

PERINATAL DISTHYROIDISM AND ACTIVE AVOIDANCE LEARNING IN WISTAR RATS

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INTRODUCTION

Active avoidance learning has been considered as an animal anxiety model

This procedure has been induced to genetically select rat strains differing on their emotivity¹. On the other hand, changes in the emotional state of the animals induce changes on the results obtained in this test. Therefore, handling within the perinatal period, concretely in the so-called "stress hypo responsive period", improves performance in the two way avoidance test on adult animals^{2,3}.

Neurobiological mechanisms underlying active avoidance learning are sensitive to changes on thyroid hormones

In fact, neonatal handling increases the expression of the glucocorticoid receptor, an effect which is blocked by the administration of an anti-thyroid drug⁴. Moreover, neonatal administration of thyroid hormones increases the density of hippocampal mossy fibres^{5,7}, which leads to an impairment in this learning⁸. Otherwise, hippocampal lesions increase the active avoidance response⁹⁻¹⁰, which can be explained by a decrease in the anxiety levels of the animal.

Perinatal disthyroidism provokes changes on the adult animal emotivity

Previous research carried out in our laboratory showed that the induction of perinatal hypothyroidism provokes a decrease on the animal emotivity¹¹. However existing data among the bibliography show impairment in the active avoidance learning when hypothyroidism state is induced¹², although in another experiment with rehabilitated animals this was not observed¹³.

AIM: To analyze the effects of perinatal disthyroidism upon the two way active avoidance test.

MATERIAL AND METHODS

SUBJECTS: 24 male rats and 23 female rats distributed in three experimental groups (thyroxine, methimazole and control).

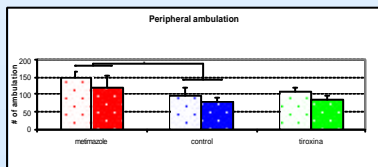
DISTHYROIDISM INDUCTION: drugs were administrated diluted in water, in order to avoid stressing effects of the other methods. The treatment started on the 9th day of pregnancy and ended on the 21st after-birth day. Doses were: 0.3 mg. of L-thyroxine or 20 mg. of methimazole per 100 ml. of water.

BEHAVIOURAL ASSESMENT: Was started when the animal was 42 days old and consisted in:

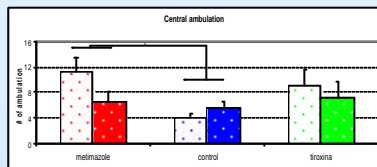
OPEN FIELD: This test is used in order to assess the locomotive activity and the emotional reactivity of the animal. This test was performed 4 consecutive days for 2 minutes. Ambulation and rearing were measured.

TWO-WAY ACTIVE AVOIDANCE LEARNING: The learning which is measured with this test is very liable of being influenced by the emotivity level of the subject. Ten daily assays were carried out thru 4 consecutive days. Twenty-one days later the retention test was carried out, which also consisted of 10 assays. Each assay started with a sound (CS) of 10 sec., if the animal responded within these 10 seconds the sound and the assay were ended. On the other hand, if the animal did not respond, then an electric shock of 0.5 mA was presented (US). This shock was removed if the animal responded, and if it was not the case, the shock had a maximum duration of 30 seconds. The learning criterion was three consecutive avoidance responses.

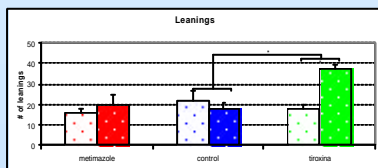
□ Rats which reach the learning criterion
■ Rats which do not reach the learning criterion



Methimazole > Control p=0'008

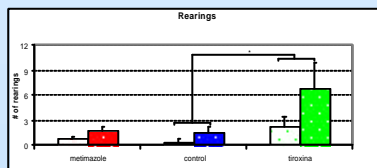


Methimazole > Control p=0'05



L-Thyroxine > Control p=0'02

Reach the criterion > Do Not reach the criterion p=0'021



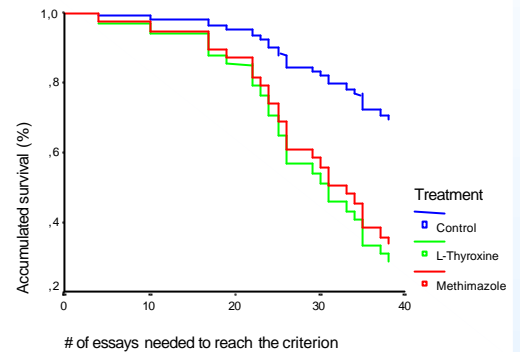
L-Thyroxine > Control p=0'006

Reach the criterion > Do Not Reach the criterion p=0'024

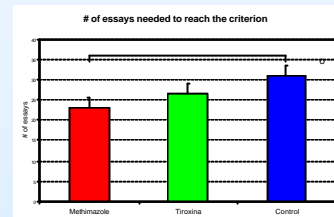
DISCUSSION AND CONCLUSIONS

- No learning differences are observed between male and female subjects. This result could be related to, among other factors, the fact that these animals have not reached the sexual maturity.
- Perinatal disthyroidism increases the number of subjects which reach the learning criterion. Although among subjects which do, animals treated present less effectiveness and poorer learning consolidation than the control group.
- Methimazole-treated animals show an increased ambulation respect to the other two groups, especially among the animals which reach the learning criterion. This fact could explain their greater speed achieving the criterion.
- Rearing behaviour is greater in the animals that do not reach the learning criterion than in the ones that reach it, especially in the thyroxine treated group. This exploratory behaviour could interfere with the learning.

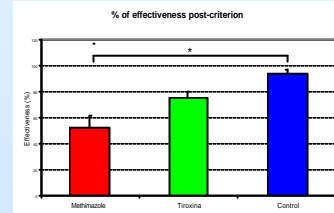
Survival function



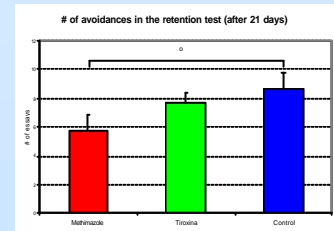
of essays needed to reach the criterion



Methimazole < Control p=0'082



Methimazole < Control p=0'002



Methimazole < Control p=0'085

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