

Self-administration of cocaine and methamphetamine in Drosophila melanogaster



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Ministarstvo znanosti, obrazovanja

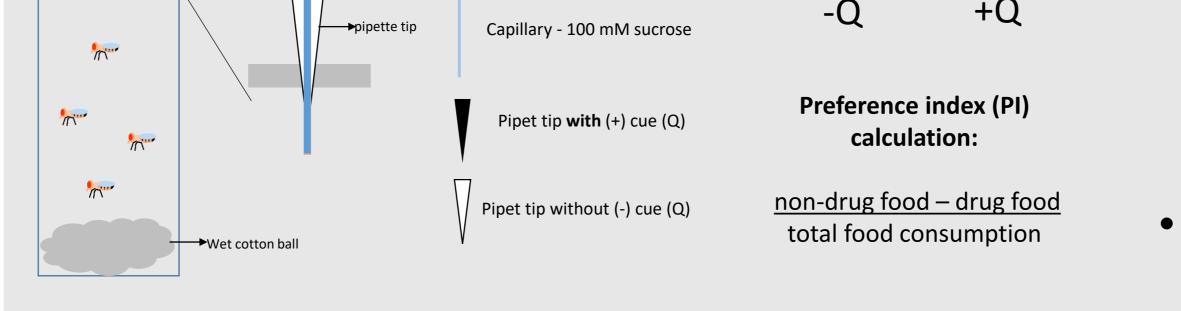


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Introduction	Meth	ods
Drosophila preferentially consumes ethanol-	To test if flies will voluntarily self-administer psychostimulants we used the two-choice Capillary	We measured:
	Feeder (CAFE) assay, where flies can choose between capillaries with drug- or a non-drug containing food.	a) Preferential consumption for COC and METH
methamphetamine (METH), bitter compounds with		b) Features of addiction:
no nutritional relevance, can induce preferential consumption. If <i>Drosophila</i> preferentially consumes COC or	Capillary - 100 mM sucrose with COC 0,15 mg/mL or METH 0,20 mg/mL	 consumption against negative consequence (quinine) relapse induced by drug deprivation

METH-containing food it would indicate that drug activates motivational and/or reward circuits. This would allow for an unbiased gene discovery for genes involved in preferential drug consumption.



c) Mutants for:

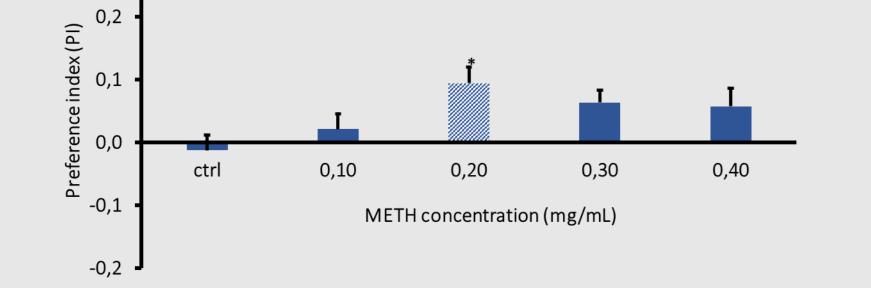
Europska unija Ulaganje u budućnost

• circadian genes *per⁰¹, tim⁰¹, clk^{Jrk} and cyc⁰¹* monoamine neurotransmission using *fmn,dumb* and

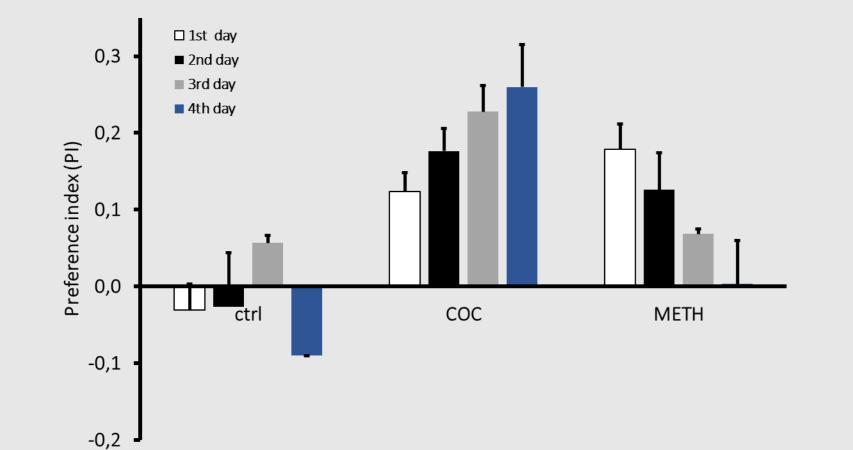
DDC-VMAT

Results preferential consumption of COC is greater with greater preferential consumption of METH after two Preferential consumption of COC and METH \bullet fixed location days of deprivation wt flies preferentially and dose dependently 0,5 • 0,3 🗆 1st day ······ METH dep consume COC and METH 2nd day 3rd day 0,4 — METH no dep 0,2 0,3 (Id) 0,3 (ы ă 0,1 (Pl) 0,2 . 9,0,2 월 0,1 -2nd 1st 0,05 0,10 0,15 0,20 0,50 1,00 ctrl -0,1 u 4 -0,1 0,0 COC concentration (mg/mL) sides fixed diagonally -0,1 J -0,2 -0,2 J **Genetic screen** Flies develop features of addiction 0,3

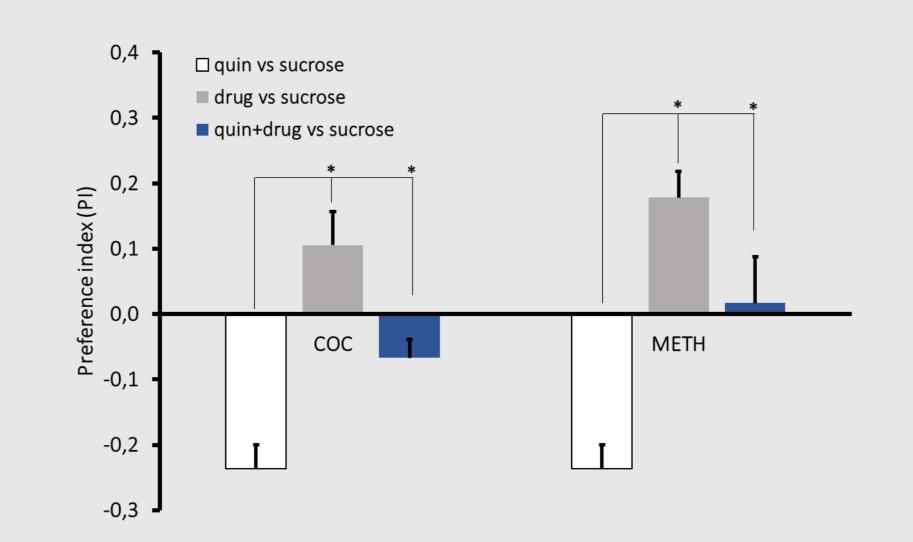
preferential consumption of METH depends on *per*,



preferential consumption of COC increases, while for METH decrease over several days

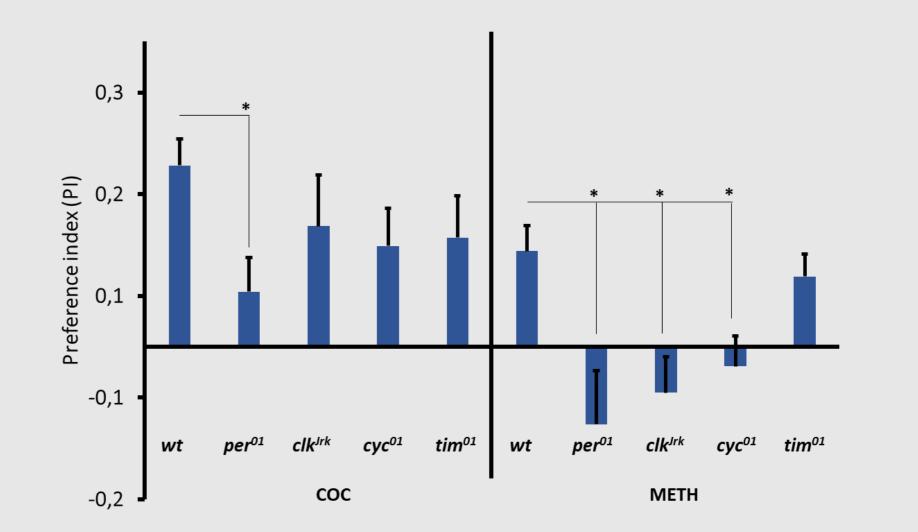


preferential consumption of COC and METH in spite of added bitter taste



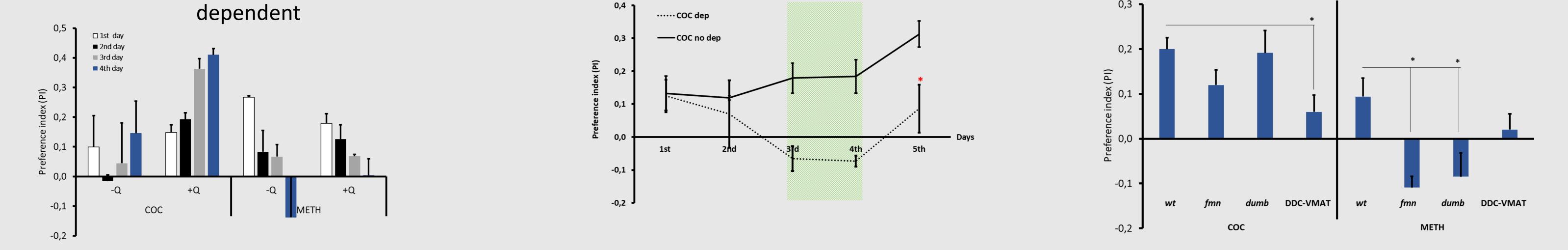
same preferential consumption of COC after two days of deprivation

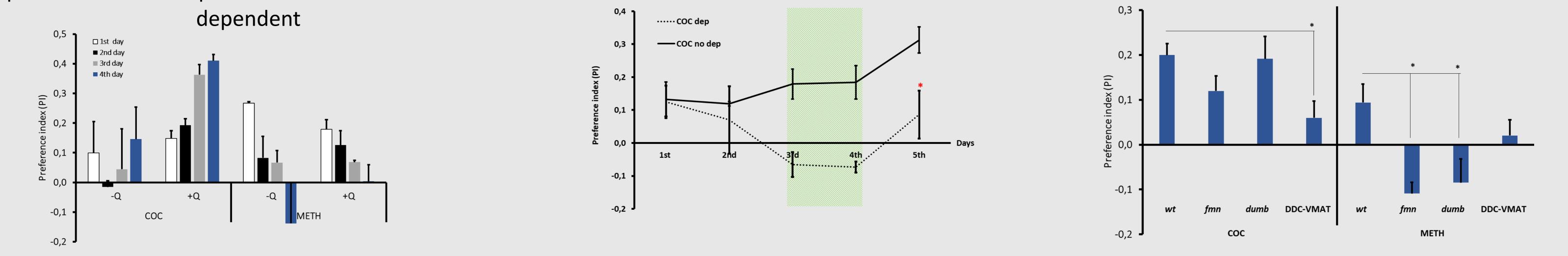
Clk and cyc gene, while for COC it depends on per

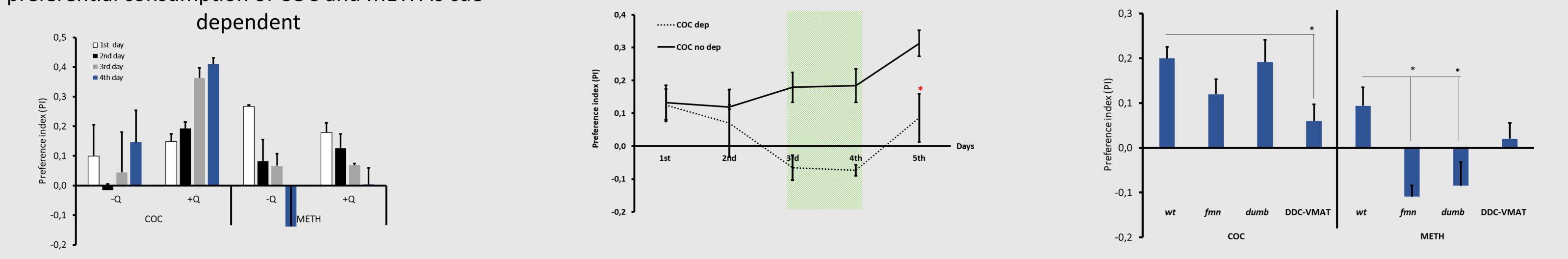


preferential consumption of COC depends on VMAT in DDC neurons, and METH depends on DAT and DA1R

preferential consumption of COC and METH is cue-







Conclusion

- Drosophila shows difference in preferential consumption of COC and METH suggesting mechanistic difference of action on motivational circuits.
- Dependence of preferential consumption on cue and location suggests inflexibility of behavior and/or involvement of mechanisms of learning and memory.
- Flies overcome bitter taste of quinine to self-administer COC and METH. 3
- Different circadian genes and components of monoaminergic signaling are involved in preferential consumption for COC and METH. 4
- These data show that self-administration can be studied in Drosophila. COC and METH act on neuronal circuit controlling motivation for consumption of drugs. 5 Neural mechanism underlying drug taking can be dissected in *Drosophila* using many genetic tools available in this model organism.

AUTHORS DECLARE NO CONFLICT OF INTEREST