Development of a DSM-V Porcine Model of Alcohol Use Disorder

Xiaobo Liu1,3, Ana Gutierrez2,5, Joshua O. Willms1,3, Brittany Backus4, Jackson Driskill2,5, Jordan Sanchez2,5, Praneetha Panthagani1,3, Angelica L. Rodriguez3, Jeremy D. Bailo2 and Susan E. Bergeson2

1Department of Pharmacology & Neuroscience, School of Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas; 2Department of Cell Biology & Biochemistry, School of Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas; 3Graduate School of Biomedical Science, Texas Tech University Health Sciences Center, Lubbock, Texas; 4Department of Animal & Food Science, Texas Tech University, Lubbock, Texas; 5Department of Biological Sciences, Texas Tech University, Lubbock, Texas

Introduction

AUD severity is significantly higher for equivalent exposure in females and generally develops over a shorter time than for men.

- AUD is a complex disorder and consequently, existing therapeutics are variable in their efficacy.
- Research into AUD has predominantly used rodent models.
- Before clinical trials can be performed in humans, the Food and Drug Administration requires that safety and efficacy is evaluated in another mammalian animal (the animal rule).

Pigs are a logical and tractable mammalian species for such investigations given their biological and physiological similarities to humans.

Preliminary Data

![Figure 1. Svine metabolize ethanol similarly to humans while mice metabolism is about 10-20 times faster than humans or other. The blue line was generated from our farm pig data, the green line is styled mammalian human ethanol metabolism, and the orange line is isosteric murex ethanol from literature.](image)

![Figure 2. The farm pigs reached intoxication, free-choice binge drinking levels and showed a strong preference for ethanol solution over water.](image)

Animal & Design

![Figure 3. (A) Miniature swine for model development. (B) Two-Bucket Choice setup.](image)

Methods & Results

DSM-V Diagnosis:

Mild AUD: 2 to 3 Symptoms; Moderate AUD: 4 to 5 symptoms; Severe AUD: 26 symptoms.

![Table 1. The DSM-V criteria for diagnosis of AUD. We tested 7 criteria, and out of those 7 criteria, all pigs presented with moderate AUD. If any of the pigs met 1 out of the remaining 4 criteria, they would be classified as severe AUD. Together, our results highlight this novel pig AUD model is exciting avenue for the investigation of therapeutic strategies (* = meets criteria, ≠ does not meet criteria, TBD = to be done). Moderate AUD using tools to measure DSM-V criteria.](table)

1. Drinks larger amounts of alcohol than intended.

2. Difficulty controlling drinking.

3. Spends a considerable amount of time drinking or recovering from drinking.


5. Fails to fulfill major roles/obligations due to alcohol use.

6. Continued alcohol use despite having persistence/recurrent social or interpersonal problems.

7. Recreational activity is given up or reduced because of alcohol use.

8. Alcohol use in physically hazardous situations.


10. Development of pharmacokinetic/pharmacodynamics tolerance to alcohol.

Pharmacokinetic tolerance will be measured following a 1.5 g/kg dose of alcohol given by gavage of 15% ethanol in water. Blood samples will be taken in intervals throughout 24 hours and analyzed for blood ethanol concentration.

Pharmacodynamics tolerance will be evaluated by the ability test described in (4). We hypothesized that the performance of the task will improve once it developed. (No pig met criteria.)

11. Experiencing withdrawal symptoms when drinking is stopped.

Discussion

To date, all 5 pigs have been evaluated on 7 of the 11 DSM-V criteria for an AUD diagnosis in humans; a full severity assessment will be completed when the other 4 criteria are performed. Thus far, however, all 5 pigs satisfy the criteria for moderate AUD (4 to 5 symptoms of 11). These results highlight that mini-pigs can develop significant AUD when given free-choice alcohol exposure. Thus, the minipig may be an improved translationally relevant model species over rodents for pre-clinical evaluation of therapeutic strategies for AUD.

Acknowledgements

Supported by the Laura W. Bush Institute of Women’s Health, Kayla Weitlauf Endowment for Women’s Health and NIH AA027491 (SEB).