The use of HiSPECT in the investigation of the 5-HT2A receptor and DAT status in the Mongolian gerbil.

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01 | Background

Stereotypies are ethologically defined as repetitive, invariant behaviours, apparently without function (Ödberg 1978). A number of studies show that stereotypies in animals are caused by a chronic frustration resulting from a stimulus-poor captive environment (for a review see Mason 1991). Humans also display stereotypies, in relation to mental conditions such as schizophrenia, bipolar disorder, dementia (Mendez et al 2005), autism (Lewis & Bodfish 1998),... or during moments of inner tension (Soussignan et al 1988). The involvement of the dopaminergic and serotonergic system in the occurrence of drug-induced and even spontaneous stereotypies has been widely accepted (reviewed in Cabib 2006, Pogorelov et al. 2005, Meers & Ödberg 2005).
Therefore, gaining more insight in the serotonergic and dopaminergic status in animal models of stereotypy is useful for the future study of animal stereotypies, but can also point out which markers are additionally useful in the study of certain human psychiatric conditions.

02 | Aims

1) Investigate the feasibility of using multi-pinhole high resolution SPECT imaging in Mongolian gerbils and verify whether a conventional perfusion tracer will allow us to anatomically identify gerbil brain structures.
2) Investigate the appropriateness of the radioligand for DAT imaging.
3) Investigate the appropriateness of the radioligand for 5-HT2A imaging.

03 | Materials and Methods

Animals

- 16 group-housed (2-3) Mongolian gerbils (355 ± 65 days)
- Makrolon IV cages, standard laboratory conditions
- Reversed 14:10 light-dark cycle (light: 19:00 - 9:00)
- Environmental Enrichment: chewing blocks, paper tissue and hay
- General anaesthesia during scans: (4% isoflurane for induction, 1,8% for maintenance)

High-resolution SPECT

- HiSPECT (Bioscan) using conventional triple head gamma camera with multi-pinhole collimation (6 holes with 1,5mm diameter)
- Step & Shoot: 36°, 10 steps, 120 s per step, 256 x 256 matrix
- Image reconstruction using a dedicated OSEM algorithm (Scivis)
- IV injection of tracer into femoral vein

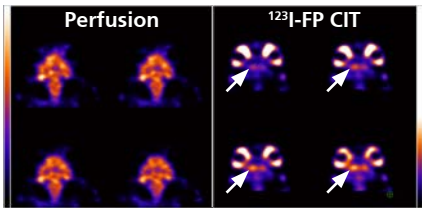
04 | Results

1) Perfusion data for anatomical identification

- 4 gerbils
- 24,42 ± 5,92 MBq ^{99}Technetium Ethylcysteinate Dimer
- Scanning 15 min after injection
- Perfusion image shows that spinal cord, cerebellum and cortical structures are easily distinguished.

2) DAT

- 5 gerbils (1 for scanning optimum confirmation)
- 44,33 ± 11,66 MBq ^{123}I-FP CIT
- Scanning optimum: 4 ½ hours after injection
- Specific binding to the DAT sites observed by the regional distribution of the radioactivity in the brain which correlated well with the known presence of DAT sites (basal ganglia, white arrows).

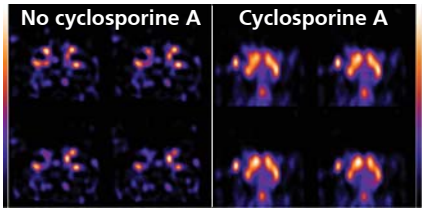


3) 5-HT2A

- 4 gerbils
- 22,2 ± 3,7 MBq ^{123}I-R91-150
- 90 min after injection

Two problems were encountered:

- First, the images were initially of poor quality. This problem was solved using Cyclosporine A (50 mg/kg) to block the P-glycoprotein pump in the blood-brain barrier.



- Second, when determining the scanning optimum, the cortex/cerebellum ratio of activity reached a rather unstable plateau. Further studies are being conducted looking into the second problem.

05 | Conclusion

1) It is feasible to use the conventional ECD tracer to perform perfusion imaging for anatomical identification.
2) The FP CIT tracer is appropriate to monitor the DAT status in the gerbil.
3) The results for the 5-HT2A receptor were less straightforward, but nonetheless promising and are being investigated further.

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