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RECENT ADVANCES IN EVALUATION OF ALCOHOLISM IN RODENTS - A REVIEW

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ABSTRACT

Rodent models remain central to mechanistic studies of alcohol use disorder (AUD). Over the last decade major methodological advances -refinements of voluntary intake paradigms (intermittent access two-bottle choice, drinking-in-the-dark), dependence induction (chronic intermittent ethanol vapor and newer voluntary vapor paradigms), and operant self-administration — have improved face and construct validity. Parallel technological progress (optogenetics, chemo genetics/DREADDs, fibre photometry, in vivo calcium imaging, and single-cell transcriptomics) now allows circuit- and cell-type-specific evaluation of alcohol drinking, withdrawal, and relapse-like behaviours. Emerging evidence also highlights the role of neuroimmune signalling and the gut microbiome in modulating alcohol intake and related behaviours, opening new biomarker and interventional avenues. This review synthesizes recent methodological and conceptual advances and discusses limitations and translational considerations.

Introduction:

Alcohol use disorder is a multifaceted pathology involving motivational, affective, cognitive, and somatic processes. Rodent models are indispensable for dissecting causal mechanisms and for preclinical evaluation of potential therapeutics. Recent years have seen both refinements to classical behavioural paradigms and the adoption of powerful neuroscience tools that permit temporally precise and cell-type specific manipulation and measurement during drinking, withdrawal, and relapse. This review focuses on advances since ~2018 that enhance evaluation of alcoholism-relevant phenotypes in rodents. (V. Vierkant 2023)

1. Behavioural and Exposure Models

1.1 Voluntary intake paradigms: Intermittent Access Two-Bottle Choice (IA2BC)

IA2BC (typically intermittent access to 20% ethanol on alternating days) remains a popular model for escalation of voluntary intake and captures aspects of compulsion and escalation. Recent studies have refined classification of intake subgroups, improved analytic approaches, and validated IA2BC across strains, sexes, and species to better model human heterogeneity in drinking trajectories. Protocol standardization and improved statistical classification enhance reproducibility and interpretation. (D Peregud, 2021).

1.2 Binge-like models: Drinking-in-the-Dark (DID) and HDID lines

The DID paradigm produces binge-level blood ethanol concentrations in mice and has been extended by selectively-bred High Drinking in the Dark (HDID) lines and procedural variants to increase reproducibility and permit genetic dissection of binge propensity. Procedural variants (duration, ethanol concentration, housing conditions) and long-term characterizations of HDID mice have clarified strengths/limitations for modeling human binge drinking. (TE Thiele, 2014).

1.3 Dependence induction: Chronic Intermittent Ethanol (CIE) vapor and voluntary vapor models

CIE vapor exposure paired with withdrawal cycles remains the gold standard for producing physiological dependence and escalated intake; however, it is a forced-exposure model. Newer approaches (e.g., ethanol-vapor self-administration, hybrid voluntary+vapor methods) aim to model voluntary transition to dependence while capturing clinically relevant blood ethanol levels. These voluntary vapor paradigms improve ethological validity and bridge gaps between forced exposure models and voluntary human drinking. (T Xiao 2023).

1.4 Operant self-administration and advanced reinforcement schedules

Operant paradigms (fixed ratio, progressive ratio, punishment-resistant responding) are increasingly used to index motivational aspects and compulsive-like alcohol seeking. Combined with individual phenotyping and escalation paradigms, operant models permit the study of relapse-like behaviors (reinstatement, cue/context-induced relapse) under precise contingency control. (V. Vierkant 2023).

2. Behavioral phenotyping beyond intake: withdrawal, affect, cognition, and relapse

Contemporary evaluation routinely pairs intake measures with assays for withdrawal severity, anxiety-/depressive-like behavior, decision-making, and cognitive flexibility. Automated home-cage monitoring and refined behavioral batteries quantify intoxication/withdrawal phenotypes and identify latent subgroups (e.g., high-intake but low-withdrawal vs. high-withdrawal phenotypes). Relapse models (stress-, cue-, drug-primed reinstatement) remain central; recent work emphasizes multi-domain phenotyping to map individual risk profiles. (AMC Ho 2022).

3. Circuit and Cell-Type Tools -Precision Modulation and Measurement

3.1 Optogenetics and chemogenetics (DREADDs)

Optogenetics enables millisecond-scale control of defined projections and has been applied to dissect striatal, amygdala, and VTA circuits mediating alcohol seeking, extinction, and reinstatement. Chemogenetic approaches (DREADDs) provide longer-timescale manipulations useful during drinking sessions or prolonged withdrawal. Both techniques have moved from proof-of-principle studies to systematic circuit mapping in AUD-relevant behaviors. (V Vierkant 2024).

3.2 In vivo recording: fiber photometry, miniature microscopes, and calcium imaging

Fiber photometry and miniature head-mounted microscopes (miniscopes) allow real-time recordings of genetically defined neuronal populations during voluntary alcohol intake, operant responding, and relapse. Protocol improvements (wireless, dual-color photometry, synchronized video) and analytic pipelines enable linking neuronal dynamics to discrete drinking events and motivational states. These tools have revealed trial-by-trial neural correlates of consumption and cue-evoked craving.(M Kielbinski, 2024).

3.3 Integration of manipulation and monitoring

Combining opto/chemogenetic perturbations with fiber photometry or electrophysiology permits causal tests of circuit function while simultaneously reading out network changes — a major methodological advance for mechanistic AUD studies. Examples include projection-specific inhibition to suppress alcohol seeking and simultaneous recording of dopamine/neuronal population signals during reinstatement. (V Vierkant 2024).

4. Molecular and Cellular Advances: Transcriptomics, Epigenetics, and Single-Cell Methods

Single-cell and bulk transcriptomics, epigenomic profiling, and proteomics applied to alcohol-exposed brains have identified cell-type specific transcriptional signatures of chronic exposure, withdrawal, and relapse vulnerability. These approaches facilitate identification of molecular targets (in microglia, astrocytes, and specific neuronal subtypes) and have been combined with viral targeting to test causality. As datasets accumulate, cross-study integration is improving translational target selection. (V Vierkant, 2023)

5. Neuroimmune Signaling and the Gut-Brain Axis: Emerging Evaluative Domains

A rapidly growing literature implicates neuroimmune activation (microglial phenotypes, cytokine signaling) and gut microbiome alterations in the development and maintenance of alcohol-related behaviors. Preclinical manipulations — anti-inflammatory agents, microbiome alteration (antibiotics, fecal transplants, microbial metabolites like short-chain fatty acids) — modulate drinking and relapse-like behavior, suggesting both mechanistic roles and therapeutic potential. Integration of microbiome, peripheral immune, and central inflammatory readouts is now recommended for comprehensive evaluation. (EK Grantham, 2022)

6. Sex as a Biological Variable And Individualized Phenotypes

Sex differences in ethanol intake, sensitivity, and neurobiological responses are now robustly documented across paradigms. Recent work underscores the importance of including both sexes, reporting cycle/estrus data in females when relevant, and analyzing sex-by-treatment interactions. Additionally, latent class and individual-level classification approaches help identify high-risk phenotypes that traditional group-mean analyses can obscure. (D Peregud,2021)

7. Refinements in Experimental Design, Analytics, And Reproducibility

Community efforts have focused on protocol standardization (detailed procedural descriptions for IA2BC, DID, CIE, and operant protocols), improved blood ethanol concentration (BEC) monitoring, continuous home-cage monitoring, and advanced statistical approaches (latent class modelling, mixed effects). These refinements increase replicability and facilitate cross-lab comparisons. Open-data and standardized pipelines for photometry and imaging analysis are likewise improving reproducibility. (Shikun Hou, 2024)

8. Limitations and Translational Caveats

Despite methodological progress, rodent models cannot fully recapitulate human AUD complexity (sociocultural drivers, long human lifespan, polysubstance use). Forced-exposure dependence models (e.g., CIE) differ from human voluntary intake, and strain/species differences complicate generalization. Careful selection of model, use of multiple convergent paradigms, and attention to sex and individual variability improve translational relevance. The field is also grappling with how best to translate circuit-level findings to human treatments. (T Xiao, 2023)

9. Future Directions

Priority areas include: (1) further development of voluntary induction models of dependence to parallel human trajectories, (2) multi-omic integration (single-cell transcriptomics + epigenetics + proteomics) across time courses of exposure and withdrawal, (3) mechanistic studies linking microbiome metabolites to neural circuit function, (4) greater use of longitudinal, automated home-cage phenotyping to capture naturalistic drinking trajectories, and (5) translation of targetable neuroimmune mechanisms into early-phase clinical testing. Continued methodological standardization and data sharing will accelerate progress. (G de Guglielmo, 2023)

Conclusions:

Recent advances in behavioral paradigms, circuit-level tools, molecular profiling, and appreciation of neuroimmune/gut-brain interactions have substantially expanded the toolkit for evaluating alcoholism in rodents. Combining rigorous behavioral phenotyping with modern manipulation and recording methods yields nuanced, mechanistically-informative models of AUD. Thoughtful experimental design, inclusion of

sex and individual variability, and translationally oriented paradigms will maximize the preclinical contributions to developing new therapies.

References

1. Carnicella, Sebastien, Dorit Ron, and Segev Barak. "Intermittent ethanol access schedule in rats as a preclinical model of alcohol abuse." *Alcohol* 48, no. 3 (2014): 243-252.
2. Szabo, Gyongyi, and Pranoti Mandrekar. "A recent perspective on alcohol, immunity, and host defense." *Alcoholism: Clinical and Experimental Research* 33, no. 2 (2009): 220-232.
3. Cohen, Ami, George F. Koob, and Olivier George. "Robust escalation of nicotine intake with extended access to nicotine self-administration and intermittent periods of abstinence." *Neuropsychopharmacology* 37, no. 9 (2012): 2153-2160.
4. Holgate, Joan Y., Masroor Shariff, Erica WH Mu, and Selena Bartlett. "A rat drinking in the dark model for studying ethanol and sucrose consumption." *Frontiers in behavioral neuroscience* 11 (2017): 29.
5. Olsen, Richard W., and Jing Liang. "Role of GABAA receptors in alcohol use disorders suggested by chronic intermittent ethanol (CIE) rodent model." *Molecular Brain* 10, no. 1 (2017): 45.
6. Simms, Jeffrey A., Pia Steensland, Brian Medina, Kenneth E. Abernathy, L. Judson Chandler, Roy Wise, and Selena E. Bartlett. "Intermittent access to 20% ethanol induces high ethanol consumption in Long–Evans and Wistar rats." *Alcoholism: Clinical and Experimental Research* 32, no. 10 (2008): 1816-1823.
7. Sprow, Gretchen M., and Todd E. Thiele. "The neurobiology of binge-like ethanol drinking: evidence from rodent models." *Physiology & behavior* 106, no. 3 (2012): 325-331.
8. Holgate, Joan Y., Masroor Shariff, Erica WH Mu, and Selena Bartlett. "A rat drinking in the dark model for studying ethanol and sucrose consumption." *Frontiers in behavioral neuroscience* 11 (2017): 29.
9. KEANE, BERNADETTE, and B. E. Leonard. "Rodent models of alcoholism: a review." *Alcohol and Alcoholism* 24, no. 4 (1989): 299-309.

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