

The English Summary – Master Thesis

**Pharmacological study of protein malnutrition on the
pharmacological profile of certain antianxiety drugs in
experimental animals**

Thesis Presented By
Amira Mourad Aboyousef
Demonstrator of Pharmacology & Toxicology
Faculty of Pharmacy
Cairo University, Beni-Suef branch

Submitted for the master degree in Pharmaceutical sciences
(Pharmacology & Toxicology)

Under supervision of

Prof. Dr. Mostafa El-Sayed El-Sayed
Prof. of Pharmacology & Toxicology
Faculty of Pharmacy
Cairo University

Prof. Dr. Amina Salem Attia
Prof. of Pharmacology & Toxicology
Faculty of Pharmacy
Cairo University

Dr. Azza Abdel-Fatah Ali
Lecturer of Pharmacology & Toxicology
Faculty of Pharmacy (Girls)
Al-Azhar University

Faculty of Pharmacy – Cairo University
Cairo 2004

Summary and Conclusions

In the present study the effect of protein malnutrition alone and in presence of diazepam (5mg/Kg) as well as, buspirone (5mg/Kg) were studied in rats after 2 hours, 7 days and 14 days on behavioral and biochemical parameters.

Protein malnutrition was induced by restricting the amount of casein in the prepared diet to 7.5 % instead of 20 % in normal protein diet. Induction of protein malnutrition started just after weaning.

Three models of behavioral examinations were selected to study the possible effects of protein malnutrition on behavioral responses to drug. These models included swimming test, open field test and conditioned avoidance test.

In addition, biochemical parameters were measured in the brain namely, GABA, 5HT, NE and DA.

The main findings of the present study can be summarized as follows:

I- Behavioral tests:

• Swimming test:

- 1- Protein malnutrition increased swimming time and did not affect latency time and direction score.
- 2- Diazepam in normally-fed rats increased swimming time after 14 days of drug administration, while it did not affect latency time or direction score.
- 3- Diazepam in protein malnourished rats decreased latency time and swimming time after 14 days of drug administration and did not affect direction score.

- 4- Protein malnutrition increased the effect of diazepam on latency time after 2 hours of drug administration and on swimming time after 2 hours and 7 days.
 - 5- Buspirone in normally-fed rats decreased latency time and swimming time after 7 and 14 days of drug administration and did not alter direction score.
 - 6- Repeated administration of buspirone in protein malnourished rats decreased latency time and swimming time after 14 days of drug administration.
 - 7- Protein malnutrition, in general, decreased the effect of buspirone on latency time and swimming time.
- **Open-Field test:**
 - 1- Protein malnutrition decreased ambulation frequency, rearing frequency, self-grooming and field sniffing and licking behaviors. and did not affect defecation and urination.
 - 2- Diazepam in normally-fed rats decreased rearing frequency and self-grooming behavior after 14 days of drug administration. It increased field sniffing and licking behavior after 7 and 14 days and it had no effect on latency time, ambulation frequency, defecation and urination.
 - 3- Repeated administration of diazepam in protein malnourished rats, in general, increased latency time, ambulation frequency, self-grooming behavior and field sniffing and licking behavior. It decreased rearing frequency and had no effect on defecation and urination.
 - 4- Protein malnutrition, in general, decreased the action of diazepam on latency time, ambulation frequency, rearing frequency and self-grooming behavior and field sniffing and licking. It had no effect on the action of diazepam on, defecation and urination.

- 5- Repeated administration of buspirone in normally-fed rats increased rearing frequency, field sniffing and licking. It decreased latency time, defecation and urination. It had no effect on ambulation frequency and self-grooming behavior.
- 6- Repeated administration of buspirone in protein malnourished rats decreased latency time and urination. It increased rearing frequency and had no effect on ambulation frequency, self-grooming, field sniffing and licking and defecation.
- 7- Protein malnutrition, in general, increased the action of buspirone on ambulation frequency, rearing frequency, field sniffing and licking and defecation. It increased the action of buspirone on latency time after 2 hours and it had no effect on self-grooming behavior and urination.

• **Conditioned-Avoidance test:**

- 1- Protein malnutrition increased number of trails to avoid electric shock in the first day of training and had no effect on retrieval ability.
- 2- Repeated administration of diazepam in both normally-fed and protein malnourished rats, in general, increased percentage failure to avoid electric shock and did not alter percentage failure to escape after electric shock.
- 3- Protein malnutrition decreased the action of diazepam on percentage failure to avoid electric shock.
- 4- Buspirone in normally-fed and protein malnourished rats, in general, decreased percentage failure to avoid electric shock and had no effect on percentage failure to escape after electric shock.
- 5- Protein malnutrition had no effect on the action of buspirone on percentage failure to avoid electric shock.

II- Biochemical Tests:

- 1- Protein malnutrition decreased brain serotonin, norepinephrine and dopamine contents. It increased brain GABA contents.
- 2- Repeated administration of diazepam in normally-fed rats increased brain GABA content.
- 3- Diazepam in protein malnourished rats had no effect on brain GABA content.
- 4- Protein malnutrition increased the action of diazepam on brain GABA content.
- 5- Repeated administration with buspirone in both normally-fed and protein malnourished rats increased brain GABA content.
- 6- Protein malnutrition increased the action of buspirone on brain GABA content.
- 7- Repeated administration of diazepam in normally-fed rats decreased brain serotonin content after 14 days of drug administration.
- 8- Repeated administration of diazepam had no effect on brain serotonin content in protein malnourished rats.
- 9- Protein malnutrition increased the action of diazepam on brain serotonin content after 2 hours of drug administration.
- 10- Repeated administration of buspirone decreased brain serotonin content in both normally-fed and protein malnourished rats.
- 11- Protein malnutrition increased the action of buspirone on brain 5HT content after repeated administration.
- 12- Repeated administration of diazepam in normally-fed rats decreased brain norepinephrine content.
- 13- Treatment with diazepam in protein malnourished rats had no effect on brain norepinephrine content.

- 14- Protein malnutrition increased the action of diazepam on brain norepinephrine content after 2 hours of drug administration.
- 15- Repeated administration with buspirone in both normally-fed and protein malnourished rats increased brain norepinephrine content after 7 and 14 days of drug administration.
- 16- Protein malnutrition increased the action of buspirone on brain norepinephrine content after different durations of drug administration.
- 17- Treatment with diazepam in normally-fed rats increased brain dopamine content after 14 days of drug administration.
- 18- Repeated administration with diazepam in protein malnourished rats, in general, increased brain dopamine content.
- 19- Protein malnutrition, in general, decreased the action of diazepam on brain dopamine content.
- 20- Repeated administration with buspirone increased brain dopamine content after 14 days of drug administration in normally-fed rats.
- 21- Treatment with buspirone in protein malnourished rats, in general, did not alter brain dopamine content.
- 22- Protein malnutrition, in general, decreased the action of buspirone on brain dopamine content.

Depending on the results of the present study, it could be concluded that:

- 1- Protein malnutrition decreases motor activity and learning ability but does not affect retrieval ability.

- 2- Protein malnutrition decreases brain monoamines but increases brain GABA content.
- 3- Diazepam in normally- fed rats decreases locomotor activity and retrieval ability (tranquillizing action).
- 4- Diazepam in protein malnourished rats increases locomotor activity and to a lesser extent decreases retrieval ability than normally-fed rats.

It follows that protein malnutrition decreases the action of diazepam

on both motor activity and retrieval ability.

- 5- Diazepam decreases brain norepinephrine and increases brain GABA contents in normally-fed rats and to greater extent in protein malnourished rats.

It follows that protein malnutrition synergizes the action of diazepam on GABA brain content.

- 6-Diazepam, in general, increases brain dopamine content in both normally-fed and protein malnourished rats after repeated administration.

It follows that protein malnutrition has no effect on the action of diazepam on brain dopamine content.

- 7-Buspirone in normally- fed rats decreases motor activity and retrieval ability.

- 8-Buspirone in protein malnourished rats decreases motor activity to a greater extent than in normally-fed rats and decreases retrieval ability.

It follows that protein malnutrition synergizes the action of buspirone

on motor activity and has no effect on retrieval ability.

- 9-Buspirone decreases brain norepinephrine and increases GABA

contents in normally-fed rats and to greater extent in protein malnourished rats .

It follows that protein malnutrition synergizes the action of buspirone

on brain norepinephrine and GABA contents.

10-Buspirone in general decreases brain serotonin content and increase brain dopamine content in normally-fed rats.

11-Buspirone in protein malnourished rats decreases brain serotonin content.

It follows that protein malnutrition synergizes the action of buspirone on serotonin brain content and antagonize the action of buspirone on brain dopamine content.

Dr. Amira Mourad Abo- Youssef

Pharmacology and Toxicology Dept.