Difusion of neuroactive substances in the extracellular space (ECS) is constrained by two factors: extracellular space volume and geometry. We have shown changes of diffusion parameters and extracellular concentrations of energetic metabolites and glutamate in two pathological states accompanied by significant ECS volume changes – in combined hypoxia/ischemia and in status epilepticus.

In the model of hypoxia/ischemia, we have shown time courses of diffusion parameters, concentrations of glucose, lactate, lactate/pyruvate ratio and glutamate during hypoxic/ischemic insult and after reperfusion. The time course of glutamate extracellular concencetration in transient hypoxia/ischemia correlated well with time course of changes in diffusion parameters. The decrease in the ECS volume fraction can therefore contribute to an increased accumulation of toxic metabolites, which may aggravate functional deficits and lead to damage of the central nervous system.

In the model of pilocarpine-induced status epilepticus our results show changes in the extracellular space diffusion parameters, K+, energy-related metabolites and glutamate during the initiation and first hours of the propagation. Our results also show that the first minutes after a pilocarpine injection are followed by an increase in extracellular K+ and a decrease in ECS volume. When extracellular volume fraction decreases from 19 % to 15 %, high amplitude epileptic discharges appear. The shrinkage of the ECS could contribute to an increase in extracellular metabolite concentrations, with all its deleterious consequences, leading to the start of epileptic discharges. The interval from the start of ECS volume changes to first epileptic discharges presents a possible terapeutic window; proper intervention in this period could be useful to prevent initiation of epileptic activity.