6th Croatian Neuroscience Congress, Osijek, Croatia, 16.-18. September, 2017.

Interaction between redox status and psychostimulants-induced neural plasticity in *Drosophila*

Ana Filošević, Josipa Kolobarić, Sabina Al-samarai and Rozi Andretić Waldowski

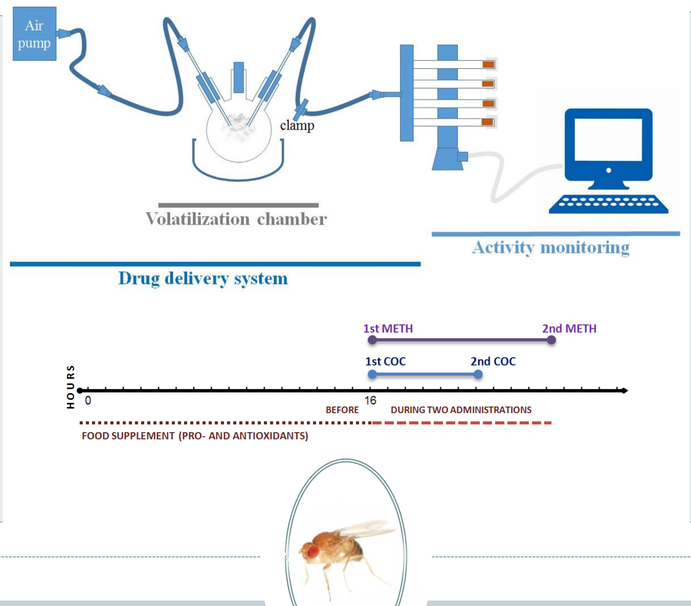
University of Rijeka, Department of Biotechnology, Laboratory for behavioral genetics, Radmile Matejčić 2, 51 000 Rijeka, Croatia,
e-mail: randretic@biotech.uniri.hr

OUR INTEREST

• Cocaine and methamphetamine-like psychostimulants induce neural plasticity and enhance dopaminergic neurotransmission which contributes to the development of addiction.

• Locomotor sensitization (LS) represents an endophenotype of neuroplastic change which can be objectively measured in Drosophila.

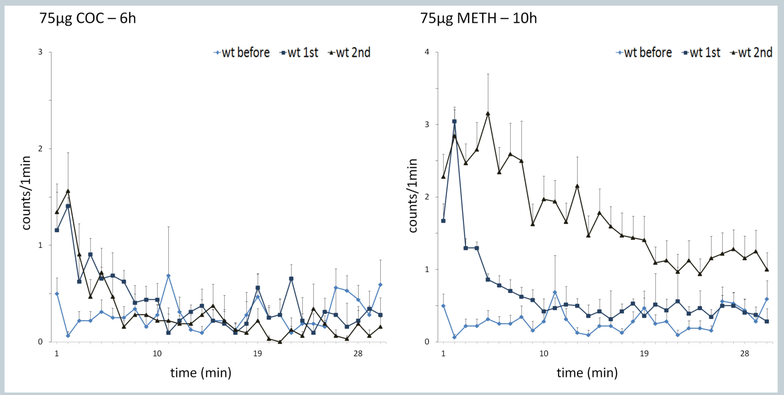
Hypothesis: Changes in redox status can modulate neural plasticity which will be evident as a change in LS to psychostimulants.



APPROACH

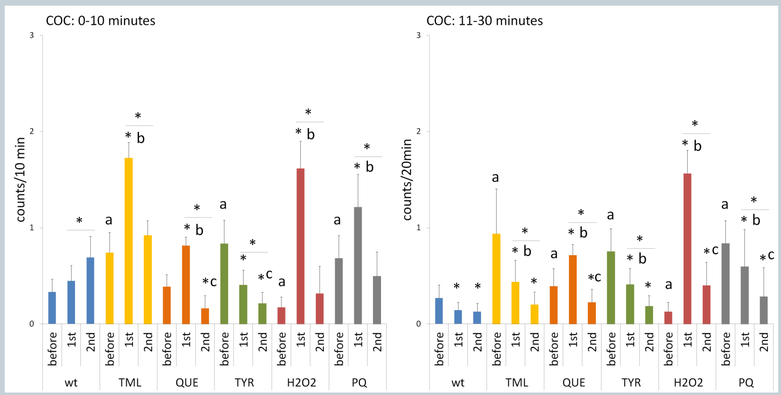
• Our newly developed high throughput locomotor assay "FlyBong" was used to quantifying locomotor activity induced by volatilized cocaine (COC) and methamphetamine (METH).
• Flies were fed with prooxidants and/or antioxidants before and during two administrations of volatilized COC or METH.
• Hydrogen peroxide (H_2O_2) and paraquat (PQ) were used as prooxidants, while tempol (TML), quercetin (QUE) and tyrosol (TYR) were used as antioxidants.
• The activity of antioxidative enzymes catalase (CAT) and superoxide dismutase (SOD) was measured.

Flies respond to volatilized COC or METH with robust, but transient increase in locomotor activity. Repeated administration of the same dose leads to further increase in locomotor activity and represents locomotor sensitization (LS).



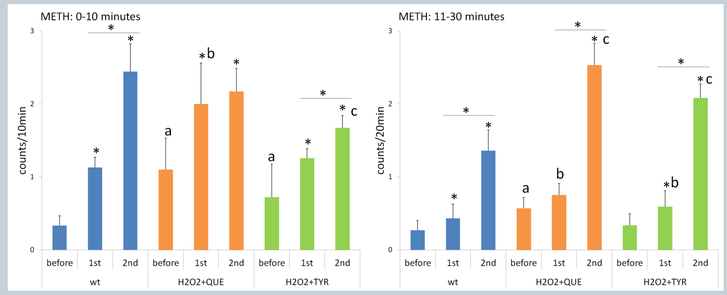
We show for the first time that flies develop LS to METH, with distinct temporal profile from COC.

LS to COC and METH is abolished in flies treated with antioxidants, as well as in flies treated with prooxidants.

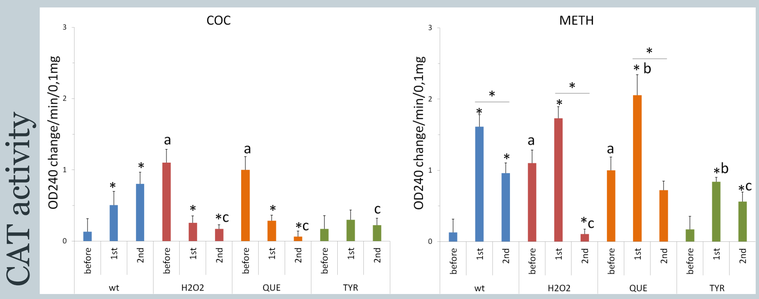


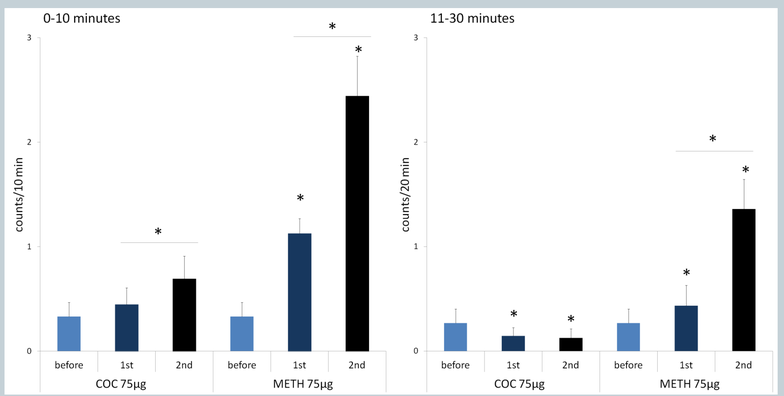
Treatment with prooxidants and antioxidants has an effect on basal locomotor activity. Treated flies show enhanced locomotor response after first administration of COC in first 10 minutes.

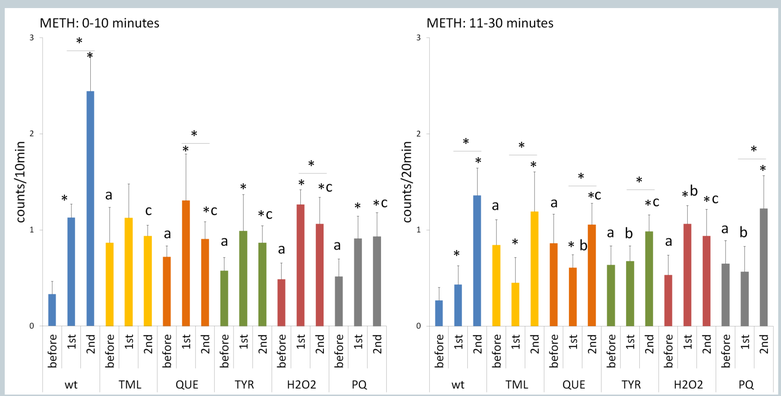
Combined treatment with prooxidant and antioxidant restores LS to METH.



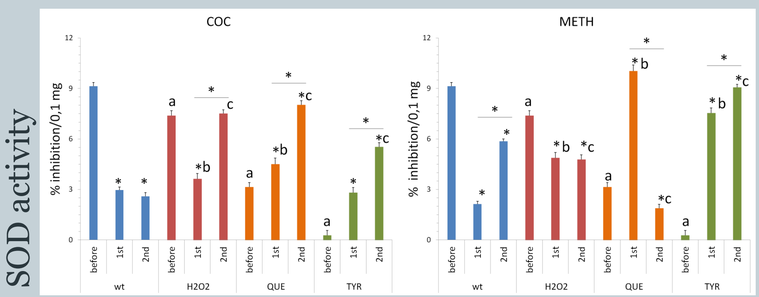
Repeated administration of COC and METH increase the activity of CAT (wt), while treatments have an opposite effect.







COC and METH decrease the activity of SOD (wt). Treatments with antioxidants counteract the SOD activity compared to wt.



Statistical significance p<0,05; a-compared to before wt, b-compared to 1st wt and c-compared to 2nd wt

INTERPRETATION

• Impairment in redox status with exogenous exposure to prooxidants or antioxidants results in changes in neural plasticity, evident as lack of LS to COC or METH.
• LS to COC or METH can be restored with the combined treatment with pro- and antioxidants.
• Anti-oxidative treatments showed opposite effect on the activity of CAT and SOD enzymes suggesting their involvement in redox processes that control LS to COC and METH.

CONCLUSION

• Neural plasticity is dependent on redox status which can be influenced exogenously.
• Identifying changes in redox status that lead to changes in behavioral response will help explain the complexity of drug-induced neural plasticity.
• Further work will focus on the investigation of neural mechanisms of neural plasticity using genetic mutants and transgenic flies involved in dopaminergic neurotransmission (TH, DAT, VMAT) and for antioxidative defense (CAT, SOD).

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.