# Substitution of 8-OH-DPAT in Quinpirole Model of Obsessive-Compulsive Disorder

Ahmad AlKhatib, Pieter Beerepoot, Derek Jacklin, Mark Tucci, Renee Sharma,
Anna Dvorkin, Dawn Graham, and Henry Szechtman
Department of Psychiatry & Behavioural Neurosciences, McMaster University, Hamilton, Ontario, Canada

## Introduction

Obsessive-compulsive disorder (OCD) is a psychiatric affliction with a prevalence rate of 1% to 3%. Compulsive checking is the most common symptom of OCD; it generally involves the performance of routines related to security, orderliness, and accuracy but without resolution[1]. In the quinpirole sensitization model of OCD, the chronic administration of quinpirole **(D2/D3 agonist)** induces compulsive checking behaviour in rats, which is characterized by exaggerated pre-occupation with one place in the environment (a large open field) to which the animal returns repeatedly. The spatiotemporal structure of this rat behavior corresponds to the structure of compulsive checking in OCD patients[1]. The criteria defining the spatiotemporal structure of compulsive checking in the rat are[1] :

- excessive number of returns to place-object
- excessive rapid return time to place-object
- few visits to other places
- motor rituals
- context specificity

There exists another OCD animal model based on the change in spontaneous alternation behaviour induced by 8-hydroxy-2-(dipropylamino)tetralin hydrobromide **(8-OH-DPAT; 5-HT$_{1A}$ agonist)**[2]. The behavioural paradigm of spontaneous alternation reflects the natural tendency of most species of animals to explore novel places sequentially and in succession[2]. This behaviour is captured in a T-maze, where rats will tend to visit one arm, and then another one[2]. Acute injections of 8-OH-DPAT cause a deficit in spontaneous alternation by producing an increased tendency for animals to repeat a choice of the same goal arm[2]. Such a perseverative tendency is suggested to be analogous to the repetitive motor patterns seen in human OCD patients[2].

The ability of 8-OH-DPAT to bring about perseverative tendencies raises the question of whether it can produce compulsive checking behaviour in a large open field, as produced by quinpirole, since positive findings would suggest that this compulsive behavior can be driven by stimulation of either dopamine or serotonin neurotransmitter systems.

## Methods

**Subjects:** Subjects were 36 adult male Long-Evans rats weighing an average of 325 g at the beginning of the study.

**Drugs:** Quinpirole hydrochloride (0.2 mg/kg) and 8-OH-DPAT (1 mg/kg) were dissolved in physiological saline and administered subcutaneously at a concentration of 0.2 mg/ml and 1 mg/ml, respectively.

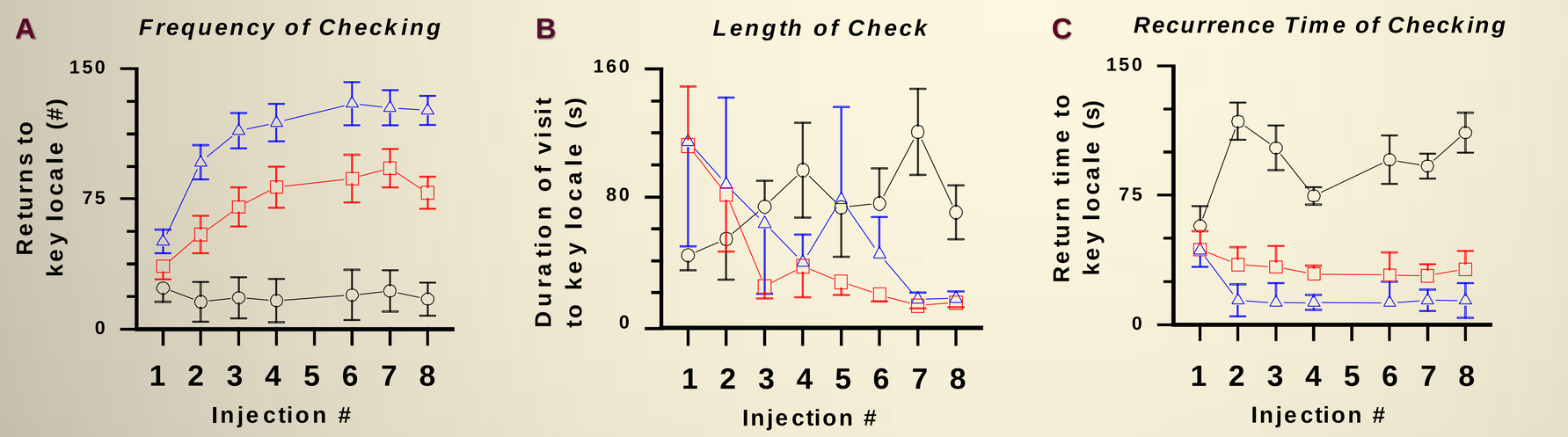
**Apparatus:** Rats were tested on an open-field table (160 cm. x 160 cm) with 4 objects placed in fixed locations (2 objects in corners and 2 objects away from corners).

**Design:**

- Compulsive Checking: Subjects were exposed to 8 injections of either 8-OH-DPAT (n=12), quinpirole (n=12), or saline (n=12), as per the standard protocol of the quinpirole model of OCD; Injections were administered twice a week over a four week period.
- Cross-Sensitization Test: Half of each chronic regimen group was then exposed to an acute administration of either 8-OH-DPAT or quinpirole to determine whether the effects of the two drugs exhibit cross-sensitization.

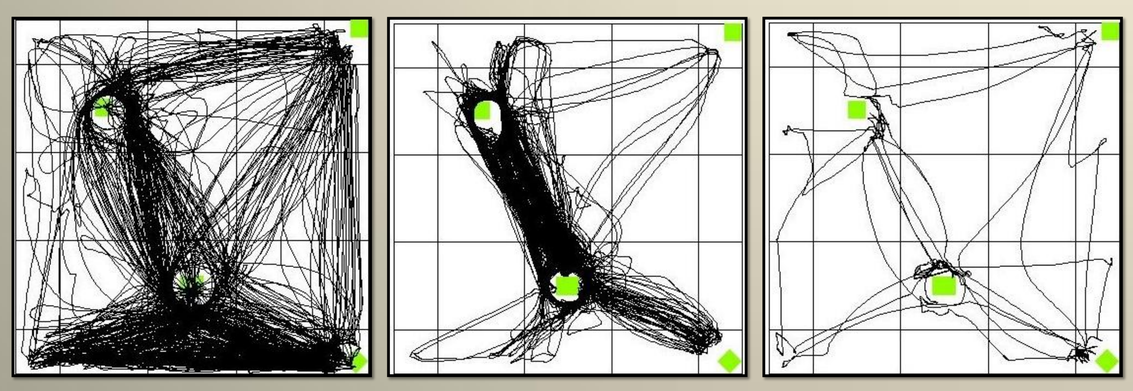
## Results

### *Development of Compulsive Checking*



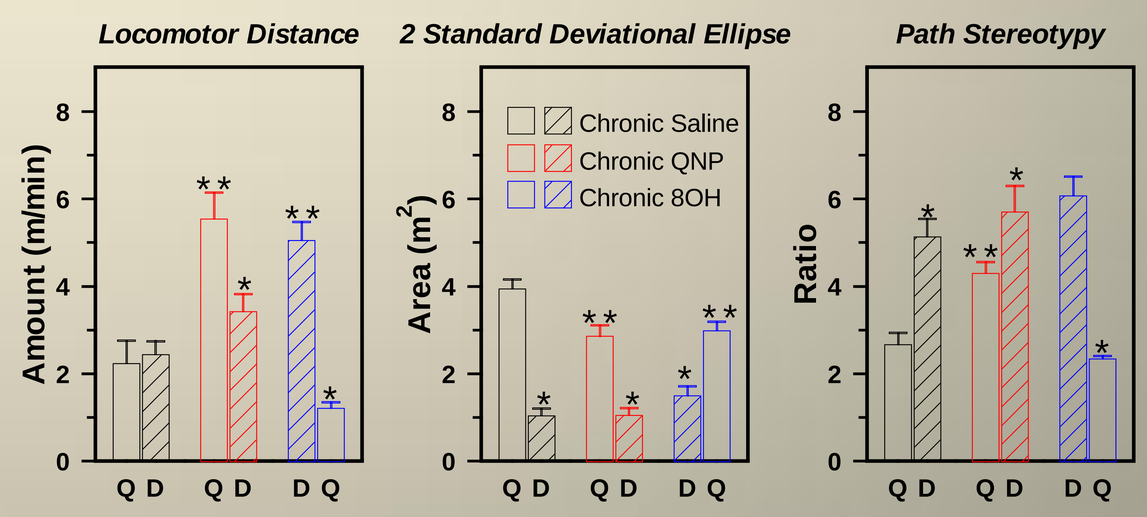

While both quinpirole and 8-OH-DPAT induced compulsive checking, for three of the measures (A, C, D), results showed that treatment with 8-OH-DPAT is a more potent inducer of compulsive checking behavior.

### *Path Plots on Test of Compulsive Checking*




Path plots of selected animals from each chronic regimen at the end of treatment (injection 8). The spatial distribution of locomotor paths in 8-OH-DPAT animals was more confined and invariant than in quinpirole rats

### *Cross-Sensitization Test*




Results showed that the effects of the drugs do not exhibit cross-sensitization, as shown in the above figures for measures of locomotion, as well as for measures of compulsive checking (data not shown). *p<.05 *vs* other drug the group received, **p<.05 *vs* saline group injected with same drug.

## Conclusion

Results showed that treatment with 8-OH-DPAT produced compulsive checking at a faster rate than injections of quinpirole, suggesting that 8-OH-DPAT is a more potent inducer of compulsive checking. Moreover, the spatial distribution of locomotor paths in 8-OH-DPAT animals was more confined and invariant than in quinpirole rats. Finally, there was no cross sensitization between the quinpirole and 8-OH-DPAT treatments. These findings suggest that the mechanisms of compulsive behavior can be triggered and driven relatively independently by hyper stimulation of dopamine or serotonin receptors and thus there may exist distinct psychopathologies of compulsive checking.

## References

[1] Szechtman H, Sulis W, & Eilam D. (1998). Quinpirole induces compulsive checking behavior in rats: a potential animal model of obsessive-compulsive disorder (OCD). *Behavioral Neuroscience*, *112(6)*, 1475-1485.

[2] Yadin, E, Friedman, E, & Bridger, WH. (1991). Spontaneous alternation behavior: an animal model for obsessive-compulsive disorder. *Pharmacology Biochemistry and Behavior*, *40*, 311-315.