Automated detection of compulsive checking behavior in rats

G.G. de Haas^{1,2}, A. Nijdam³, T. Westra¹, M.J.H. Kas², and H.G.M. Westenberg¹

Department of Psychiatry, UMC Utrecht, Rudolf Magnus Institute of Neuroscience, The Netherlands,

G.G.deHaas-2@umcutrecht.nl

Obsessive compulsive disorder (OCD) is a psychiatric disorder with a prevalence lifetime of 2 to 3%. People with OCD suffer from strong obsessive thoughts and perform rituals (compulsions) to get in control of these obsessions. OCD rituals vary from "washing behavior" (in combination with obsessions related to the fear of being contaminated with germs or dirt) to "checking behavior" or "counting". Of course checking can be a normal behavior, but OCD patients perform these rituals so excessively that it interferes with their normal daily functioning. Currently, selective serotonin reuptake inhibitors (SSRI's) are the most effective treatment of OCD patients, but still 30-40% does not respond to this medication [1].

Pre-clinical research with valid animal models for OCD is necessary to gain more insight in the pathogenesis of OCD and to discover new therapies. At this point there are no well validated OCD animal models available. Szechtman et al. [2, 3] have preformed research on a candidate animal model in which quinpirole sensitized rats develop compulsive checking behavior. The aim of this study is to investigate the compulsive checking behavior in this model in more detail and evaluate the potential use of Theme [4] for automated detection of behavioral patterns in this animal model.

In this model rats are injected twice a week with the D2/D3 receptor agonist quinpirole 0.5 mg/kg for 5 weeks. After each injection, the animal is placed on a large open field (160X160 cm) with 4 objects and is tracked for 60 min with EthoVision. During the course of treatment the animals will develop compulsive checking behavior. The EthoVision data is fed into the software package Theme (Noldus Information Technology, The Netherlands) which is a tool for pattern detection and analysis in time-based data.

Data analysis in Theme results in a set of hierarchical time patterns, also called T patterns, for individual animals at different time points (sessions). Our data showed that quinpirole treated animals had significantly fewer variations in their behavioral repertoire compared

with saline animals (Mixed model: P < 0.0001) and that the patterns of their behavioral sequences are less complex. The mean occurrences per pattern showed a significant treatment effect, in which quinpirole treated animals showed a 2-fold higher mean occurrence per pattern compared to control (throughout all sessions), indicating that quinpirole animals repeat their patterns more often (Mixed model; P < 0.0001). Most used level and length of patterns are higher in the saline than quinpirole treated animals (Glimmix Poisson; P=0.0007, P=0.0027), indicating that quinpirole treated animals have shorter and less complex patterns. Related to these results is the mean maximum time of a pattern which is significantly longer in saline treated animals (Mixed model; P < 0.0001), which can be explained by the longer length and higher complexity of these patterns. We can conclude that T pattern analysis is a useful tool in the development of an animal model for compulsive behavior. It not only adds a valuable measurement, but also provides a new dimension in the behavioral data that translates to OCD.

References

- Pallanti, S., Hollander, E., Bienstock, C., Koran, L., Leckman, J., Marazziti, D., Pato, M., Stein, D., Zohar, J., International Treatment Refractory OCD Consortium (2002). Treatment nonresponse in OCD: methodological issues and operational definitions. *Int J Neuropsychopharmacol.* 5, 181-91.
- Szechtman, H., Sulis, W., Eilam, D. (1998). Quinpirole induced compulsive checking behavior in rats: A potential animal model of Obsessive Compulsive Disorder (OCD). *Behavioral Neuroscience* 112, 1475-1485.
- Dvorkin, A., Perreault, M.L., Szechtman, H. (2006). Development and temporal organization of compulsive checking induced by repeated injections of the dopamine agonist quinpirole in an animal model of obsessive-compulsive disorder. Behavioural Brain Research 169, 303-311.
- Magnusson, M.S. (2000). Discovering hidden time patterns in behavior: T-patterns and their detection. Behavior Research Methods, Instruments & Computers 32, 93-110.

Department of Neuroscience and Pharmacology, Rudolf Magnus Institute of Neuroscience, The Netherlands
 Department of Animals, Science and Society, Ethology and Animal Welfare, Faculty of Veterinary Medicine,
 Utrecht University, The Netherlands