

# Postnatal Exposure to Clonazepam Leads to Cognitive Deficits in Adult Rats

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## INTRODUCTION

Benzodiazepines (BZs) belong to widely prescribed drugs in all age groups. Under the specific condition they can be used during pregnancy and early postnatally in humans [1].

Clinical studies suggest possible risk of BZs exposure in early postnatal period for further development and behavior. Therefore, we designed the present study to examine possible cognitive alterations in adult rats after the short-term exposure to clonazepam (CZP) during development period (P7-P11).

## METHODS

### Animal and Drug

Wistar immature male rats were daily injected with CZP for five consecutive days (P7-P11). CZP, freshly suspended in saline with Tween 80, was administered intraperitoneally in three doses – 0.1, 0.5, 1.0 mg/kg. Control group received a corresponding volume of saline. Body weight was checked daily during the CZP administration.

### Habituation Test

Habituation is defined as a response decrement following continuous or repeated exposure to spatial novelty [2]. In our experiment, habituation was assessed in two ways: within-session and between-session habituation [3]. Between-session habituation to a novel environment is used as a model of non-associative learning.

We tested rats (P67-P70) for four consecutive days in an open field (OF). We placed rats individually in the center of OF and registered their behavior for 10 minutes. We evaluated following parameters: locomotor activity (distance moved in OF), exploratory activity (rearing) and displacement behavior (grooming). The evaluation was

carried out using Ethovision software (Noldus Information Technology).

### Morris Water Maze (MWM)

This test was used to investigate spatial memory. It is based on the premise that animal evolves an optimal strategy to explore the water maze and escape from the water onto submerged platform [4, 5].

Animals were tested at the age of P81-P85. Each rat received 8 consecutive trials per day for 5 consecutive days. A trial began by placing the animal into 1 of 4 randomly selected sectors (north, west, south, or east; each starting point was used no more than 2 times per session) with the head facing towards the wall. The rat was allowed to swim until it found the escape platform or had swum unsuccessfully for 60 s. In the latter case, we guided a rat to the platform by hand and recorded its latency as 60 s.

## RESULTS

Irrespective of the treatments, all animals showed within-session habituation in the 4<sup>th</sup> session. Between-sessions habituation was found only in control animals. CZP exposed animals had deficit between-sessions habituation.

In the acquisition sessions (MWM), all animals reached the platform across sessions which suggest that they learned the task i.e. to escape onto the platform. However, animals exposed to CZP in dose of 1.0 mg/kg spent more time swimming. In retention test performed 10- and 40 days after acquisition sessions no differences were found between controls and CZP rats.

In conclusion, postnatal exposure to CZP led to cognitive deficit in a dose and task dependent manner.

## ACKNOWLEDGMENTS

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