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ORIGINAL PAPERS

Behavioural and Metabolical Changes Associated with the Pathophysiology of Alzheimer's Disease in Zebrafish

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Abstract

Background. Affecting 60% of the people diagnosed with dementia, Alzheimer's disease is a neurodegenerative pathology that negatively impacts the cognitive function. It is characterised by symptoms as memory loss, locomotor difficulties, behavioural changes, and even rationalization issues. This disease has been studied on both rodents and fishes. Rodents helped science people establish the basic neurobiology of dementia, while fishes (*Danio rerio* – the zebra fish, especially) were more appropriate as transgenic models. Recent studies proved that transgenically induced Alzheimer's disease at zebra fishes is not defined only by cognitive decline but also by motor function disorders. **Objectives.** This study aims to analyse how iron chloride and sucrose impact zebra fishes' locomotion and memory by using the T maze. **Methods.** 50 zebra fishes were purchased from a local pisciculturist and randomly divided in 4 experimental groups. They were accommodated in the Ecotoxicology laboratory at "Alexandru Ioan Cuza" University for 3 weeks according to the European Union Commission and European Union Council recommendations regarding experimental purposes animals' protection and accommodation. Fishes' possible behavioural changes were analysed after they were given sucrose and iron chloride separately and in their combination. **Results.** We observed that sucrose administration negatively impacted the locomotory activity while iron chloride surprisingly increased it. The possible explanation is the fact that iron chloride generated anxiety - an early-stage Alzheimer's disease

symptom, and therefore improved fishes' swimming performance. Successive sucrose and iron chloride administration also led to increased locomotor activity.

Keywords: *Alzheimer's disease, dementia, zebra fish, behaviour, sucrose, iron chloride*

Introduction

In 1910, the term 'Alzheimer's disease' was used for the first time, naming the neurodegenerative disease after Alois Alzheimer – German psychiatrist and neurologist. Initially, this pathology was described as an 'unusual disease affecting the cerebral cortex', observed at a 51-year-old female patient who had symptoms such as: memory issues, behavioural changes, difficulties in doing usual activities and other symptoms that were not noticed before at young people, comparing to elders who had dementia. Years later, after the patient's death, the autopsy proved that there was massive brain damage, especially in the parietal and frontal regions (Hippius & Neundorfer, 2003).

Known as the 21st century disease, Alzheimer's disease is represented by a neurodegenerative process that slowly contributes to the loss of the cognitive function, leading to the patients' death. It affects around 60% of the people suffering with dementia, being specific mostly to elders, although young people tend to be diagnosed with it as well (Marica, 2011).

The main risk factor generating Alzheimer's disease is the presence of apolipoprotein E (APOE) allele. Out of its 3 forms: E2, E3 and E4, E4 type is considered to be involved in Alzheimer's disease pathophysiology, judging by the fact that it APOE has important functions such as: motor coordination, cholesterol distribution, growth, repair and maintenance of myelin sheath and brain cells. There are 9% chances that an individual that lacks E4 allele has Alzheimer's disease, while the risk rises to 29% for people who have it (Cummings & Cole, 2002). Besides repeated, serious cranio-cerebral trauma, other risk factors in developing this disease could be biological: low levels of folate and vitamin B12, high levels of homocysteine and cholesterol, type 2 diabetes, hypertension, and social factors: poor education and low income for example (Marica, 2011) (Apostolova, 2016).

Alzheimer's disease early clinical examination is characterized by symptoms as apathy and generally decreased interest or concern. Around 50% of the patients also have depression related symptoms and 25% can hallucinate, while mobility abnormalities are observed during the last phase of the disease (Cummings & Cole, 2002). According to a 2019 study, patients' symptoms vary with the disease phase as it follows: early stage – organizing issues, forgetting dates, names, details about him/herself, getting lost in familiar places; middle stage: hallucinations, compulsive behaviour, anxiety, reading and writing issues,