MICHAEL D BERQUIST, Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences College of Medicine, Little Rock, AR, 72205, MITCHELL R MCGILL, Department of Environmental and Occupational Health, University of Arkansas for Medical Sciences Fay W. Boozman College of Public Health, Little Rock, AR, 72205, ANNA MAZUR, Department of Biomedical Sciences, Marshall University School of Medicine, Huntington, WV, 25755, DAVID L FINDLEY, Department of Pharmaceutical Science and Research, Marshall University School of Pharmacy, Huntington, WV, 25701, GREG GORMAN, Department of Pharmaceutical, Social and Administrative Sciences, Samford University McWhorter School of Pharmacy, Birmingham, AL, 35229, CYNTHIA B JONES, Department of Pharmaceutical Science and Research, Marshall University School of Pharmacy, Huntington, WV, 25701, and MICHAEL D HAMBUCHEN, Department of Pharmaceutical Science and Research, Marshall University School of Pharmacy, Huntington, WV, 25701. Liver dysfunction effects on methamphetamine pharmacokinetics in male and female rats.

Disease states such as hepatitis C and HIV are both associated with methamphetamine (METH) use and are known to produce liver dysfunction. Indeed, bile duct ligation (BDL)-induced liver dysfunction enhances METH effects in rats. While female rats are more sensitive to METH, male rats are more prone to BDL-induced liver damage. The objective of this study was to determine if BDL disproportionately affects METH pharmacokinetics in male compared to female rats.

On day 0, sham or BDL surgery was performed on male and female rats. On day 7, serum biomarker samples were collected prior to pharmacokinetics studies with 3 mg/kg subcutaneous METH. METH-induced weight loss was measured on day 8. On day 9, samples were collected for liver histology and brain METH concentration measurement.

While BDL surgery produced significantly elevated alanine aminotransferase and bile duct proliferation in male versus female rats, there were no significant interactions between sex and liver function in the pharmacokinetic parameters. Both liver dysfunction and female sex, however, were associated with significantly slower serum METH clearance and higher brain METH concentrations ($p<.05$). While there were no sex-dependent differences, there was a significant reduction in post-METH weight in BDL compared to sham animals ($p<.05$).

BDL-induced hepatic dysfunction produces substantial elevations in serum and brain METH exposure in both male and female rats. This inexpensive model could potentially be used to find and correct liver dysfunction-related issues with future METH use disorder medications prior to expensive clinical trials. Funding: Marshall University School of Pharmacy Faculty Research Seed Grant.