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

Preferential consumption of psychostimulants in *Drosophila melanogaster*: introduction of self-administration paradigm

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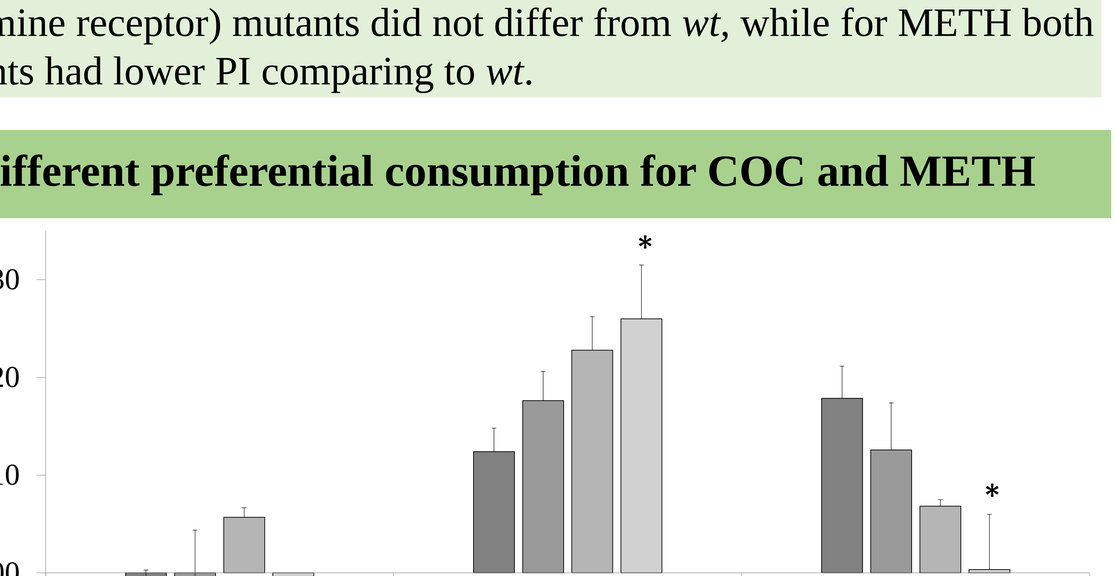
Background

The self-administration paradigm is a behavioral phenotype that can be measured in laboratory animals and models features of addiction. *Drosophila* preferentially consumes ethanol–containing food, however it is not known if the same is true for psychostimulants, cocaine (COC) and methamphetamine (METH).

Methods

To test if flies will voluntarily self-administer psychostimulants we modified the two-choice Capillary Feeder (CAFE) assay, where flies can choose between capillaries with drug-food or a non-drug food. Liquid non-drug food contained 100 mM sucrose aqueous solution, while drug-food contains 100 mM sucrose solution with COC (0,15 mg/mL) or METH (0,20 mg/mL). Capillaries containing drug-food were placed in pipet tips marked with cue (dark marking on a pipette tip). Preference Index (PI) was calculated based on the consumption of drug-food minus non-drug food, normalized by consumption of all food. There were 6 flies per tube, capillaries were changed daily and PI was calculated per tube.

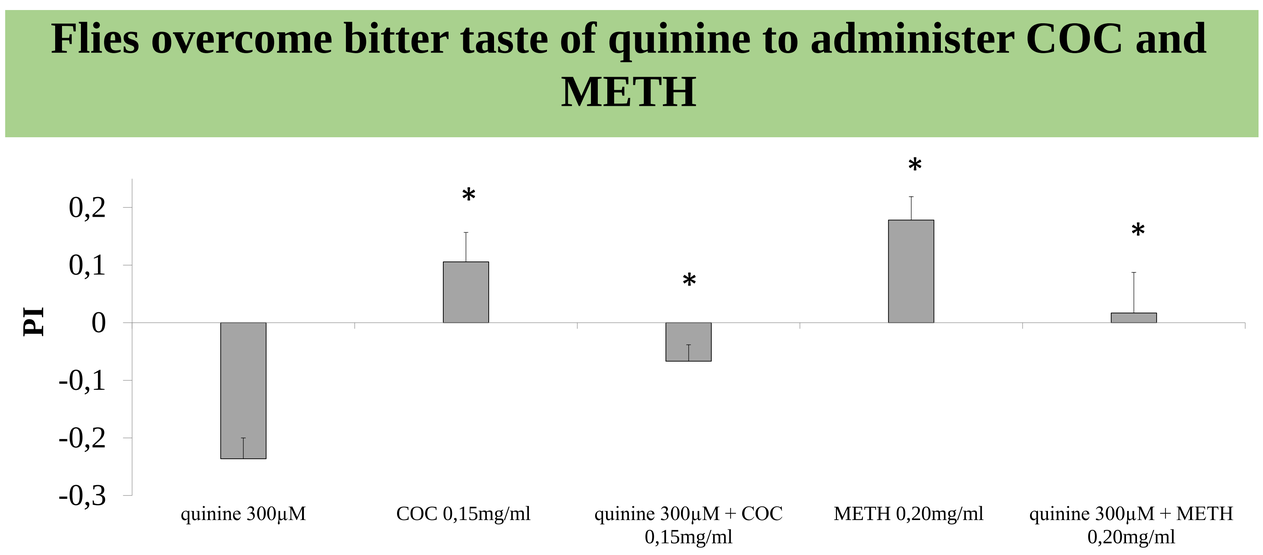


Results

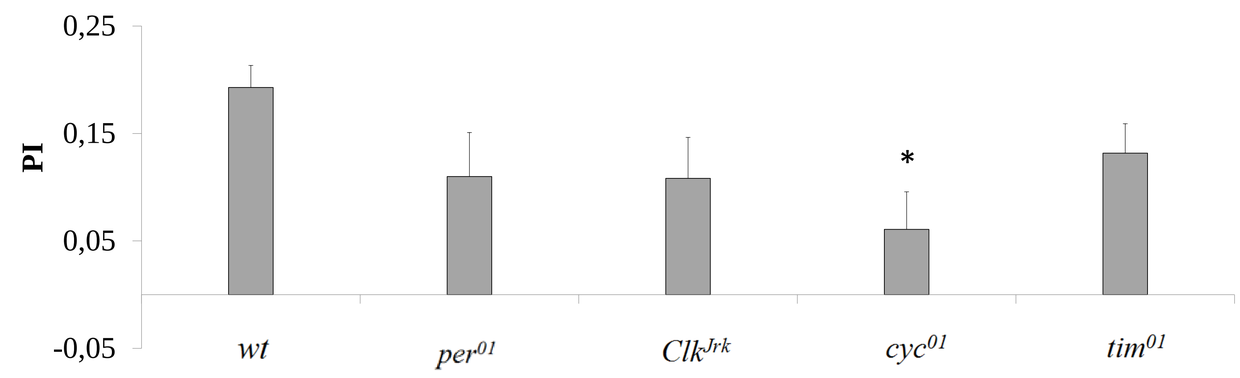
PI for COC is positive and increases over consecutive days, while PI for METH is positive on day one, but then decreases over consecutive days. Flies continue to consume substantial amounts of drug-food even when quinine is added, though preference is decreased. Clk^{Jrk}, cyc^{01} and per^{01} mutants had negative average PI for METH-containing food, while only cyc^{01} had significally lower PI for COC-containing food. Preferential consumption for COC of *fmn* (dopamine trensporter) and *dumb* (D1-like dopamine receptor) mutants did not differ from *wt*, while for METH both mutants had lower PI comparing to *wt*.

Different preferential consumption for COC and METH

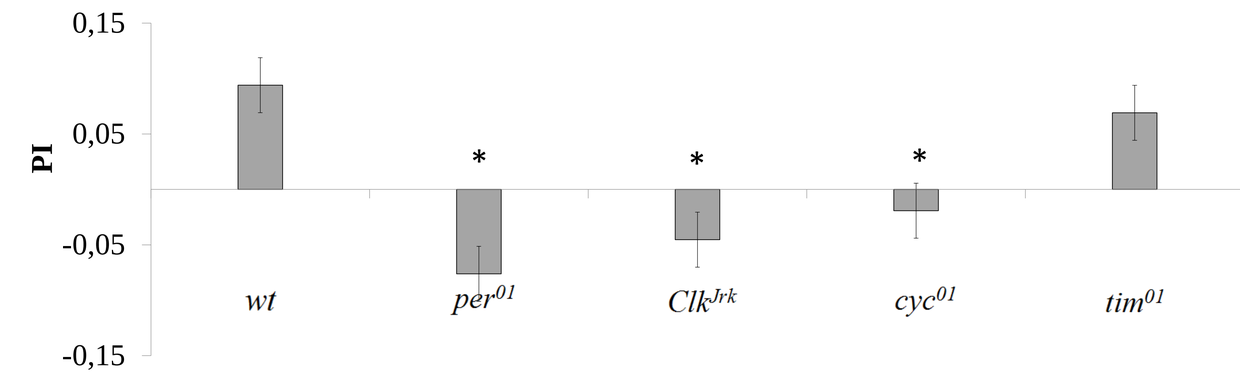
Flies overcome bitter taste of quinine to administer COC and METH



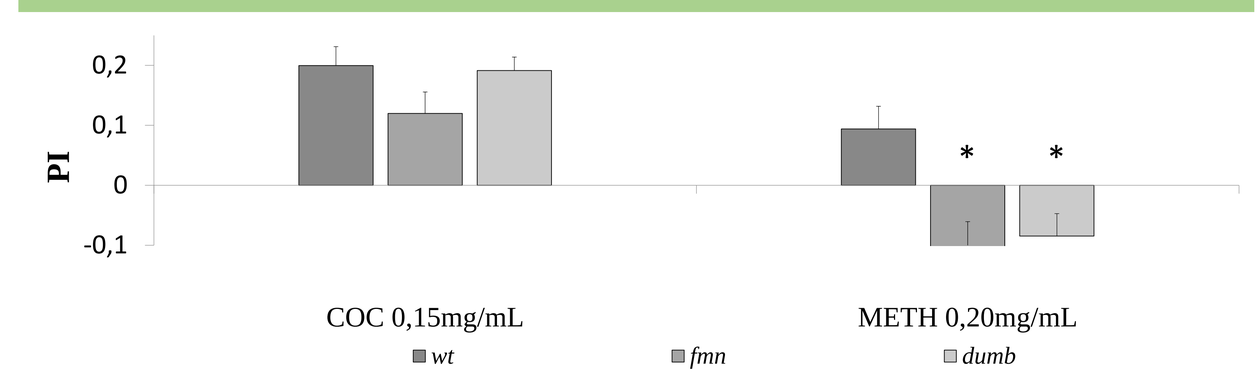
Preferential consumption of circadian mutants for COC



Preferential consumption of circadian mutants for METH



Preferential consumption of *fmn* and *dumb* mutants for COC



Conclusion

1. Drosophila preferentially consumes COC and METH containing food over sugar-food, but there is a difference in preferential consumption of METH and COC suggesting mechanistic difference of action.
2. Flies overcome an aversive stimulus in order to obtain COC and METH.
3. Different circadian genes are involved in preferential consumption for COC and METH.
4. Dopamine transporter and dopamine receptor D1 are involved in preferential consumption for METH, but not for COC, suggesting role for other molecules.
5. Drosophila can be used as a model organism to investigate neural mechanism of rewarding effects of psychostimulants.

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

Croatian Science Foundation

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