Секция «Экспериментальные исследования»

Effects of sertraline exposure on adult zebrafish in the aquatic tail immobilization test

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Introduction: Rodents' despair-like behavior is widely used as a phenotype for antidepressants screening. At the same time, fish despair-like behavior remained unknown. Recently we proposed new way of zebrafish (Danio rerio) behavioral phenotyping. The results of such studies (e.g. fluoxetine) strongly support use of Zebrafish Tail Immobilization (ZTI) test to study and screening of antidepressants and suggest high sensitivity of this test [1, 2]. Here we study SSRI sertraline effects on the behavior of zebrafish using the ZTI test and automatic behavioral screening using Noldus Ethovision XT 11.5 and compare the results with former sertraline screening with the usage of ZTI test and manual scoring, reported earlier. Methods: Wild-type naïve short-fin zebrafish (3-5 month old) housed in standard care conditions were used in the study. Briefly, in ZTI fish caudal half was immobilized for 5 min using the sponge that was placed right on the water surface in such way that cranial part of the fish remained in a small tank filled water. Prior to test fish were pre-exposed to 2, 10, 50 mg/L sertraline dissolved in DMSO (10 mg/L) or in drug-free vehicle containing 10 ml/L DMSO in 0,25 L beakers filled with water for 20 min (n=15) or in drug- and DMSO free water. Trials were recorded on action camera and activity (relation of changing pixels to the arenas area) were studied. Fish that successfully escaped were excluded from further analyses. Data were analyzed by the Kruskal-Wallis ANOVA test. The Mann-Whitney U-test was used to compare DMSO and control groups. Results and discussion: The data, analyzed using the Kruskal-Wallis ANOVA test, have demonstrated a statistically significant increase in percentage of activity for the 10 and 15 mg/L concentrations compared to the DMSO vehicle group (0.41 ± 0.08 and 0.52 ± 0.05 vs. 0.16 ± 0.06, respectively, with $p<0.0001$. Dunn's test for significant KW data. KW: 0,0259 and 0,0001 for the 10 and 15 mg/L respectively, with $p<0,0001$). The usage of DMSO as a solvent did not affect behavior in a statistically significant manner in the Mann-Whitney U-test when compared against the control group (U=109, p=0.9). Furthermore, the results allow for the activity threshold of sertraline in zebrafish to be established as being between 2 and 10 mg/L, as no statistically significant differences in mean activity were demonstrated by the KW test between 10 mg/L and 15 mg/L (KW-H = 0.826, $p<0.0001$). Thus, sertraline exposure improves zebrafish performance in ZTI test. Other assay methods (in compare with former study) prove sensitivity of the ZTI to antidepressant screening and efficiency of sertraline as an antidepressant. Since manual scoring was insensetive in assesing overall behavioral differences and relied on perminute analyses automatic scoring may be seen as superior for studying ZTI behavioral responses.

Источники и литература

1) Demin K.A., Lakstigal A.M., Chernysh M.V. et al. The zebrafish tail immobilization (ZTI) test as a new tool to assess stress-related behavior and a potential screen for drugs affecting despair-like states// J Neurosci Methods. 2020 Feb 17:108637

2) 26th Multidisciplinary International Neuroscience and Biological Psychiatry Conference "Stress and Behavior": https://drive.google.com/file/d/1oc8Vfeiwt6RTegqTgufr9dAWmfkw9HvM/view