P7.12.

Mapping whole-brain activity in behaving rats using activity-induced manganese-enhanced MRI in a 3T clinical scanner

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Manganese accumulates in excited cells, such as activated neurons, through voltage-gated calcium channels in an activity-dependent manner. Mn2+ can be delivered outside the MRI, preceding the scanning, in contiguity with behavioral activation of the animal, and the pattern of neuronal activation is retained for a long time. Since a major disadvantage of this method is the toxicity of Mn2+, in the present series of experiments, we wanted to find the most effective dose of Mn with the lowest toxicity effects and best image contrast. T1 maps were calculated in association with performing a sustained attention demanding task. MnCl2 solution (20 mg/kg, 1 ml/h) was i.p. infused, and the infusions were repeated twice in 48 hours. Serum levels of total-protein, albumin, total-bilirubin, GOT, GPT, and glucose were measured. Neurological examinations were also performed. Significant increase was found only in the levels of GOT, GPT, and total-bilirubin. Rats did not exhibit neurological impairments. T1 maps showed dose-dependent contrast increase. In the sustained attention demanding task, 20 and 40 mg/kg MnCl2, though decreasing the number of correct responses, did not cause substantial learning deficit. Our results indicate that the activity-induced manganese-enhanced MRI is a reliable method to detect local activity changes of neuronal circuits in the central nervous system with only moderate side effects on metabolism and behavior.