Relevance of choice of brain region and time point of analysis after MPTP lesioning in wild type mice

Jan Kehr[1,3], Victoria Schiffer[2], Shimako Yoshitake[1], Tina Loeffler[2], Vera Niederkofler[2], Stefanie Flunkert[2], Ewald Auer[2], Takashi Yoshitake[3], Birgit Hutter-Paier[2]

[1]Pronexus Analytical AB, Grindstuvägen 44, 167 33 Bromma, Sweden; [2]QPS Austria GmbH, Neuropharmacology, Parkring 12, 8074 Grambach, AUSTRIA;
[3]Dept. Physiology and Pharmacology, Karolinska Institutet, Biomedicum C5, 171 77 Stockholm, Sweden

BACKGROUND

Parkinson's disease (PD) is a common neurodegenerative disorder which cardinal clinical features include tremor, slowness of movement, stiffness, and postural instability. These symptoms are primarily attributable to the degeneration of dopaminergic neurons in the substantia nigra pars compacta and the consequent loss of their projecting nerve fibers in the striatum. Mice treated with MPTP selectively loose significant numbers of nigrostriatal dopaminergic neurons. MPTP-induced dopaminergic cell loss in the substantia nigra mimics clinical conditions of PD and is therefore a useful preclinical model to test anti-parkinsonian drugs.

To use this model for compound tests against PD, it is important to understand the progressive development of MPTP lesioning to choose the correct timing for analysis after the MPTP lesion.

MATERIALS and METHODS

C57Bl/6 mice were treated with a MPTP regime and analyzed for Dopamine (DA), DOPAC and HVA in the substantia nigra at various time points after the last MPTP injection. Furthermore, animals were MPTP lesioned and the striatum was analyzed for the same biomarkers 4 days after the treatment. In the latter group of animals, 7-nitroindazole was used as a positive control.

RESULTS

Analyses of DA levels shortly after the MPTP lesioning resulted in increased DA levels in the substantia nigra at very early and later time points but decreased levels after 12 hours. Similar effects could be observed for DOPAC while HVA levels stayed almost constant. Evaluations in the striatum 4 day after MPTP lesioning showed severely reduced DA, DOPAC and also HVA levels that could partially be rescued by 7-nitroindazole treatment.

SUMMARY and CONCLUSION

Our results show that it is of high importance to select the correct brain region and time point after MPTP lesioning for evaluation of different readouts.

Meet QPS and Pronexus at Booth #1464 and 1466

Poster #E11

For more information about the model please visit:
www.qpsneuro.com

or send us an e-mail:
office-austria@qps.com

RESULTS

Substantia Nigra

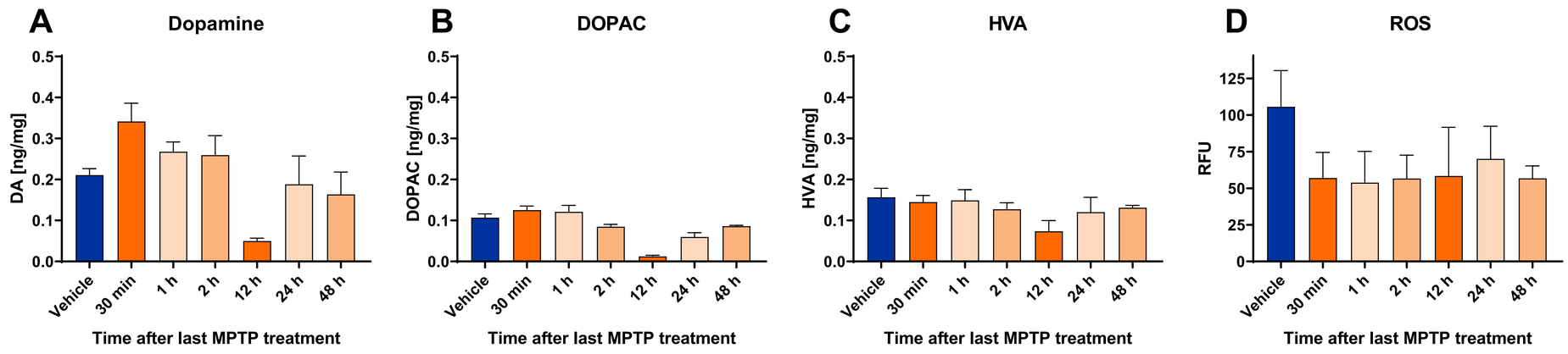

Figure 1. Quantification of dopamine, DOPAC, HVA and ROS in the substantia nigra of C57Bl/6 mice 30 min to 48 h after MPTP treatment. **A**: Dopamine, **B**: DOPAC, **C**: HVA and **D**: ROS levels in the substantia nigra of 10 week old C57Bl/6 mice 30 min, 1 h, 2 h, 12 h, 24 h and 48 h after MPTP lesioning. For MPTP lesioning, animals were treated i.p. 4 times with 20 mg/kg MPTP within 6 hours. Vehicle: PBS; n = 5; Mean + SEM. One-way ANOVA.

Striatum

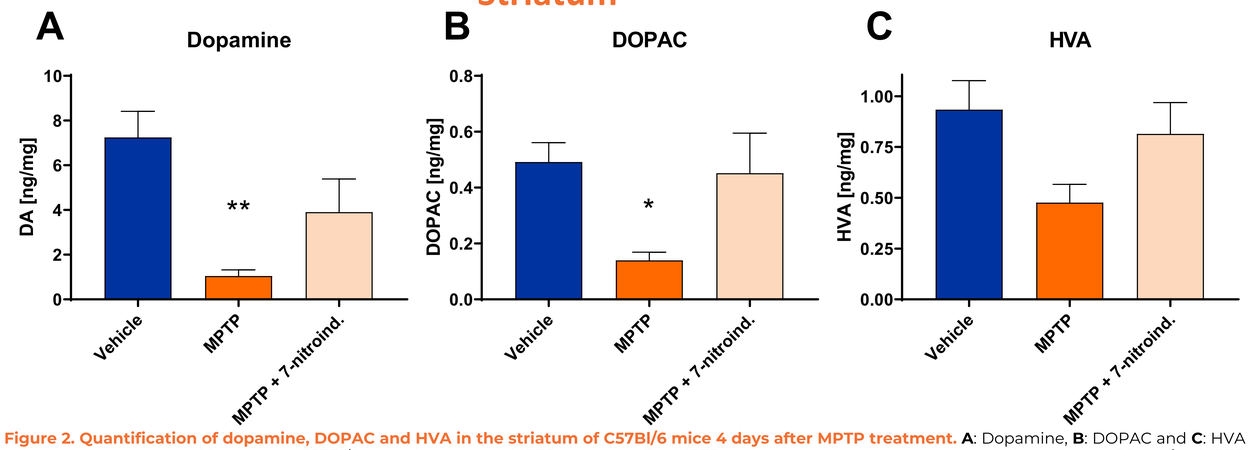

Figure 2. Quantification of dopamine, DOPAC and HVA in the striatum of C57Bl/6 mice 4 days after MPTP treatment. **A**: Dopamine, **B**: DOPAC and **C**: HVA levels in the striatum of 10 week old C57Bl/6 mice 4 days after MPTP lesioning. For MPTP lesioning, animals were treated i.p. 4 times with 20 mg/kg MPTP within 6 hours. 7-Nitroindazole in peanut oil was given i.p. 30 min before and 90 min after first MPTP treatment. Vehicle: PBS; n = 5; Mean + SEM. *p<0.005; **p<0.01; One-way ANOVA with Tukey's multiple comparison test. compared to vehicle treated animals.