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EVOLUTION OF BLADDER DYSFUNCTION IN A MODEL OF UNILATERAL DOPAMINERGIC NEURONS LESION

Hypothesis / aims of study
Parkinson's disease (PD) is one of the most common neurological entities causing voiding dysfunction, often resulting in detrusor overactivity and an impairment of relaxation of the striated urethral sphincter. Lower urinary tract symptoms may be as high as 50-70% in PD patients. Hydroxydopamine (6-OHDA), a selective dopaminergic neurons' toxin, is used to induce PD in animals. We used a model of unilateral injection of 6-OHDA and evaluated bladder function 3 and 14 days after central lesion.

Study design, materials and methods
Female Sprague-Dawley rats (250-300 g) underwent a stereotaxic injection of 6-OHDA (12 µg) or saline (sham group) into the medial forebrain bundle on the left side. At the same time or 10 days post injection, PE 50 tubes were inserted into the dome of the bladder, held in place with a purse string suture, tunneled subcutaneously and anchored to the skin of the back. Healthy controls underwent bladder catheterisation, without the stereotaxic lesion. Three days after bladder catheterization, urodynamic evaluation was performed without anesthesia.

Results
3 days after lesion 6-OHDA rats (n=8) showed higher threshold (TP) and maximum pressures (MP) compared to controls (n=6) (33.6±15 and 50.3± 19 cmH_2O vs. 19.1±3 and 27.9±4.6 cmH_2O; $p<0.05$) as well as higher spontaneous activity (SA) (7.9±8 vs. 2.2±1; $p<0.05$). 14 days after lesion 6-OHDA rats (n=7) still showed increased TP, MP and SA (42.3±29.3, 63.9±38.3 and 6.1±2.7 cmH_2O, $p<0.05$). Additionally they then demonstrated increased micturition frequency, decreased bladder capacity and micturition volume compared to controls (16.2±3.8 h^{-1}, 0.64±0.15 and 0.58±0.16 mL vs. 10.8±1.8 h^{-1}, 0.95±0.18 and 0.88±0.13 mL, $p<0.05$).
Sham operated animals (d3 n=7; d14 n=7) equalled controls animals, despite an increased TP at day 3 (31.5±11.7 cmH_2O, $p<0.05$) and an increased MP at day 14 (61.5±20.6 cmH_2O, $p<0.05$).

Interpretation of results / Concluding message
These findings suggest that 6-OHDA lesion in the medial forebrain bundle increases detrusor activity, characterized by higher spontaneous activity, with a possible sphincter dyssynergia, reflected by higher micturition pressures, as early as three days after lesion. Two weeks after 6-OHDA lesion increased detrusor activity is more pronounced with low bladder capacity and high micturition frequency. Sham operation does not increase detrusor activity. This model of PD may be useful to study evolution, pathophysiology and treatment of bladder dysfunction in PD.

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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
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