Advances in Biomedical Research, MedILS, Split, Croatia, July 3rd – 7th, 2017.

Circadian Genes and Redox Regulate Neuroplasticity to Psychostimulants in *Drosophila*

Ana Filošević, Josipa Kolobarić, Sabina Al Samarai and Rozi Andretić Waldowski

University of Rijeka, Department of Biotechnology, Center for high-troughput technologies, Laboratory for behavioral genetics, Radmile Matejčić 2, 51 000 Rijeka, Croatia, e-mail: randretic@biotech.uniri.hr

OUR INTEREST

Addictive drugs engage mechanisms of neural plasticity to change the function and structure of the brain resulting in addiction.

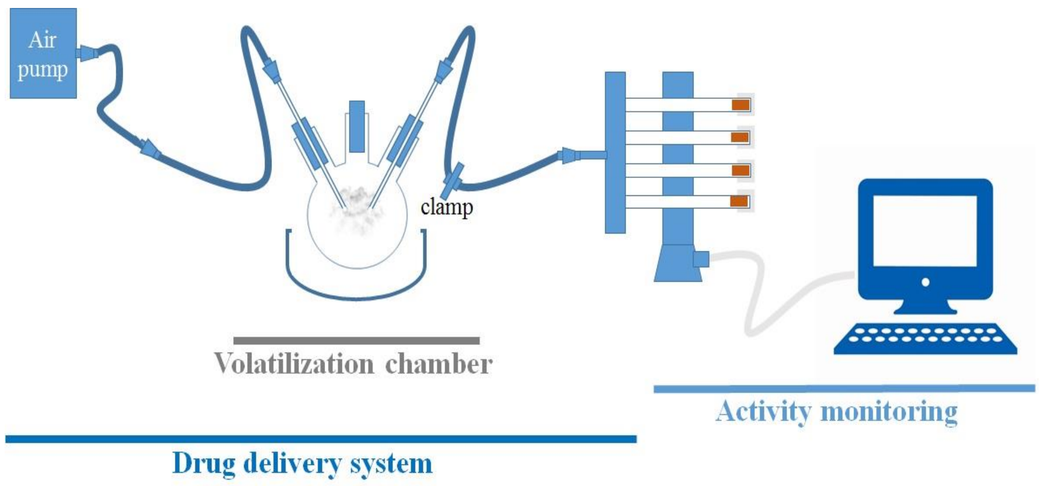
Addiction is a complex behavior and in the lab we study the endophenotype, a form of neuroplastic change: locomotor sensitization (LS).

To investigate the genetic basis of LS we use Drosophila melanogaster.

Hypothesis: Interaction between circadian genes and redox state regulate LS to cocaine (COC) and methamphetamine (METH).

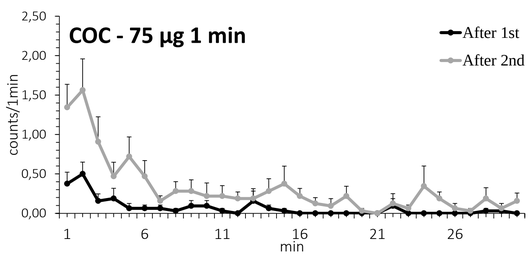
HOW WE STUDY IT

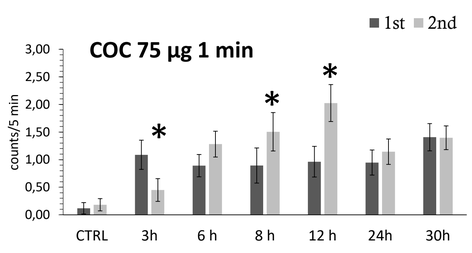
We have developed a high throughput behavioral assay for quantifying locomotor sensitization induced by volatilized COC or METH, that we named FlyBong.

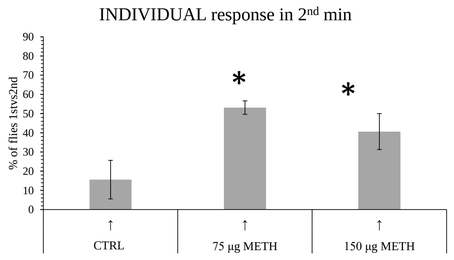


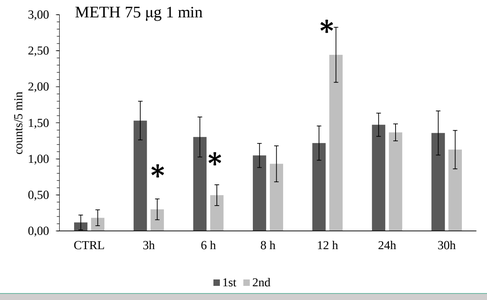
WHAT WE DISCOVERED

1. Repeated administrations of volatilized COC or METH induce locomotor sensitization.



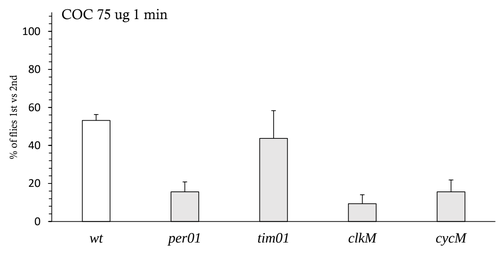


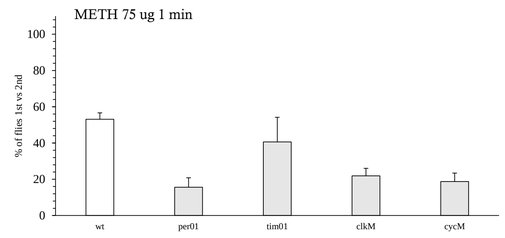




SIGNIFICANCE: Validation of the FlyBong for development of LS to COC. New discovery that shows that repeated METH administration induces LS.

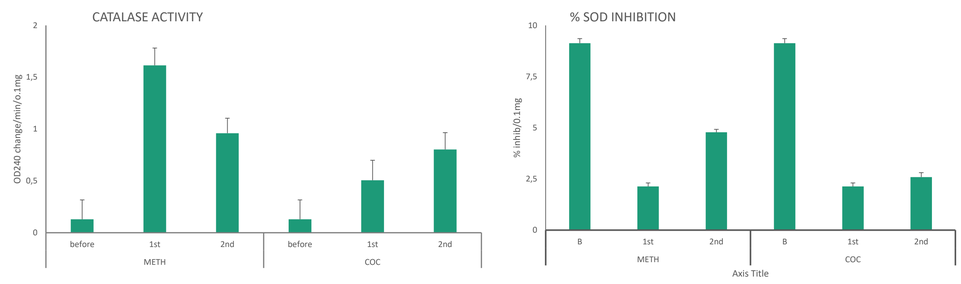
2. Locomotor sensitization is dependent on circadian genes: period, Clock and cycle and dopamine transporter.





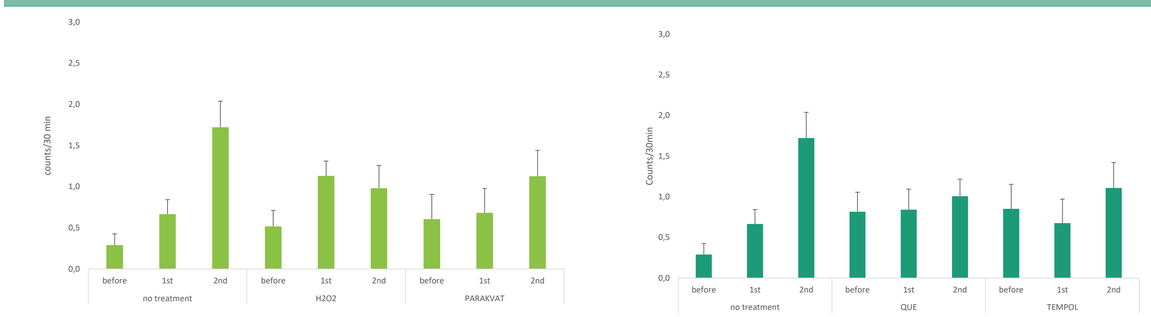
SIGNIFICANCE: Validation of the FlyBong assay.
Circadian genes regulate and are regulated by redox state.

3. COC and METH induce activity of Catalase and decrease activity of Superoxid dismutase



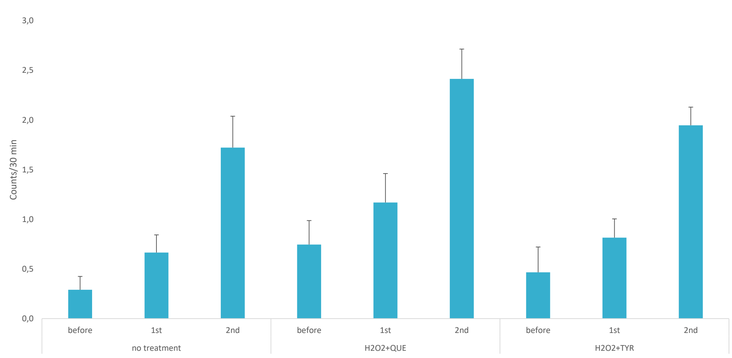
SIGNIFICANCE: After COC and METH administration antioxidative enzymes are activated to maintain redox balance.

3. Locomotor sensitization is dependent on redox status. Pro and anti-oxidants abolish sensitization.



SIGNIFICANCE: When redox balance is further disturbed with exogenous substances, LS does not develop.

5. Locomotor sensitization develops when there is a balance of pro and antioxidants.



SIGNIFICANCE: Homeostatic balance of redox is permissive for LS. Decrease in oxidative status is not as permissive.

INTERPRETATION

1. COC and METH change the activity of antioxidant enzymes to keep the redox balance.
2. When antioxidant enzymes can not keep up with change in redox LS does not develop.
3. Orally administered antioxidants could influence effects that addictive drugs have on brain functioning and addiction.

WHAT WE WOULD LIKE TO KNOW

1. What is the consequence of lack of LS on rewarding aspects of drug taking, such as craving (self-administration).
2. Where in the brain do redox changes occur which influence LS.
3. Circadian genes and redox show mutuall regulation. Is the redox influence on neuronal plasticity mediated by circadian genes?
4. Which other genes do circadian genes interact with in the regulation of neuronal plasticity.

FINANCIAL SUPPORT: Research Grant of Croatian Scientific fondation number: 4920; Doctoral Support Croatian Scientific fondation 2015., University of Rijeka grant

Projekt je sufinancirala Europska unija iz Europskog fonda za regionalni razvoj. Sadržaj ove publikacije isključiva je odgovornost Sveučilišta u Rijeci.