Abstract

Roles of $GABA_B$, Muscarinic and Nicotinic Receptor Signaling in the Acquisition and Expression of Fructose and Fat-Conditioned Flavor Preferences and Acquisition of Quinine-Conditioned Flavor Avoidances in Rats.

By

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In addition to increased intake of sweet solutions by mammals, learning, particularly classically-conditioned Pavlovian learning, also plays an important role. An orosensory conditioned flavor preference (CFP) can be elicited by pairing one novel flavor (conditioned stimulus, CS+) with a fructose solution and a second novel flavor (CS-) with a saccharin solution. Rats will prefer the CS+ flavor in a subsequent 2-bottle choice test with both flavors mixed in saccharin. Previous pharmacological analyses revealed that systemic administration of dopamine (DA) D1 and D2 as well as NMDA, but not opioid, receptor antagonists eliminated the acquisition (learning) of fructose-CFP. Further, expression of an already-acquired fructose-CFP was significantly reduced by systemic DA D1 or D2, but not NMDA or opioid receptor antagonists. This dissertation research extended the pharmacological substrates of fructose-CFP by examining whether systemic administration of muscarinic (scopolamine: SCOP) and nicotinic (mecamylamine: MEC) cholinergic receptor antagonists, or a $GABA_B$ receptor agonist (baclofen: BAC) affected the learning and maintenance of fructose-CFP. Whereas fructose-CFP acquisition was eliminated by SCOP, but not MEC or BAC, fructose-CFP expression was only marginally reduced by SCOP, MEC and BAC.

In addition to sugars, fats can also elicit CFP by pairing two novel flavors with different concentrations (e.g., 3.5% and 0.9%) of corn oil (CO). Previous studies indicated that acquisition of CO-CFP was eliminated by NMDA recptor antagonistm, it was significantly reduced by DA D1 and D2, but not opioid receptor antagonists. Expression of CO-CFP was mildly reduced by DA D1, DA D2, NMDA or opioid receptor antagonists. In similar fashion, the effects of SCOP, MEC and BAC were evaluated upon acquisition and expression of CO-CFP. Interestingly, a similar pattern of results emerged for fat-CFP as was found for fructose-CFP. Thus, whereas CO-CFP acquisition was eliminated by SCOP, but not MEC or BAC, CO-CFP expression was significantly but marginally reduced by SCOP, MEC and BAC.

In addition to learned preferences, a conditioned flavor avoidance (CFA) can be produced by pairing a CS+ flavor with the bitter taste of quinine. The present studies evaluated whether fructose-CFP, CO-CFP and quinine-CFA share common neurochemical substrates by determining the systemic effects of DA D1 (SCH23390: SCH), DA D2 (raclopride: RAC), NMDA (MK-801), opioid (naltrexone: NTX), muscarinic (mAch: SCOP) or nicotinic (nAch: MEC) receptor antagonists as well as $GABA_B$ (BAC) agonists on the acquisition of quinine-CFA. We first demonstrated that DA D1, NMDA and opioid, but not DA D2 receptor antagonism enhanced the CFA produced by the bitter taste of quinine, and then subsequently found that whereas MEC and BAC enhanced this avoidance, SCOP failed to alter quinine-CFA.

Therefore, this dissertation demonstrated the differential involvement of major neurotransmitter systems in two forms of preference-based and one form of avoidance-based learning. Accordingly, whereas the acquisition of sugar- and fat-preferences is

primarily mediated by DA D1, DA D2, NMDA and mAch receptors, and their expression is primarily mediated by DA D1, DA D2, mAch and nAch receptors, the acquisition of quinine-avoidance is primarily mediated by DA D1, NMDA, opioid, nAch and $GABA_B$ receptors.