SY40-3
MGLUR5 POSITIVE ALLOSTERIC MODULATORS: PRECLINICAL EVIDENCE FOR PRO-COGNITIVE EFFECTS IN ALCOHOL AND COCAINE ADDICTION
M. F. Olive¹, J. T. Gass² and P. R. Kufahl¹
¹Psychology, Arizona State University, USA and ²Medical University of South Carolina

Introduction. mGluR5 positive allosteric modulators (PAMs) facilitate hippocampal synaptic plasticity and reverse NMDA antagonist-induced cognitive deficits. We sought to determine the effects of mGluR5 PAMs on extinction learning, the reinstatement of drug-seeking, and synaptic plasticity in the prelimbic (PrL) and infralimbic (IfL) cortex.

Method. The effects of the mGluR5 PAM CDPPB (10–30 mg/kg) on extinction responding following self-administration (SA) of either alcohol, cocaine, or methamphetamine was examined in rats. We also tested the effects of CDPPB on the reinstatement of alcohol-seeking, and potential mediation of any effects by the PrL and IfL. Finally, we assessed the effects of CDPPB alone and or in combination with extinction on dendritic spine density, morphology, and AMPA-mediated transmission in the PrL and IfL.

Results. CDPPB reduced extinction responding following alcohol or cocaine SA, but had minimal effects on extinction following methamphetamine SA. CDPPB prevented cue-induced reinstatement of alcohol-seeking, and these effects were reversed by mGluR5 antagonism in the IfL. CDPPB selectively increased IfL AMPA-mediated transmission, dendritic spine density, and spine maturity.

Conclusion. mGluR5 PAMs facilitate extinction learning and produce adaptive plasticity in the IfL, and therefore may represent a novel class of pro-cognitive compounds for possible use in the treatment of substance use disorders.