

EFFECT OF EXERCISE ON THE DOPAMINERGIC SYSTEM: RELEVANCE FOR THE PREVENTION OF ANERGIA IN ANIMALS MODELS

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Resumen

La práctica de actividad física está relacionada con la mejora de la salud física, la satisfacción personal, el rendimiento cognitivo y el bienestar psicológico. El sistema de dopamina mesolímbico (DA), desempeña un papel crucial en la regulación de la activación del comportamiento y los procesos asociados al esfuerzo en la conducta motivada. Por eso, el deterioro o disminución de DA puede inducir anergia en tareas de toma de decisiones que requieren esfuerzo. En el presente estudio se evalúa el impacto del enriquecimiento ambiental y la depleción de DA, inducida por TBZ, sobre la preferencia por reforzadores activos en ratones machos CD1 criados en condiciones de ambiente enriquecido y ambiente neutro. Los animales recibieron una inyección peritoneal de TBZ (8 mg/kg) o vehículo (0,9% solución salina) administrada 120 min antes de la prueba y se evaluó su comportamiento en el laberinto en T de tres opciones para evaluar las preferencias espontáneas por distintos estímulos situados en diferentes brazos: un olor neutro, comida palatable y una rueda para correr (RW). Los resultados muestran que la TBZ redujo el tiempo en RW en comparación al grupo control pero solo en el tiempo dedicado a interactuar con los estímulos. Por lo que en general, no se muestran diferencias significativas a la resistencia de los efectos de la TBZ en animales en condiciones de AE comparado al grupo control, es decir, los animales siguen prefiriendo el reforzador que contiene un mayor valor motivacional, correr. Los resultados obtenidos contradicen las evidencias científicas por lo que sería interesante controlar la variable de ejercicio realizado en el AE antes de las pruebas.

Palabras clave: Anergia, Dopamina, Esfuerzo, Ambiente enriquecido, Ejercicio, Tetrabenazina.

Abstract

The practice of physical activity is related to improved physical health, personal satisfaction, cognitive performance and psychological well-being. The mesolimbic dopamine (DA) system plays a crucial role in the regulation of behavioral activation and effort-associated processes in motivated behavior. Therefore, impairment or decrease in DA can induce anergy in effortful decision-making tasks. The present study evaluates the impact of TBZ-induced environmental enrichment and DA depletion on the preference for active reinforcers in male CD1 mice reared in enriched and neutral environment conditions. Animals received a peritoneal injection of TBZ (8 mg/kg) or vehicle (0.9% saline) administered 120 min before the test and their behavior in the three-choice T-maze was assessed to evaluate spontaneous preferences for different stimuli located in different arms: a neutral odor, palatable food, and a running wheel (RW). The results show that TBZ reduced the time in RW compared to the control group but only in the time spent interacting with the stimuli. Therefore, in general, there are no significant differences in the resistance of the effects of TBZ in animals in AE conditions compared to the control group, that is, the animals still prefer the reinforcer that contains a higher motivational value, running. The results obtained contradict the scientific evidence, so it would be interesting to control the variable of exercise performed in the AE before the tests.

Key words: Anergy, Dopamine, Effort, Enriched environment, Exercise, Tetrabenazine.

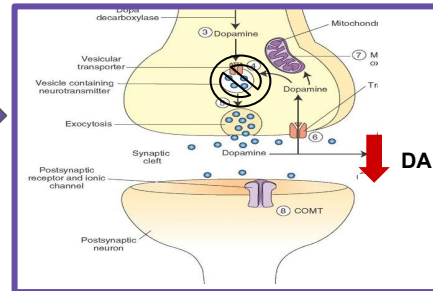
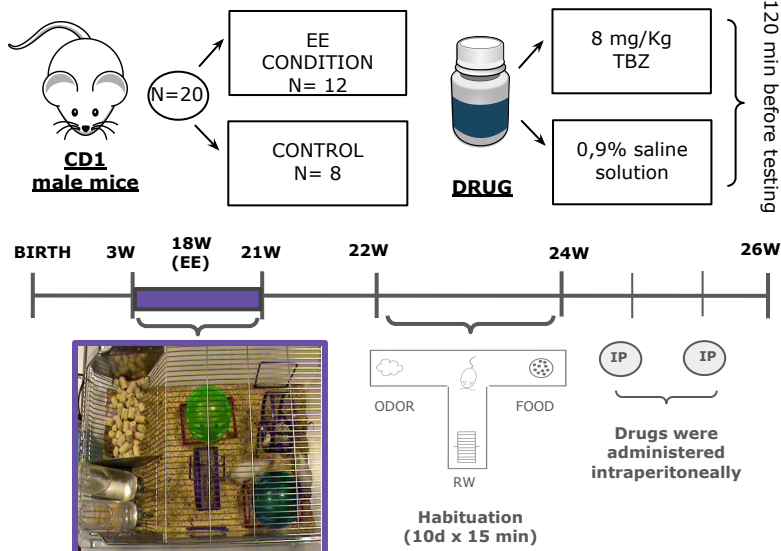
INTRODUCTION

Physical activity has been consistently shown to be associated with improved physical health, life satisfaction, cognitive functioning, and psychological well-being. Exercise compares favorably to antidepressant medications as a first-line treatment for mild to moderate depression (Carek et al., 2011). **Mesolimbic dopamine** is essential for the regulation of behavioural activation and effort-related processes in motivated behaviour. Therefore, impairment of mesolimbic dopamine leads to fatigue and anergia (Correa et al., 2020). **TBZ** acts by inhibiting vesicular monoamine transporter type 2 (VMAT-2), leading to a blockade of the vesicular storage and monoamine depletion, with its greatest effects at low doses on striatal DA in rats and mice (López-Cruz et al., 2018)

OBJECTIVES

The aim of our study was to assess the impact of environmental enrichment and DA depletion, induced by TBZ, on preference for active reinforcers.

METHODS



RESULTS

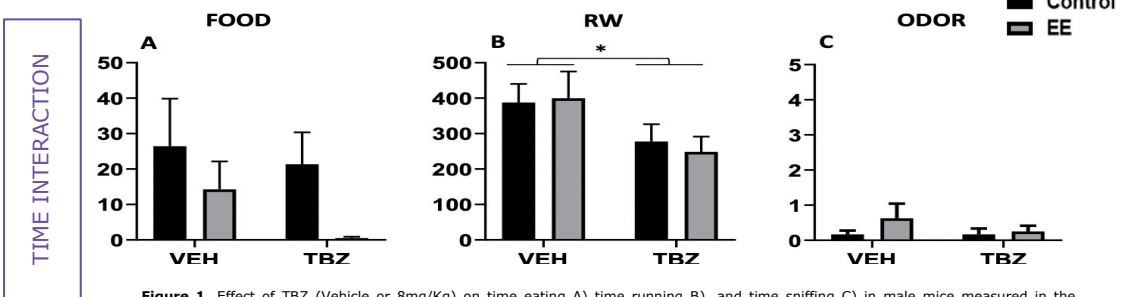


Figure 1. Effect of TBZ (Vehicle or 8mg/Kg) on time eating A) time running B), and time sniffing C) in male mice measured in the 3-choice-T-maze task. Bars represent the mean ± S.E.M. of accumulated seconds interacting with each stimulus in 15 minutes *p<0.05, significant differences between treatments.

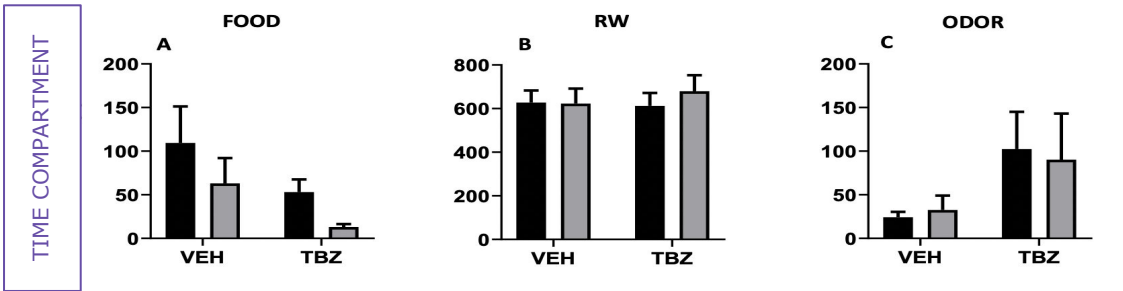


Figure 2. Effect of TBZ (Vehicle or 8mg/kg) on time in food compartment A), RW compartment B), and odor compartment C) in male mice measured in 3-choice-T-maze task. Bars represent the mean ± S.E.M. of accumulated in 15 minutes.

CONCLUSIONS

- In general, all animals **prefer** the reinforcer that requires more activity, the **RW**.
- Only in the time spent interacting with stimuli did **TBZ reduce** the time spent in the RW compared to the vehicle group.
- Despite the evidence in the scientific literature, in this study, it is not observed that animals in the **EE condition** show greater resistance to the effects of TBZ than the control group.
- For **future research**, it would be interesting to control the variable of the exercise done by each of the animals in the EE before testings.

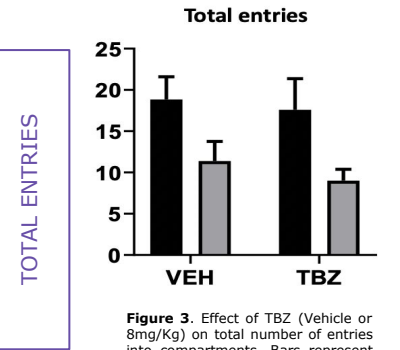


Figure 3. Effect of TBZ (Vehicle or 8mg/Kg) on total number of entries into compartments. Bars represent the mean ± S.E.M. of total entries.

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