accompanied with oral explanation.

Conclusions: results show that pictograms are generally well understood in DS population. The use of the selected pictograms (including oral explanation) constitutes a valid instrument to assess the presence of self-reported symptoms by DS population.

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Conflict of interest:

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IMPACT OF DUAL SPECIFICITY TYROSINE PHOSPHORYLATION REGULATED KINASE 1A OVEREXPRESSION ON THE COMORBIDITY OBSERVED IN INDIVIDUALS WITH DOWN SYNDROME RELATED TO COGNITIVE DYSFUNCTION AND OBESITY

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Down syndrome (DS) is the major genetic cause of intellectual disability that co-occurs with other pathological features. Among others, the prevalence of obesity in DS individuals is higher respect to general population which leads to severe metabolic disturbances. The presence of an extra copy of human chromosome 21 suggests that specific genetic mechanisms associated to trisomy 21 predispose to this comorbidity. DYRK1a is a DS dose-sensitive candidate gene involved in neuronal differentiation and proliferation and the regulation of lipids and glucose metabolism. Our aim is to unravel the role of Dyrk1A to regulate obesity development in DS and its link to cognitive impairment.

Transgenic mice overexpressing Dyrk1A (TgDyrk1A) and their respective controls were fed ad libitum with high fat diet (RD 12492) or standard chow from 9 weeks old for four months. Along those months, mice of both sexes were submitted to a standardized pipeline combining cognitive behavioral tests and metabolic measurements. Behavioral tests included novel object recognition, spontaneous alternation, marble burying and sucrose preference test. The pipeline was completed with the oral glucose tolerance and insulin sensitive tests to address disturbances in glucose metabolism. Two-way ANOVA was used for statistical analysis.

Our results indicate that overexpression of Dyrk1A could protect from obesity development upon high caloric diet, since the weight increase was statistically reduced compare to control mice fed with high fat diet. In spite of the protective effect, glucose metabolism was altered specially in TgDyrk1A females as shown by maintained higher glucose levels after glucose load in the oral glucose tolerance test and the lack of the recovery of glucose levels after insulin administration in the insulin sensitive test. Regarding cognitive performance, TgDyrk1a mice showed slight impairment in spontaneous alternation and object discrimination compared to control mice that were not affected upon high fat feeding. Similarly, TgDyrk1A mice were prompt to show a compulsive behavior in the marble burying test being higher the number of buried marbles compare to control mice. Control mice upon high fat diet showed an increase in the number of buried marbles compare to controls with standard chow, effect that was not observed in the TgDyrk1a mice. Finally, no relevant differences in the sucrose preference test were observed in any of the experimental groups suggesting not changes in anhedonia in our mice in spite of the administration of high fat diet. Our results indicate that overexpression of Dyrk1A mediates the glucose metabolism impairing it. However, a significant weight increase was not observed upon hyper caloric diet, so it was difficult to establish the relationship between obesity and cognition in our model. Due to Dyrk1A function in glucose and lipid metabolism we cannot discard the possibility of targeting Dyrk1A to modulate metabolic disturbances in DS individuals, but further experiments are required.

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OXYTOCIN TREATMENT IMPROVES DEXAMETHASONE-INDUCED DEPRESSION-LIKE SYMPTOMS IN FEMALE MICE

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Aims: Stress is a major risk factor for depression, which is among the leading causes of disability globally, and is twice as common in women as in men. It is crucial in the hunt for improved antidepressant medicines because only approximately half of the patients treated with traditional antidepressants achieve remission. Chronic stress and glucocorticoid exposure are risk factors for depression. Oxytocin (OT) is mainly formed in the paraventricular nucleus (PVN) of the hypothalamus and its neurons project to the hippocampus. Oxytocin has been revealed to have antistress and antidepressant-like effects in male rodents. However, women are twice as likely to experience depression as males, and it is still unknown whether OT has benefits similar to those of an antidepressant in depressed women. As a result, in this study, we explored the therapeutic effect of chronic OT administration in a female mouse model of dexamethasone (DEX)-induced depression.

Methods: After 1 week of acclimatization, the animals were divided into the following three experimental groups (n = 8 for each group) at random. 1) Saline was administered to the vehicle group. 2) DEX was administered to the DEX group. 3) The OT + DEX group received OT and DEX treatment. After the termination of drug administration, all animals were exposed to a series of behavioral tests (open field test, elevated plus maze test, and forced swimming test). Then, the mice were sacrificed under anesthesia with sodium pentobarbital (50 mg/kg), and the blood sample, dorsal, and ventral hippocampus were obtained. Trunk blood samples were collected from the mice into a tube containing 5-μL heparin. Then, the samples were centrifuged at 3,000 rpm for 15 min at 4 °C to separate the plasma, which was assayed using a commercially available CORT ELISA kit based on the manufacturer's instructions. Furthermore, we also analyzed the hippocampal levels of phosphorylated cAMP response element-binding protein (p-CREB) and brain-derived neurotrophic factor (BDNF), which are critical mediators of the response to antidepressants. Data were examined using StatView software Ver.5 (HULINKS). When needed, Bonferroni–Dunn posthoc analysis was used to compare groups using parametric tests such as one-way factorial analysis of variance (ANOVA). All data are represented as mean ± standard error of the mean (S.E.M). Statistical significance was set at $P < 0.05$.

Results: The DEX exposure increased the anxiety-, depression-like behaviors, and plasma CORT levels, while simultaneous OT treatment prevented the aversive effects of DEX and improved p-CREB and BDNF levels of the dorsal and ventral hippocampus. These results have demonstrated that chronic OT treatment counteracted the aversive effects of DEX-induced depression.

Conclusion: OT may exert antidepressant-like effects by stimulating hippocampal CREB-BDNF signaling in a female mouse model of depression. Our findings strongly demonstrate the significance of the OT systems as a potential target for a new therapeutic approach for depression in females.

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