Exploring Sex Differences in Gonadal Phthalate Metabolizing Enzymes Expression and the Impact of Di-2-ethylhexyl Phthalate

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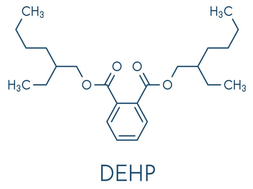
INTRODUCTION

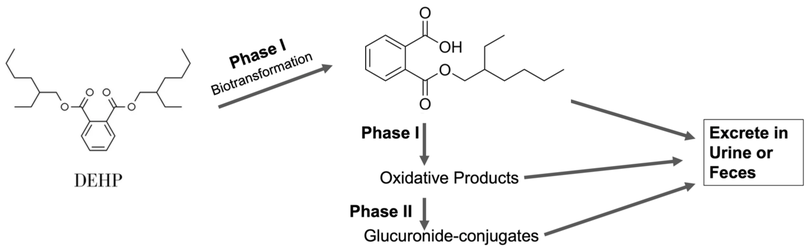
- Global infertility rates are rising, with approximately 68.6 million couples affected. Fertility treatments are not often covered by insurance and are cost-prohibitive for many infertile couples and can lead to decreased quality of life.
- Phthalates are chemicals commonly found in food packaging, cosmetics, and medical supplies (e.g., dialysis tubing).
- Di-2-ethylhexyl phthalate (DEHP), a common endocrine disruptor, has been linked to hormone regulation disruptions and germ cell development issues, potentially affecting fertility.



DEHP

OBJECTIVE

Are there sex-specific differences in key phthalate-metabolizing enzymes within the gonads, and how does DEHP influence these enzymes in male and female CD-1 mice?



METHODS

60-day-old female and male CD-1 mice (N=5)

DEHP or vehicle control pipette fed for 12 days (males) or 10-14 days (females)

Vehicle Control:
- Corn oil

DEHP Dosage:
- **20 µg/kg/day**
- **200 µg/kg/day**
- **1000 mg/kg/day**

Euthanized after final dose and gonads were collected (females euthanized in the proestrus/estrus stages)

1. **qPCR for metabolizing genes** (*Lpl*, *Adh1*, *Aldh1a1*, and *Cyp1b1*)
2. **Data analysis using GraphPad** (Student's t-test; One-Way ANOVA)

RESULTS

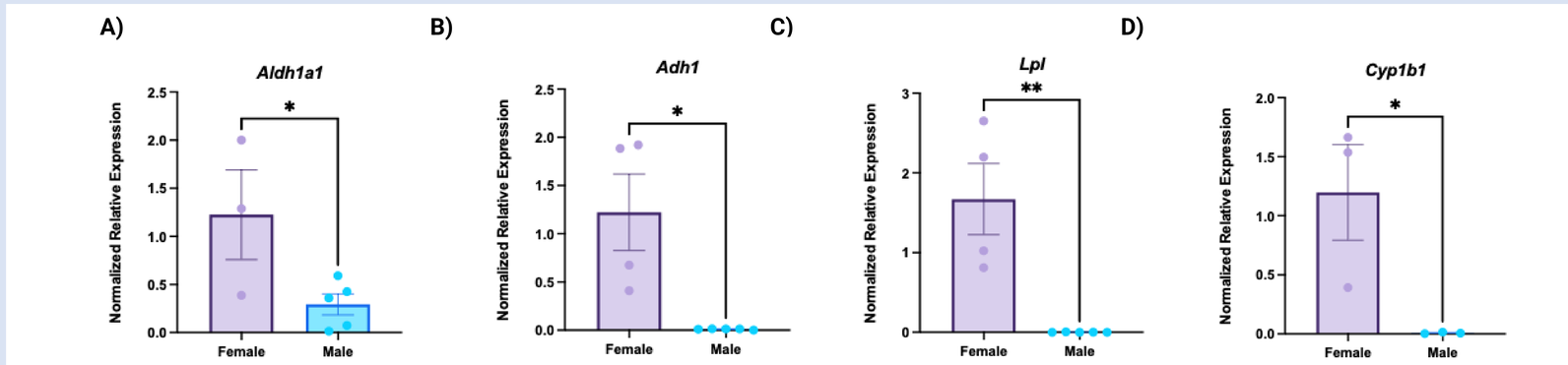


Fig. 1. Sex differences in the expression of phthalate metabolizing enzymes in the gonads. Expression of *Aldh1a1* (A), *Adh1* (B), *Lpl* (C), and *Cyp1b1* (D) were compared between the testis and ovary of adult control mice. Expressions were normalized to the housekeeping gene *Tbp.* Data are presented as mean normalized relative expression + SEM. Asterisks (*) indicates statistically significant (*p<0.05). Comparisons were made using Student's t-test (n=3-5).

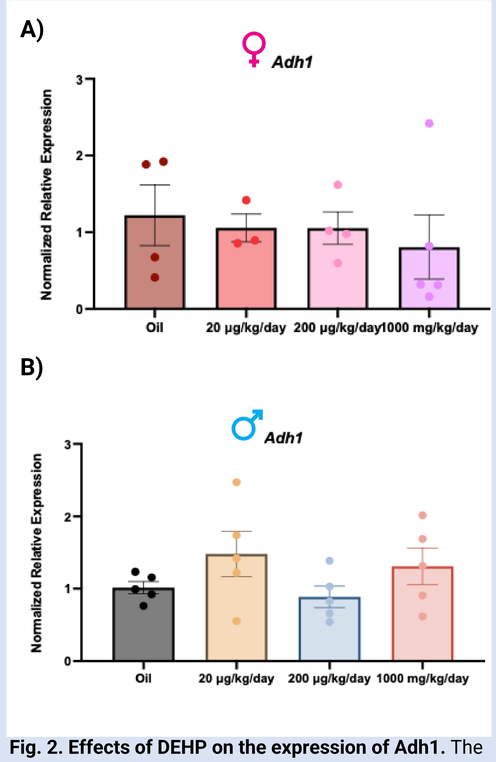


Fig. 2. Effects of DEHP on the expression of Adh1. The expressions of*Adh1* (A, B), in the testis and ovary were compared between DEHP-treated and control mice. Expressions were normalized to *Tbp*. Data are presented as mean normalized relative expression + SEM (n=3-5).

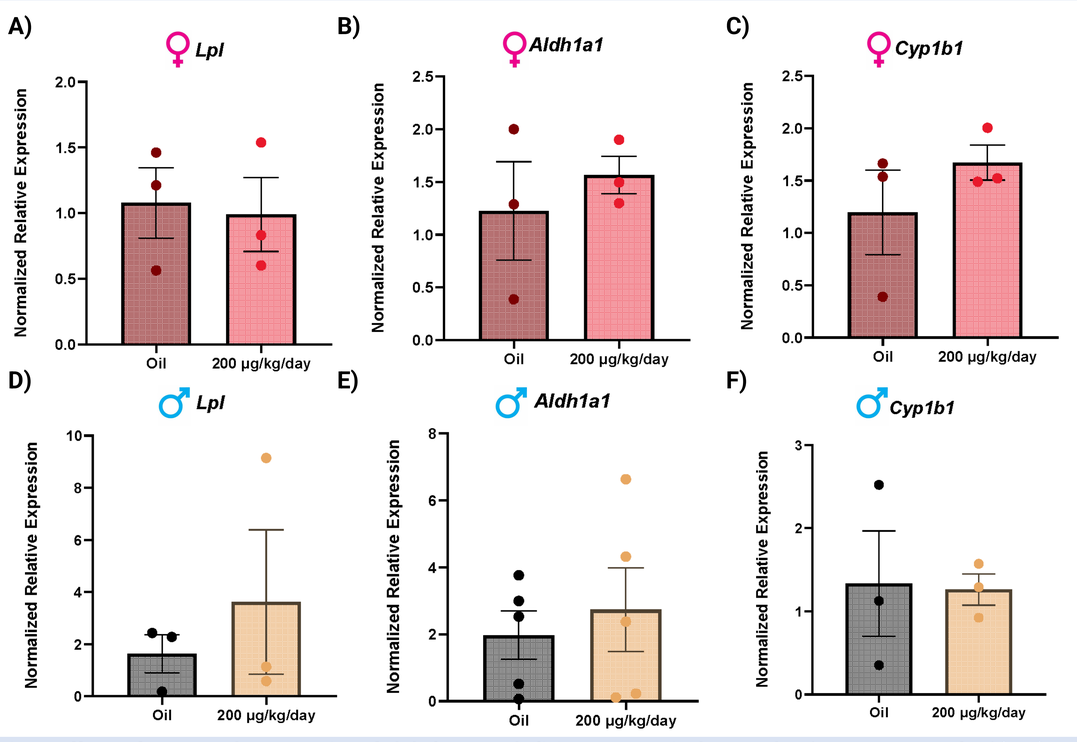


Fig. 3. Effects of DEHP on the expression of phthalate metabolizing enzymes in the gonads. The expressions of *Lpl* (A, D), *Aldh1a1* (B, E), and *Cyp1b1* (C, F) in the testis and ovary were compared between DEHP-treated and control mice. Expressions were normalized to the housekeeping gene *Tbp*. Data are presented as mean normalized relative expression + SEM (n=3-5).

CONCLUSION

Gene expression analysis revealed significant sex-specific differences in *Lpl, Adh1*, *Aldh1a1*, and *Cyp1b1*, with higher expression in the ovaries compared to the testes ($p < 0.05$). However, DEHP treatment did not significantly alter gene expression in either male or female gonads. These intrinsic sex differences in phthalate metabolism suggest distinct vulnerabilities to exposure, warranting further research into their impact on infertility and endocrine-related conditions.

ACKNOWLEDGEMENTS

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