



MEDICINE
TEXAS A&M HEALTH SCIENCE CENTER

Beyond Maternal Factors: The Overlooked Role of Fathers in FASD

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Historical Neglect of Paternal Contributions to FASD



1918

Stockard & Papanicolaou, 1st
Experimental Report (guinea pigs)



20th Century

Maternal-only focus following
1973 clinical description of FASD



Early 2000s

Paternal interest grows



Early Paternal Alcohol Findings

- 1 Birth Metrics
- 2 Organ Development
- 3 Neurological and Hormonal Changes
- 4 Behavioral Phenotypes
- 5 FASD-Like Outcomes

Evidence from Other Paternal Exposures



Chronic Stress

Stress → offspring stress reactivity



Diet

Poor diet → metabolism & weight problems



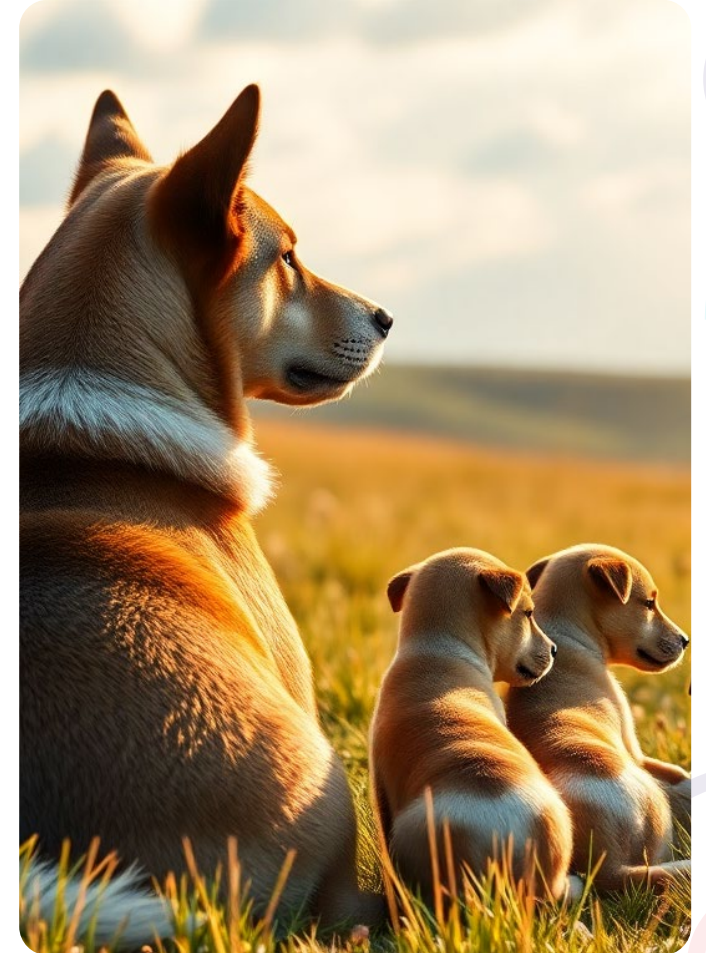
Pollutants

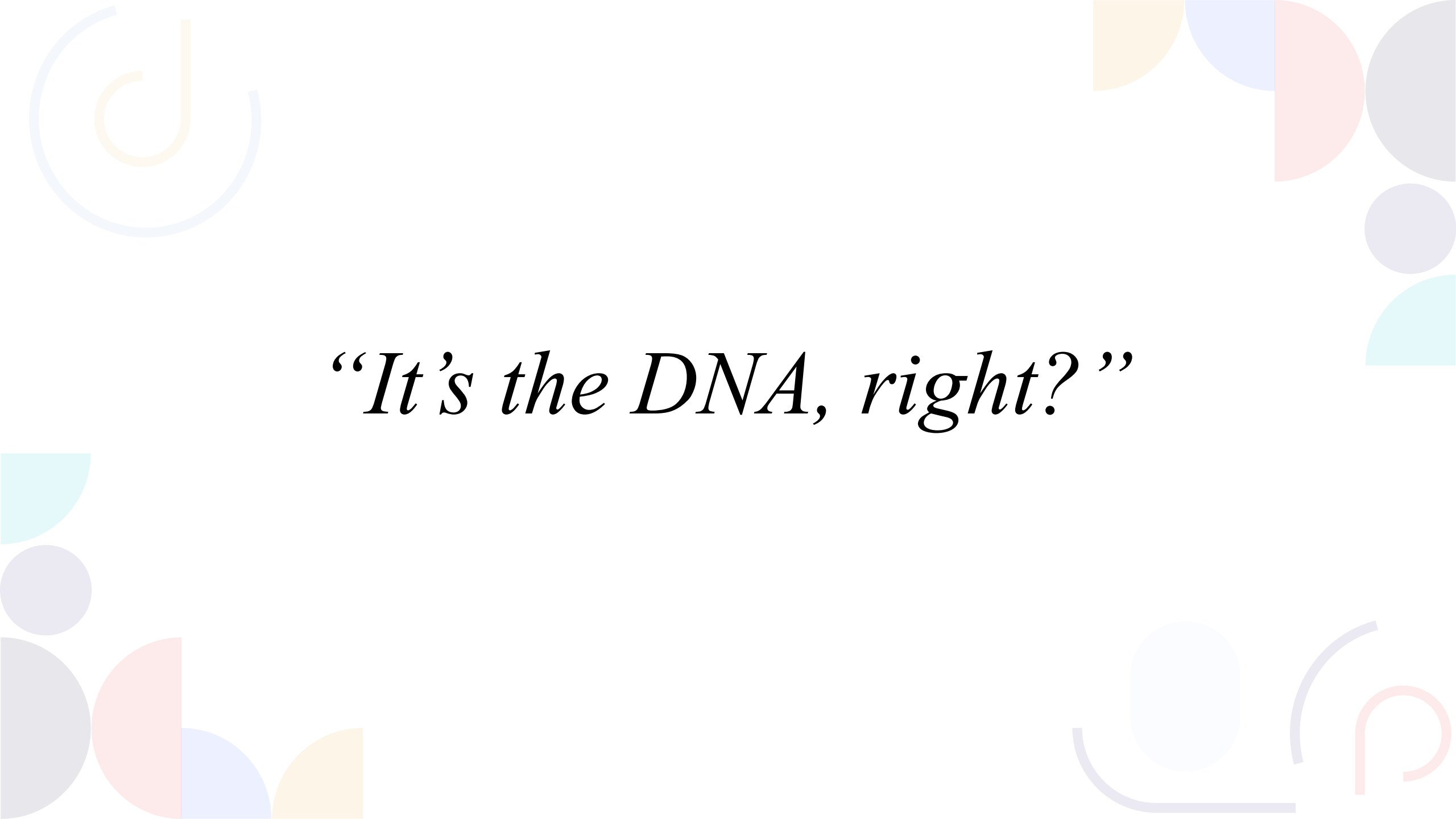
Pesticides & air pollution → altered brain development.



Substance Use

Drugs (e.g., cocaine, nicotine) → behavior & reward pathways



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“It’s the DNA, right?”

The 'Missing Heritability' Problem

Heritability Estimate for AUD

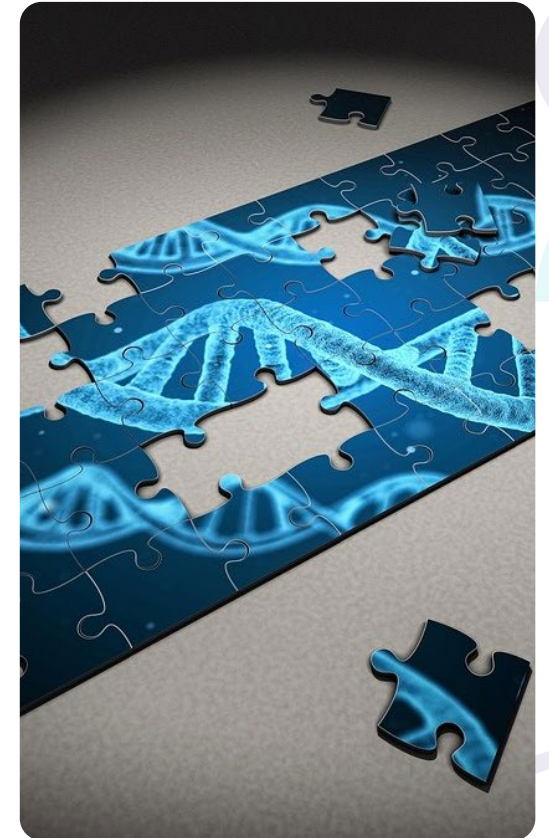
Twin and adoption studies estimate alcohol use disorder (AUD) heritability at ~50%.

GWAS Findings on AUD

Genome-wide association studies (GWAS) account for < 1% of this heritability.

The Concept of Missing Heritability

There must be other mechanisms beyond DNA sequence variation that contribute to familial AUD risk.





Sperm Carry More than DNA



Chemical “tags” on genes

DNA methylation determines when and where genes are turned “on” or “off”.



Proteins that “hang out” with DNA

Up to 10% of histones in human sperm are passed to offspring.



Small (but mighty!) RNAs

Tiny RNA can control which genes are turned “on” or “off” during the first few days after fertilization.

RESEARCH ARTICLE · Volume 67, Issue 1, P105-113, July 2024 · *Open Access*

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Paternal Preconceptional Alcohol Use Disorder With the Offspring's Mortality Risk

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[Affiliations & Notes](#)  [Article Info](#) 

- **Nationwide Danish study**
- **2 million births (1980-2012)**
- **Father with AUD *before* conception**

**Increased Odds of
Stillbirth**

23%

**Higher Infant
Mortality Risk**

23%

**Elevated Mortality
After First Year**

28%

Impact of Timing on Offspring Mortality



- **Timing of AUD diagnosis *does* matter**
- **AUD <1 year before conception → greatest risk**
- **85–111% higher mortality ages 15–40**
- **↑ deaths from infections & circulatory disease**

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RESEARCH ARTICLE



Does paternal alcohol consumption affect the severity of traits of fetal alcohol spectrum disorders?

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J. Phillip Gossage² | Wendy O. Kalberg² | Marlene De Vries³ | Luther K. Robinson⁴ |
David Buckley² | Melanie Manning^{5,6} | Charles D. H. Parry^{2,7}  | H. Eugene Hoyme⁸ |
Barbara Tabachnick⁹ | Soraya Seedat³

Paternal Drinking Patterns

Fathers of Children with FASD

- Drank alcohol during pregnancy: **73%**
- Average 12oz drinks per session: **11.5**
- A higher prevalence of reported past and current drinking problems.

Fathers of Unexposed Controls

- Drank alcohol during pregnancy: **48%**
- Average 12oz drinks per session: **8**
- Fewer reported past and current drinking problems.

Links to Child Outcomes

“Binge” Drinking

Paternal binge drinking is defined as consuming five or more drinks per occasion.

Physical Impacts on Children

Children of fathers who binge drink tend to be shorter in stature and have smaller head circumferences.

Cognitive Impacts on Children

These children score lower on verbal intelligence assessments.

Independent Influence of Paternal Drinking

The harmful effects persist even after accounting for maternal alcohol use and tobacco exposure.



The Risk Is Highest When Both Parents Drink



The most prominent effects were seen when alcohol exposure occurred through *both parents*.



ELSEVIER

Contents lists available at ScienceDirect

Alcohol

journal homepage: <http://www.alcoholjournal.org/>



Maternal, paternal, and dual-parental alcohol exposures result in both overlapping and distinct impacts on behavior in adolescent offspring

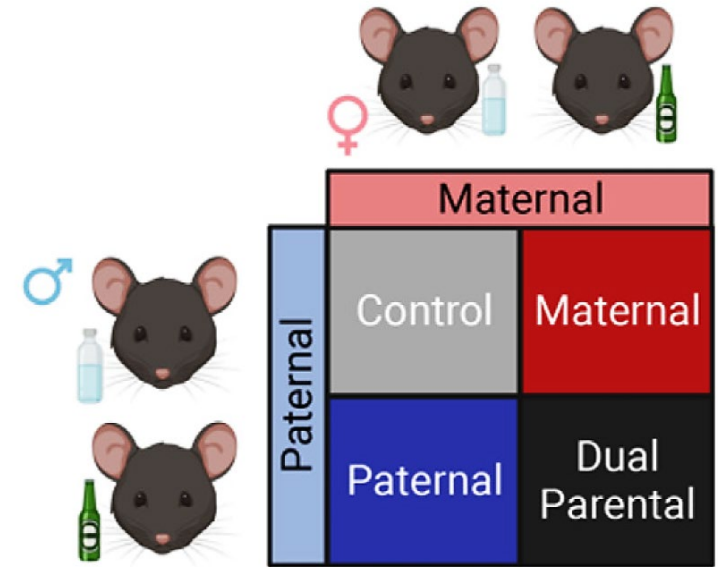


Kara N. Thomas^a, Alison Basel^a, Hayden Reitz^a, Rachel Toler^a, Kelly R. Thomas^a,
Luke J. Dotson^a, Tyler Brown^a, Alan Nguyen Pham^a, Siara K. Rouzer^b,
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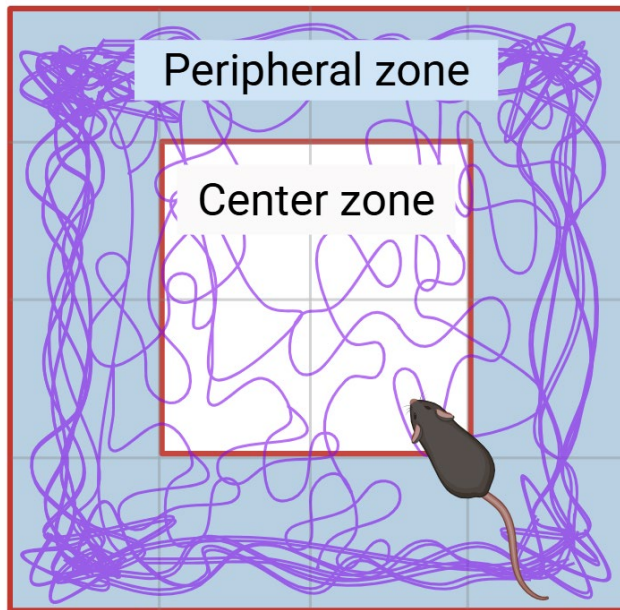
Modeling Dual-Parent Exposures in Mice

Alcohol Exposure: Voluntary Drinking

Goal: Test single vs **dual** exposure effects on adolescent offspring

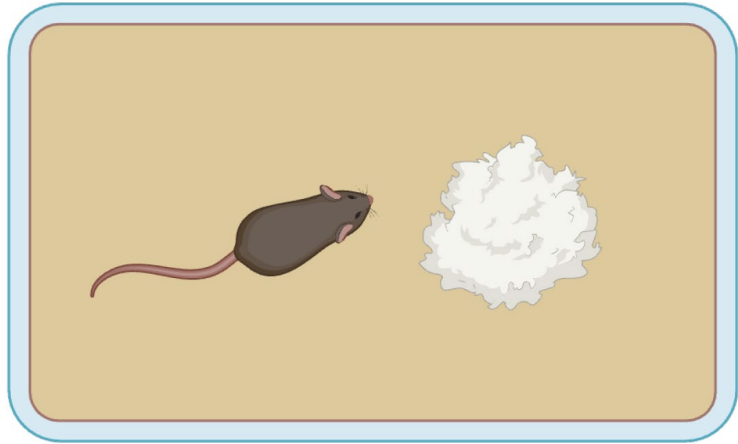


Anxiety-like Behavior (Open Field Test)



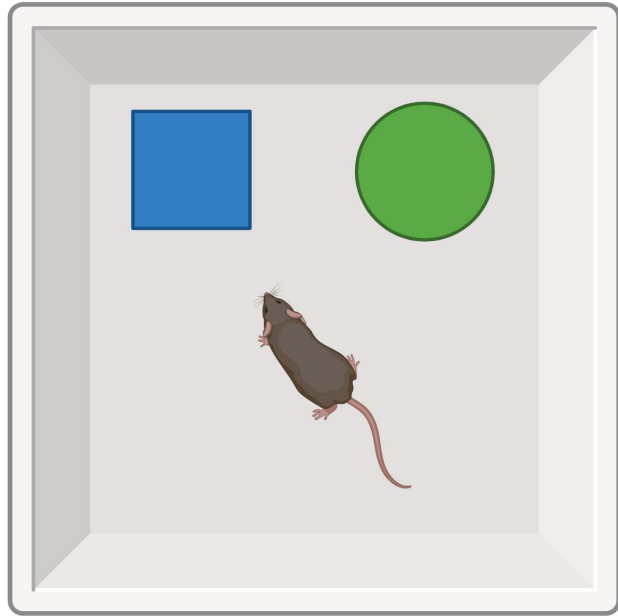
- **Males:** Paternal exposure → less anxious (more center time)
- **Females:** No change
- **Dual Exposure:** No distinct outcomes

Compulsive-like Behavior (Nestlet Shredding Test)



- **Males:** ↑ with Maternal; ↑ with Paternal
- **Females:** ↑ with Paternal
- **Dual Exposure:** No distinct outcomes

Risk-taking Behavior (Novel Object Preference)



- **Dual Exposure:** Both males and females prefer the novel object - controls preferred the familiar object

Activity Levels & Circadian Phasing (Running Wheel)



- **16 weeks of voluntary, monitored exercise**
- **Males:** Dual Exposure ↓ running activity, specifically during the nighttime (when mice are most active)
- **Females:** No effect of exposure

Of Mice & Men: Synergizing Research on Paternal Alcohol Exposure

- Human fathers with AUD → ↑ infant mortality, developmental problems
- Fathers' drinking → sperm changes → offspring brain & behavior
- Shared biological pathways?



Where Research Should Go Next



Study how alcohol alters
sperm epigenetics and
RNA content

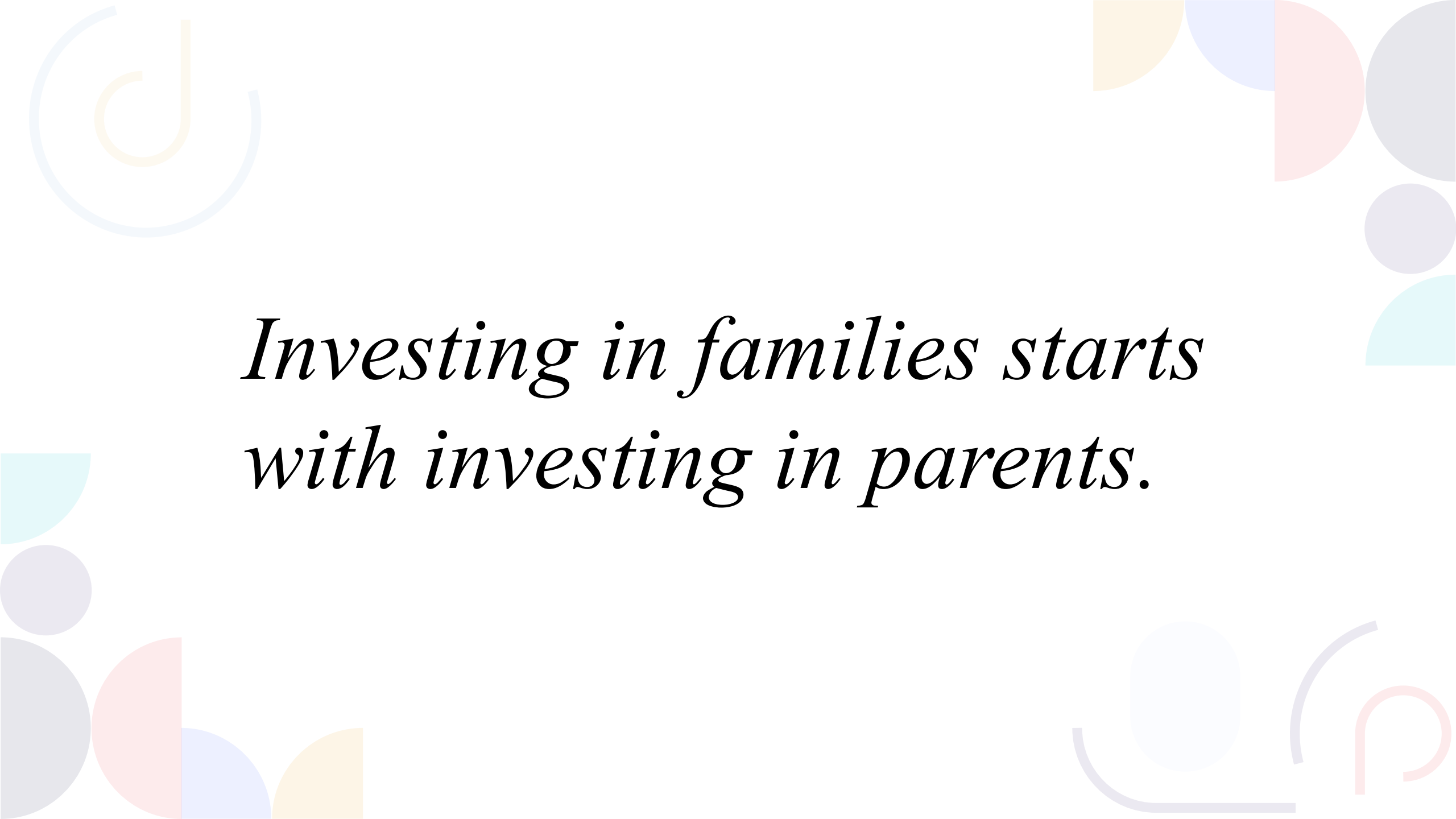


Longitudinally follow
children born to fathers
with alcohol exposure



Integrate paternal alcohol
use screening into FASD
risk assessments

We need more models that incorporate both parents.

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*Investing in families starts
with investing in parents.*

Thank you!

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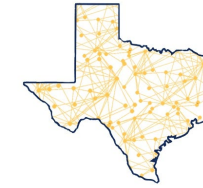
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