

The developmental changes of endogenous opioid system associated with altered sensitivity to reward during adolescence

Adolescence as a period of transition between childhood and adulthood is a time when young people discover how to adapt within environment, face new challenges and approach new social situations. It is also a time of intense brain reorganization when complex changes occur in the brain structures responsible for emotional regulation, decision-making and learning. The intensified sensation-seeking and risk-taking behaviors observed in human teenagers make adolescence a phase of increased propensity to emergence of mental disorders. This adolescent susceptibility may be due to an altered sensitivity to reward - a stimulus that induces pleasurable feelings.

One of the brain systems particularly involved in reward system modulation is the opioid system. An enhanced sensitivity to reward and an increased propensity for substance abuse during adolescence suggest that rapid developmental changes in the opioid system occurs. Molecules involved in opioid signaling are abundant in the prefrontal cortex (PFC) and nucleus accumbens (NAcc) - key structures for the reward system that develop dynamically during puberty.

As far as sensitivity to social reward is concerned, in adolescents in the so-called "teenage rebellion" period, there is an increased motivation to establish contacts with peers and a decrease in affect associated with being among family members. In our study, we saw a similar phenomenon in mice - the rewarding effects of sibling contact temporarily diminish during adolescence. Interestingly, we were able to restore it by administering the opioid drug, cyprodime. This result indicates that social reward is mediated by opioid signaling.

Given our current knowledge, as well as our previous results, we believe that altered sensitivity to rewarding stimuli during adolescence is associated with developmental changes in the opioid system. However, these changes are not yet well described.

Therefore, in this project, we want to investigate how the opioid system changes during adolescence. To address this issue, we will measure the opioid genes in PFC and NAcc in three stages of mice development corresponding to childhood, adolescence and adulthood. Interpretation of the obtained results will concern the general changes occurring in selected brain structures involved in reward processing. Due to the lack of detailed reference data on the ontogenesis of the opioid system in adolescence, even broader conclusions will be very valuable and will enable us to formulate hypotheses about the mechanisms of the opioid system.

This project will help to identify neuronal populations that should be the subject of further human research in the context of mental disorders, the first symptoms of which appear already in adolescence. In addition, since our previous results have shown the possibility of restoring the rewarding effects of social interactions with opioid drug, we hope that the results of this project will boost further molecular research in this direction, contributing to the development of new pharmacological therapies for mental disorders.