The effect of one month riboflavin administration on thermonociceptive behavior and locomotion in mice

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INTRODUCTION

Certain neurotransmitters, including serotonin, norepinephrine or dopamine (fig. 1) are metabolized by the monoamine oxidase (MAO), a mitochondrial outer membrane enzyme, dependent on FAD, the coenzyme form of riboflavin [1, 2].

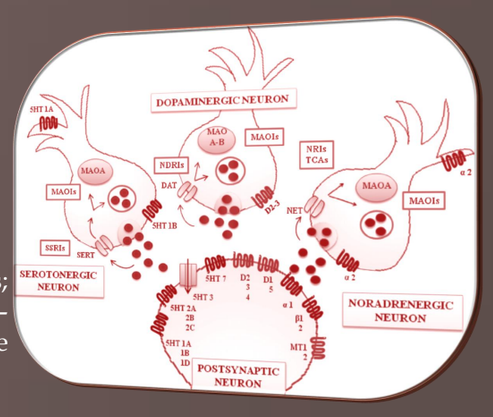
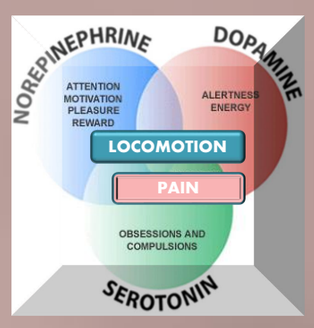


Fig.1 Schematic representation of MAO dependent neurotransmitters. TCAs, tricyclic antidepressants; TeCAs, tetracyclic antidepressants; SSRIs, selective serotonin reuptake Inhibitors; NDRIs, noradrenaline–dopamine reuptake inhibitor; MAO-A, monoamine oxidase inhibitor-A; MAO-B, monoamine oxidase inhibitor-B; SNRIs, serotonin–noradrenaline reuptake inhibitor (dupa Felice et al 2015)



All MAO dependent neurotransmitters are involved in depression, pain and locomotion control fig 2.

Fig.2 Interferences between pain, locomotion and psychiatric disorders

It is documented that riboflavin administration restores and stimulates MAO activity [3] so we decided to explore the effect of repeated riboflavin administration (four weeks) on thermonociception, motor coordination and locomotor activity.

METHODS

20 male BALB/c mice, weight 33±2 g, were divided in 2 : groups: - the riboflavin group (n=12),
- the control group (n=8).

The mice received daily riboflavin (50mg/kg b.w.) or saline (the same volume as riboflavin treated mice) intraperitoneal injections and were evaluated for thermonociception, motor coordination and locomotor activity before treatment (baseline) and every two days thereafter, for a 28 day period.

Nociception was evaluated using tail flick latency test (**TFLT**) and hot plate test (**HPT**).

Motor coordination has been assessed by the rotarod test (RT).

The Ugo Basile Activity Cage was used to measure horizontal (**HLA**) and vertical (**VLA**) locomotor activity. The cut off was set at 12s for TFLT, 15 s for HPT and 300s for RT. The locomotor activity was evaluated for 3 minutes. The data for days 7, 14, 21, and 28 are presented in percentage changes from baseline (PBC)

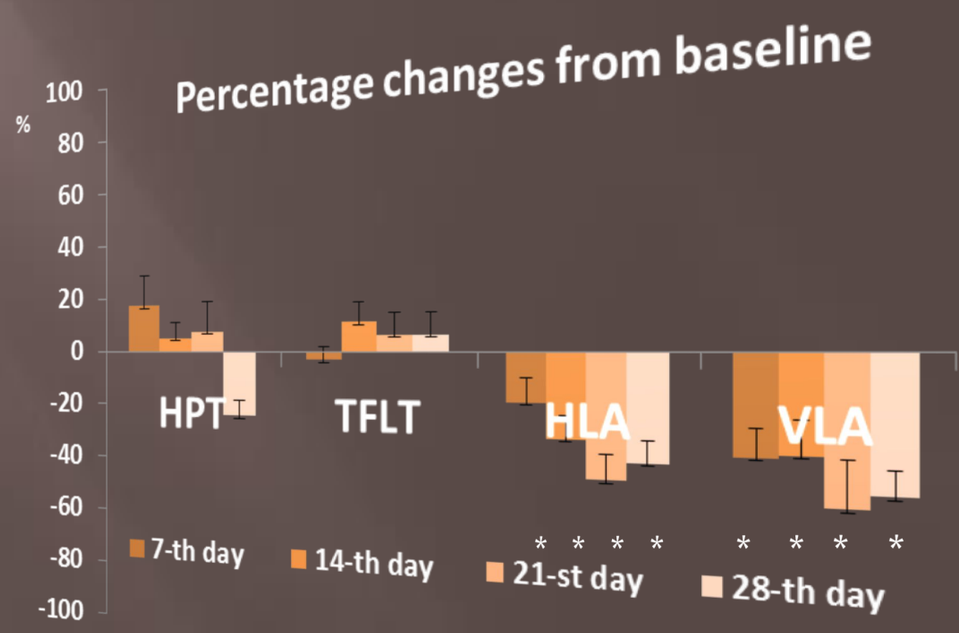
PBC = (treated- baseline) x 100/baseline.

Statistical significance was assessed by paired ttests or ANOVA as appropriate.

RESULTS

Riboflavin had no statistically significant effect on thermonociception neither when compared with baseline nor with control group.

However, the PBC for HPT in the saline group varied from 2% to +10%, while in the riboflavin group from 23% to 5%, whereas for TFLT, variations were 3 7.5% and 2 to 10%, respectively. We noticed a tendency towards hyperalgesia in the last week of treatment on the HPT. No changes on motor coordination were observed during riboflavin/saline treatment. By contrary, a significant decrease in rearing (day 28, 43.97 ± 54.4%, p=0.03) and horizontal movements (day 28, 36.1 ± 13%, p=0.02) were noticed in the riboflavin treated mice when compared with baseline or with control group. Starting from the first week, the decrease was significant for both vertical and horizontal movements.



CONCLUSION

Our results show that one month of riboflavin treatment has no significant effects on nociception, no effect on motor coordination and has a powerful effect on mice's exploratory behavior – the animals preferred to stay into the unprotected center area of the activity cage thus indicating that riboflavin has an anxiolyticlike behavior [3].

Even though riboflavin controls MAO metabolism through a mitochondrial FAD dependent enzymes, it seems that it has different effects on MAO dependent neurotransmitters, being more important for those involved in anxiety than those involved in pain and locomotion control.

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