

Obsessive-compulsive disorder (OCD) is a serious psychiatric condition manifested by repeated thoughts followed by stereotypic compulsive behavior. Alterations to cortico-thalamo-striato-cortical circuits are most often implicated in the pathophysiology of OCD. However, many studies have also found a changed volume, shape and activity of the hippocampus in OCD patients. This work focused on the activity of hippocampal CA1 cells during stereotypical checking behavior and on cognitive flexibility in a quinpirole (QNP) sensitization model of OCD.

The activity of CA1 hippocampal cells during stereotypical checking was assessed in an enriched open-field test in QNP sensitized rats. *Arc+* (activity - regulated cytoskeletal associated protein, or Arg 3.1) mRNA expression profiles were determined in CA1 coronal hippocampal sections following stereotypical checking. After the establishment of stereotypical checking (10 sessions), rats were exposed to the arena and sacrificed after 5 minutes. QNP sensitized animals visited the same objects with the same frequency as during previous sessions, while control rats did not. Locomotor activity was comparable between QNP treated rats and controls. Following sacrifice, rat brains were flash frozen and sliced to 20 μm thick sections. Sections, mounted on slides, were hybridized with anti-*Arc* riboprobes, and visualized using tyramid amplification. Both control rats and rats treated with QNP displayed low baseline *Arc+* positive cells in CA1. Importantly, there was a significant interaction between QNP and the environment – QNP treated rats displayed a lower number of *Arc+* nuclei in CA1 during exploring/checking the open-field compared to control rats; while in the baseline condition there was no significant difference in *Arc+* cells in CA1 between QNP treated rats and control rats.

To assess cognitive flexibility, a hippocampus-dependent Carousel arena task with reversal was employed. Animals were to avoid a sector on rotating arena that was not directly perceptible and could only be localized by spatial relationships to distal landmarks. The number of entrances into the sector was used as a measure of learning. Rats treated with QNP displayed a severe, but transient, increase in the number of errors in reversal. Treatment with clomipramine, a drug commonly used to treat OCD, further impaired reversal and impaired acquisition of the Carousel arena task. On the other hand, a combination of clomipramine and risperidone improved the rats' performance. Furthermore, two-way active avoidance task confirmed hippocampal impairment in QNP treated rats.

Although direct causality cannot be inferred from present results, this work highlights the possibility of hippocampal involvement in generation of stereotypical behavior similar to behavior observed in OCD patients.