spontaneous and the KCl(35 mM)-evoked efflux of [³H]-D-asp in MOG-treated (MOG+) and sham-control mice. Results are expressed as mean ± SEM of fractional rate (FR) for spontaneous efflux and of overflow for the evoked release. Our preliminary results show that at 13 days, the KCl-evoked release in MOG+ slices was significantly (30%) lower than that measured in controls ($0,905 \pm 0,06$ vs $1,309 \pm 0,101$, respectively). This difference was slightly increased at 21 days (40%; $0,911 \pm 0,069$ vs $1,530 \pm 0,125$). In this latter case, also the spontaneous efflux was significantly diminished (20%; $0,856 \pm 0,04$ vs $1,077 \pm 0,04$). At 52 days, no significant differences were observed. Thus, our data do not seem to support that an enhancement of GLU release occurs in the spinal cord during the evolution of EAE.

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