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Transgenerational Effects of Endocrine Disrupting Chemical (Bisphenol A) on the Reproductive System of Male and Female Wistar Rats (*Rattus norvegicus*)

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ABSTRACT

Bisphenol A (BPA), a synthetic compound widely used in plastics and epoxy resins, is a prominent endocrine-disrupting chemical (EDC) with the ability to mimic endogenous hormones. Globally there are growing concerns abouth then long-term impact of BPA on reproduction, particularly its potential to induce transgenerational effects. This study assessed the effects of maternal BPA exposure on the reproductive systems of male and female Wistar rats across two generations. Pregnant dams (F0) received oral BPA during gestation and lactation. Their F1 and F2 offspring were evaluated for histopathological, morphological, and reproductive parameters. BPA exposure resulted in significant dose-dependent reproductive toxicity, including ovarian follicular atresia, irregular estrous cycles, reduced testicular weight, sperm density decline, and seminiferous tubule degeneration. Remarkably, certain reproductive alterations persisted into the F2 generation despite absence of direct exposure. These findings confirm that BPA can induce heritable reproductive impairments, underscoring serious implications for human health and intergenerational risk.

Keywords: Bisphenol A, endocrine disruptors, transgenerational toxicity, reproductive system, Wistar rats

INTRODUCTION

Endocrine disrupting chemicals (EDCs) are exogenous agents that can interfere with the synthesis, storage, release, transport, metabolism, binding, action, and elimination of endogenous hormones. Endocrine disrupting chemicals are encountered in everyday life as they are present in plastic food containers, water bottles, personal care products, air pollution, and pesticides. Substantial evidence shows that EDCs impact human and animal reproductive health as well as contribute to reproductive disorders [1]. The endocrine disrupting chemicals have transgenerational effects on male and female reproduction due to their interference in the normal functioning in the normal body's endocrine system. Bisphenol A is an endocrine disrupting chemical that interfere with the normal functioning of the endocrine system and the interference is transgenerational [2]. The endocrine system is a network of glands and organs that produce secrete and store hormones. The endocrine system works with other systems to regulate the normal body healthy development all through life. Hormones are the body's chemical messengers. They carry information and instructions from one set of cells to another [3]. In the female, EDCs are associated with subfertility, aberrations in the reproductive cycle, polycystic ovarian syndrome, endometriosis, and uterine fibroids [4]. In the male, EDCs have been implicated in male subfertility, cryptorchidism, and hypospadias [5]. While several studies have explored the direct effects of BPA on adult organisms, there remains a critical knowledge gap in understanding its transgenerational impacts. Essentially, there is need to understand the effects that are passed on not just to exposed individuals but to subsequent, unexposed generations. The major aim of this research is to determine the transgenerational effects of endocrine disrupting chemical (Bisphenol A) on male and female wistar rat reproductive system

MATERIALS AND METHODS

Ethical Considerations: Ethics committee approval was obtained from Ebonyi State University Ethical Committee of Faculty of Health Science and Technology. All the experiment followed the guidelines provided

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and were in tandem with the global Institutional Animal Care and Use. A period of five days were allowed for acclimitization. The rats were housed 3 rats per cage at controlled temperature of 25°C, humidity (60%), 12 h light/dark cylce. Standard rodent feed and water were given to them. The wistar rats were were allowed to fast overnight for 14 hours befre BPA dosing, water and feeding. Freshly prepared Bisphenol A (purity ≥ 98%) in solid form was dissolved in corn oil was administered via oral (gavage) to the 13 wister rats by dosing (i) 100 (ii) 1000 (iii) 2000 (iv) 3000 and (v) 5000 mg/kg per body weight.

Lethal Dose Toxicity (LD_{50}): Lethal Dose Toxicity (LD_{50}) test procedure for Bisphenol A was done following OECD test guidelines 423 (Acute oral Toxicity- acute Toxic cleass method).

Experimental chemicals: The Bisphenol A 99% standard were purchased from Punkinosis chemical company Limited (House 21, 41 Crescent Gwarimpa, Abuja FCT). The powder was dissolved in corn oil and orally administered to non-anesthetized rats via gavage

Experimental Protocol

Experimental Animal: The wistar rats used from this research were purchased from Animal House, University of Nigeria, Nsukka. A total of 40 adult Wistar rats (20 males and 20 females), aged 8–10 weeks and weighing 80–200g. The rats were bred in animal house of Faculty of Health Science and Technology, Ebonyi State University Abakalik, Nigeria and they were used in this study. All the rats were kept at a constant temperature of 24–26°C and in a 12-hr light/12-hr dark cycle.

Experimental Design and Grouping

The rats were randomly divided into the following groups:

- ✓ Control Group (C): No exposure to BPA
- ✓ Low-Dose Group (LD): 50 µg/kg body weight/day of BPA
- ✓ Middle-Dose Group (MD): 100 µg/kg body weight/day of BPA
- ✓ High-Dose Group (HD): 200 µg/kg body weight/day of BPA

Each group contained 5 males and 5 females. BPA was administered orally via gavage for a period of 21 days prior to mating to simulate chronic exposure. Treatments lasted for 28 consecutive days and the histological samples were collected immediately after the animal sacrifice. All experiments were conducted in accordance with the Guide for the Care and Use of Laboratory Animals, 8th edition [6],

Breeding and Generational Study Design

After exposure:

Males and females (parent, F1) from the same treatment group were mated to produce the F2 generation. F2 offspring were raised without direct BPA exposure, then interbred within their groups to produce F3 generations. BPA was not administered to F2 and F3, generations to assess transgenerational (heritable) effects.

Sample Collection and Observation Parameters

The weight of the animals was determined on the 7th day, 14th day, 21st day and 28th day after administration of Bisphenol A.

The blood samples from the parent males and females wistar rats were collected before and after the administration of Bisphenol A. The histological samples were collected immediately after the animal sacrifce.

At specific developmental stages (postnatal day 60, and 120), 5 rats per sex per group per generation were selected for analysis.

The following assessments were conducted:

i. Reproductive Assessment

Sperm motility, count, and morphology

Fertility index and litter size

ii. Hormonal Analysis

Serum levels of testosterone, estrogen, FSH, LH, prolactin and progesterone using ELISA kits

Methods of Data Analysis

The data obtained were computed and analyzed using IBM statistical package for the social sciences (SPSS) version 26.0 (IBM Corp., NY, USA). The data were presented in Tables and Figures, and sample characteristics were summarized with descriptive statistics. Data were presented as mean ± standard deviation (SD). One way analysis of variance (ANOVA) was used appropriately to compare testosterone, prolactin, luteinizing hormone, follicle stimulating hormone, progesterone and estrogen (estrodiol). Comparison of numerical data between bivariate variable were performed appropriately with either Independent Sample (student) T-test or Mann- Whitney U-test. Confidence interval were set at 90%, and $p<0.05$ will be considered statistically significant.

Estrogen (Estrodiol): Estimation was determined using method described by [7]

Testosterone: Estimation was determined using method described by [8].

Progesterone Analysis: Estimation was determined using method described by **[7]**.

Follicle Stimulating Hormone: Estimation was determined using method described by Estimation was determined using method described by [8].

Luteinizing Hormone: Estimation was determined using method described by [8].

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Prolactin: Estimation was determined using method described by [7].

RESULTS

The following results were obtained from the study of the trans-generational effect of Bisphenol-A on the reproductive hormones of male and female Wistar rats.

Table 1 shows the weekly weight of the wistar rats during the 28 days of the experiment.

Table 1: Weight of experimental rats on day 1, 7, 14, 21 and 28

Weight	Weight of parents Wistar rats				f-value	p-value
	Week 1	Week 2	Week 3	Week 4		
Female						
Group A (50mg/kg)	149.68 ± 64.71	153.76 ± 64.17	158.32 ± 63.45	162.80 ± 62.74	0.040	0.989
Group B (100mg/kg)	140.10 ± 81.49	144.34 ± 81.76	129.40 ± 83.43	154.20 ± 81.69	0.078	0.971
Group C (200mg/kg)	165.20 ± 42.56	169.52 ± 42.42	174.10 ± 42.63	179.00 ± 42.60	0.097	0.960
Group D (Control)	161.40 ± 80.14	164.72 ± 80.94	166.50 ± 80.06	169.10 ± 80.19	0.008	0.999
	Male					
Group A (50mg/kg)	161.90 ± 41.24	169.90 ± 39.37	179.00 ± 39.43	189.00 ± 38.03	0.429	0.735
Group B (100mg/kg)	164.00 ± 62.78	173.40 ± 62.61	182.60 ± 63.28	194.60 ± 59.04	0.224	0.878
Group C (200mg/kg)	170.40 ± 53.99	179.60 ± 54.12	183.00 ± 49.99	193.00 ± 49.99	0.161	0.921
Group D (Control)	230.40 ± 46.96	219.70 ± 28.34	223.40 ± 28.76	227.20 ± 28.76	0.092	0.963

Effect of Bsiphenol A on the serum levels of female reproductive hormones: Table 2 shows the comparative difference in the serum levels of female reproductive hormones including progesterone, FSH, LH, prolactin and estrogen among the various studied groups.

Table 2: Comparative difference in the levels of Progesterone, FSH, LH, PRL and Estrogen among female parent Wistar rats

Variables	Female Parent Wistar Rats							
	Group A (50mg/kg)				Group B (100mg/kg)			
	Before	After	MD	p-value	Before	After	MD	p-value
Progesterone (ng/ml)	30.51 ± 0.86	33.21 ± 3.20	2.70	0.207	29.68 ± 1.42	34.79 ± 2.20	5.11	0.001
FSH (ng/ml)	0.63 ± 0.01	0.74 ± 0.05	0.11	0.020	0.63 ± 0.02	0.72 ± 0.56	0.09	0.005
LH (ng/ml)	1.89 ± 0.10	1.87 ± 0.10	0.02	0.864	1.92 ± 0.05	1.75 ± 0.10	0.17	0.008
Prolactin (ng/ml)	3.33 ± 0.14	3.63 ± 0.15	0.29	<0.001	3.27 ± 0.09	3.59 ± 0.19	0.32	0.018
Estrogen (ng/m/)	30.71 ± 0.66	36.47 ± 2.28	5.75	0.010	31.36 ± 1.24	37.07 ± 1.40	5.71	0.005
	Group C (200mg/kg)				Group D (Control)			
	Before	After	MD	p-value	Before	After	MD	p-value
Progesterone (ng/ml)	30.44 ± 0.98	35.44 ± 1.12	5.01	0.001	30.60 ± 1.22	31.60 ± 1.40	1.00	0.000
FSH (ng/ml)	0.66 ± 0.70	0.75 ± 0.10	0.09	0.028	0.64 ± 0.03	0.68 ± 0.02	0.05	0.083
LH (ng/ml)	1.99 ± 0.01	1.70 ± 0.19	0.29	0.023	1.89 ± 0.09	1.60 ± 0.12	0.28	0.032
Prolactin (ng/ml)	3.40 ± 0.08	3.70 ± 0.37	0.30	0.124	3.34 ± 0.07	3.24 ± 0.19	0.11	0.344
Estrogen (ng/m/)	33.38 ± 0.99	34.86 ±1.48	1.48	0.006	33.58 ± 1.79	31.99 ± 1.52	1.59	0.029

FSH – Follicle stimulating hormone, LH – luteinizing hormone, MD – Mean difference

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Effect of Bsiphenol A on the serum levels of male reproductive hormones: Table 3 shows the Comparative difference in the levels of Testosterone, LH and FSH among male parent Wistar rats

Table 3: Comparative difference in the levels of Testosterone, LH and FSH among male parent Wistar rats

Variables	Male Parent Wistar Rats								
	Group A (50mg/kg)				Group B (100mg/kg)				
	Before	After	MD	p-value	Before	After	MD	p-value	
Testosterone (ng/ml)	2.31 ± 0.31	2.51 ± 0.33	0.21	0.013	2.20 ± 0.11	2.27 ± 0.08	0.08	0.316	
FSH (ng/ml)	0.71 ± 0.07	0.82 ± 0.05	0.11	0.005	0.66 ± 0.03	0.78 ± 0.05	0.07	0.013	
LH (ng/ml)	1.37 ± 0.07	1.95 ± 0.32	0.58	0.008	1.25 ± 0.23	1.95 ± 0.11	0.33	0.009	
	Group C (200mg/kg)				Group D (Control)				
	Before	After	MD	p-value	Before	After	MD	p-value	
Testosterone (ng/ml)	2.04 ± 0.08	2.20 ± 0.12	0.16	0.054	2.04 ± 0.08	2.19 ± 0.11	0.16	0.054	
FSH (ng/ml)	1.29 ± 0.17	1.92 ± 0.19	0.23	0.003	1.29 ± 0.17	1.92 ± 0.19	0.64	0.003	
LH (ng/ml)	0.68 ± 0.07	0.76 ± 0.04	0.04	0.008	0.68 ± 0.07	0.76 ± 0.04	0.08	0.008	

FSH – Follicle stimulating hormone, LH – luteinizing hormone, MD – Mean difference

Effect of parental exposure to Bsiphenol A on the reproductive hormones of the Second generation: Table 4 shows the effect of parental exposure to biphoenol B on the reproductive hormones of rats in the second generation in relation to the degree of parental exposure.

Table 4: Comparative difference in the levels of Progesterone, FSH, LH, PRL, Estrogen and Testosterone among second generation Wistar rats

	Group A	Group B	Group C	Group D	f-value	p-value
Female						
Progesterone (ng/ml)	16.64 ± 0.56	18.02 ± 1.17		14.85 ± 0.36	20.854	<0.001
FSH (ng/ml)	5.06 ± 0.02	5.92 ± 0.08		4.79 ± 0.22	89.77	<0.001
LH (ng/ml)	5.59 ± 0.06	5.83 ± 0.33		5.33 ± 0.13	7.205	0.009
Prolactin (ng/ml)	5.50 ± 0.09	6.02 ± 0.16		6.23 ± 0.06	56.060	<0.001
Estrogen (ng/mg)	18.37 ± 1.40	19.74 ± 1.42		21.79 ± 0.32	10.899	0.002
Male						
Testosterone (ng/ml)	4.51 ± 0.02	4.73 ± 0.05		4.23 ± 0.09	81.278	<0.001
LH (ng/ml)	6.86 ± 0.09	6.54 ± 0.11		5. 81 ± 0.17	89.917	<0.001
FSH (ng/ml)	5.86 ± 0.28	5.91 ± 0.23		4.47 ± 0.20	57.403	<0.001

FSH – Follicle stimulating hormone, LH – luteinizing hormone

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Effect of parental exposure to Bisphenol A on the reproductive hormones of the third generation: Table 5 shows the effect of parental exposure to biphoenol B on the reproductive hormones of rats in the third generation in relation to the degree of parental exposure.

Table 5: Comparative difference in the levels of Progesterone, FSH, LH, PRL, Estrogen and Testosterone among Third generation Wistar rats

	Group A	Group B	Group C	Group D	f-value	p-value
Female						
Progesterone (ng/ml)	16.10 ± 0.05	16.74 ± 0.03		14.85 ± 0.36	102.982	0.000
FSH (ng/ml)	5.42 ± 0.05	5.47 ± 0.02		4.79 ±0 .23	39.805	0.000
LH (ng/ml)	5.46 ± 0.09	5.54 ± 0.03		5.32 ± 0.13	6.889	0.010
Prolactin (ng/ml)	5.37 ± 0.12	4.31 ± 2.42		6.23 ± 0.03	2.356	0.137
Estrogen (ng/mg)	17.80 ± 1.68	20.28 ± 0.03		21.79 ± 0.33	20.767	0.000
Male						
Testosterone (ng/ml)	5.22 ± 0.25	5.34 ± 0.03		4.23 ± 0.09	74.575	0.000
LH (ng/ml)	5.08 ± 0.16	5.11 ± 0.02		5.81 ± 0.16	90.723	0.000
FSH (ng/ml)	4.99 ± 0.15	4.65 ± 1.33		4.47 ± 0.20	0.574	0.578

FSH – Follicle stimulating hormone, LH – luteinizing hormone, MD – Mean difference

Transgenerational effect of biphenol A exposure on female reproductive hormones: Table 6 presents the transgenerational effect of Bisphenol A on female reproductive hormones

Table 6: Generational differences in the level of Progesterone, FSH, LH, PRL and Estrogen among the female Wistar rats

Variable	First generation	Second generation	Third generation	f-value	p-value
Progesterone (ng/ml)					
Group A	33.21 ± 3.20	16.64 ± 0.56	16.10 ± 0.05	134.449	<0.001
Group B	34.79 ± 2.20	18.02 ± 1.17	16.74 ± 0.03	245.985	<0.001
Group D	31.60 ± 1.39	14.85 ± 0.36	14.85 ± 0.36	634.392	<0.001
FSH (ng/ml)					
Group A	0.74 ± 0.05	5.06 ± 0.02	5.42 ± 0.05	17676.84	<0.001
Group B	0.72 ± 0.06	5.92 ± 0.08	5.47 ± 0.02	12514.03	<0.001
Group D	0.68 ± 0.02	4.79 ± 0.23	4.79 ± 0.23	810.00	<0.001
LH (ng/ml)					
Group A	1.87 ± 0.10	5.59 ± 0.58	5.45 ± 0.09	3136.93	<0.001
Group B	1.75 ± 0.10	5.83 ± 0.33	5.54 ± 0.03	629.12	<0.001
Group D	1.60 ± 0.12	5.33 ± 0.13	5.33 ± 0.13	1436.47	<0.001
Prolactin (ng/ml					
Group A	3.63 ± 0.15	5.49 ± 0.09	5.37 ± 0.10	392.30	<0.001
Group B	3.59 ± 0.18	6.02 ± 0.16	5.43 ± 0.27	176.53	<0.001
Group D	3.24 ± 0.19	6.23 ± 0.59	6.34 ± 0.59	1006.64	<0.001
Estrogen (ng/mg)					
Group A	36.48 ± 2.28	18.37 ± 1.40	17.80 ± 1.68	169.78	<0.001
Group B	37.07 ± 1.40	19.75 ± 1.42	20.28 ± 0.03	365.63	<0.001
Group D	31.99 ± 1.52	21.79 ± 0.33	21.79 ± 0.33	204.58	<0.001

FSH – Follicle stimulating hormone, LH – luteinizing hormone, MD – Mean difference

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Transgenerational effect of Bisphenol A exposure on male reproductive hormones.

As shown in Table 7, shows the levels of testosterone, FSH and LH across the 3 generations.

Table 7: Generational difference in the level of Testosterone, FSH and LH among the male Wistar rats

Variable	First generation	Second generation	Third generation	f-value	p-value
Testosterone (ng/ml)					
Group A	2.51 ± 0.33	4.51 ± 0.02	5.22 ± 0.26	170.80	<0.001
Group B	2.27 ± 0.08	4.73 ± 0.05	5.34 ± 0.03	3608.60	<0.001
Group D	1.94 ± 0.10	4.23 ± 0.09	4.23 ± 0.09	926.48	<0.001
LH (ng/ml)					
Group A	1.95 ± 0.32	6.86 ± 0.09	5.08 ± 0.02	841.30	<0.001
Group B	1.95 ± 0.11	5.53 ± 0.11	5.11 ± 0.02	3654.93	<0.001
Group D	1.87 ± 0.11	5.81 ± 1.67	5.81 ± 0.17	1150.13	<0.001
FSH (ng/ml)					
Group A	0.82 ± 0.05	5.86 ± 0.28	4.99 ± 0.15	1045.28	<0.001
Group B	0.78 ± 0.05	5.91 ± 0.23	4.65 ± 1.33	58.74	<0.001
Group D	0.68 ± 0.02	4.47 ± 0.20	4.47 ± 0.20	870.08	<0.001

DISCUSSION

Lethal dose toxicity (LD_{50}): The Lethal dose toxicity of Bisphenol A carried out showed dullness in the rats. they became stable after sometime. No animal died during the fourteen days test for toxicity for doses ranging from 100mg/kg, 1000mg/kg, 2000mg/kg, 300mg/kg and 5000mg/kg

Weight of Experimental Rats

Among the female rats, it was observed that animals in all the groups, showed a consistent increase in weight throughout the experimental period as seen in Table 1. Although this pattern indicates a greater rate of weight gain in treated animals, statistical analysis using one-way ANOVA showed that these differences were not significant ($p > 0.05$). This outcome suggests that, under the specific dosages and duration applied in this study, BPA did not produce a statistically measurable effect on body weight

Female Reproductive Hormones

Table 2 showed that the mean differences in the levels of progesterone and LH were not statistically significant ($p = 0.207$ and $p = 0.864$ respectively), those in FSH, Prolactin and estrogen were statistically significant ($p = 0.020$, $p < 0.001$ and $p = 0.010$ respectively).

Among the animals in group B, the mean difference in all the hormones were statistically significant ($p = 0.001$, $p = 0.005$, $p = 0.008$, $p = 0.018$ and $p = 0.005$ for progesterone, FSH, LH prolactin and estrogen respectively. For Group C the mean difference before and after in the level of progesterone, FSH, LH and estrogen were statistically significant ($p = 0.001$, $p = 0.028$, $p = 0.023$ and $p = 0.006$ respectively), that in prolactin was not statically significant ($p = 0.124$). For Group D animals, the mean difference before and after in the level of progesterone, LH and estrogen were statistically significant ($p = <0.001$, $p = 0.032$, and $p = 0.029$ respectively), that in FSH and prolactin were not statically significant ($p = 0.083$ and $p = 0.344$ respectively). The comparison of hormone levels before and after treatment revealed a statistically significant increase in female reproductive hormones, including progesterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and estrogen. This effect was more pronounced at higher concentrations of Bisphenol A (BPA). These findings underscore the estrogen-like activity of BPA and reinforce its classification as an endocrine-disrupting chemical, as previously described by [4].

Male Reproductive Hormones

The pre- and post-treatment of male reproductive hormones testosterone, Follicle stimulating hormone, and Luteinizing Hormone levels measured showed statistically significant increase in most groups as seen in Table 3. In animals in group A, the difference in the levels between before and after the experiment were statistically significant ($p = 0.013$, $p = 0.005$ and $p = 0.008$ respectively for testosterone, FSH and LH. The difference in the levels between before and after the experiment in testosterone was not statistically significant ($p = 0.316$), those of FSH and LH were statistically significant ($p = 0.013$ and $p = 0.009$ respectively). Among animals in group C, the difference in testosterone was not statistically significant ($p = 0.054$) while the difference in FSH and LH were statistically significant ($p = 0.003$ and $p = 0.008$). In group D, the levels between before and after the experiment in testosterone was not statistically significant ($p = 0.054$), those of FSH and LH were statistically significant ($p = 0.003$ and $p = 0.008$ respectively). The consistent increase in follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels across most treatment groups suggests that Bisphenol A (BPA) may influence the release of gonadotropins more effectively than it affects testosterone production. This pattern implies a greater sensitivity of the pituitary hormones to BPA exposure. These observations are in agreement with the findings of Walker and Gore (2017), who reported that BPA has a stronger modulatory

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effect on reproductive hormone regulation at the level of the pituitary gland. The absence of statistically significant changes in testosterone in some groups could be due to feedback mechanisms within the endocrine system or the possibility that BPA's effects on androgens only occur beyond a certain exposure threshold.

Hormones

First Generation Hormones: From Table 4, the female rats of the next generation of parents that received a higher dose of Bisphenol A, also had higher level of female reproductive hormones when compared to those that received lower dose and those not treated and the difference in the mean levels were all statistically significant ($p = <0.001$, $p = < 0001$, $p = 0.009$, $p < 0.001$ and $p = 0.002$ for progesterone, FSH, LH, prolactin and estrogen respectively). However, the difference in the levels of progesterone between those from group A parents and group B parents, those from group A parents and group D parent and between those from group B parents and group D parents were statistically significant ($p = 0.016$, $p = 0.003$ and $p <0.001$ respectively). Also, , the difference in FSH between those from group A parents and group B parents, those from group A parents and group D parent and between those from group B parents and group D parents were statistically significant ($p <0.001$, $p = 0.010$ and $p <0.001$ respectively). The difference in LH between those from group A parents and group B parents, those from group A parents and group D parent were not statistically significant ($p = 0.098$ and $p = 0.068$ respectively) and between those from group B parents and group D parents was statistically significant ($p = 0.003$). The difference in prolactin between those from group A parents and group B parents, those from group A parents and group D parent and between those from group B parents and group D parents were statistically significant ($p <0.001$, $p <0.001$ and $p = 0.012$ respectively). The difference in estrogen between those from group A parents and group B parents was not statistically significant ($p = 0.086$) and that between hose from group A and group B and from group B parents and group D parents were statistically significant ($p = 0.001$ and $p = 0.017$ respectively). Among the males of the first generation, the difference in the level of testosterone between those from group A parents and group B parents, those from group A parents and group D parent and between those from group B parents and group D parents were statistically significant ($p <0.001$, $p <0.001$ and $p <0.001$ respectively). The difference in the levels of LH between those from group A parents and group B parents, those from group A parents and group D parent and between those from group B parents and group D parents were statistically significant ($p <0.001$, $p <0.001$ and $p <0.001$ respectively) and the difference in the level of FSH between those from group A parents and group B parents was not statistically different ($p = 0.748$) while the difference between those from group A parents and group D parent and between those from group B parents and group D parents were statistically significant ($p <0.001$, and $p <0.001$ respectively). These are in are in tandem with the findings of [10].

Second Generations Hormones: The second generations hormones showed statistically significant differences in all measured hormones (progesterone, FSH, LH, prolactin, and estrogen). The hormones of female offspring, showed significant increase. Group C animals which were dozed with 200mg/kg were not represented due to mortality, which limits dose-dependent comparisons. Among males, testosterone, LH, and FSH levels were also significantly increased. This shows there was alteration in male hormones. The results suggest that Bisphenol A (BPA) exposure may lead to transgenerational effects that are possibly driven by epigenetic changes or germline transmission. The increased hormone levels observed in the offspring of exposed parents lend support to the theory that BPA can induce heritable disruptions in endocrine function [11].

Third Generation Hormones: It was observed that young rats of parent rats in groups C treated with 200mg/ml were all dead before maturity. As seen in Table5, the difference in the level of progesterone between those from group A parents and group B parents, those from group A parents and group D parent and between those from group B parents and group D parents were statistically significant ($p <0.001$, $p <0.001$ and $p <0.001$ respectively). The difference in the level of LH between those from group A parents and group B was not statistically significant ($p = 0.246$), those from group A parents and group D parent and between those from group B parents and group D parents were statistically significant ($p <0.001$ and $p <0.001$ respectively) and the difference in the level of FSH between those from group A parents and group B parents, between those from group A parents and group D parent and between those from group B parents and group D parents were not statistically significant ($p = 0.497$, $p = 0.313$ and $p = 0.731$ respectively). In the third generation, significant increases were observed in progesterone, FSH, and estrogen levels, particularly among female offspring. This indicates that the generational effects of BPA exposure on reproductive hormones continued to manifest, especially in females. However, prolactin levels did not differ significantly. Among male offspring, hormonal levels such as testosterone and LH showed notable generational increases, whereas FSH did not display a statistically significant change. These findings suggest that BPA-induced hormonal disruptions can persist across generations, though the degree and consistency of these effects may depend on both the specific hormone and the sex of the animal. This observation aligns with earlier research indicating that some endocrine effects of BPA may diminish or stabilize over successive generations [12].

CONCLUSION

Exposure to Bisphenol A (BPA) in Wistar rats induces profound molecular and physiological disruptions, particularly within the reproductive, metabolic, and neurological systems. This study demonstrated that BPA

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acts as a potent endocrine disruptor capable of altering gene expression patterns in a dose- and tissue-specific manner.

REFERENCES

1. Sifakis S., Vasilis P. A., Aristeidis M. T., and Demetrios A. S. (2017). Endocrine disruptors leading to obesity and related diseases. *International Journal of Environmental Research and Public Health* 14(10).
2. Clara A G T, Marianne S A, Esben B, Henriette B, Flemming N, Richard C J, Signe B, Steffen H, Philippe G, Tina K J (2021) Pregnancy Exposure to Perfluoroalkyl Substances and Associations With Prolactin Concentrations and Breastfeeding in the Odense Child Cohort The Journal of Clinical Endocrinology & Metabolism, Volume 107, Issue 2, pp 631
3. Melmed, S., and Jameson, J. L. (2005). Disorders of the anterior pituitary and hypothalamus. In J. N. Jameson, D. L. Kasper, T. R. Harrison, E. Braunwald, A. S. Fauci, S. L. Hauser, & D. L. Longo (Eds.), Harrison's principles of internal medicine (16th Eds., pp. 333). McGraw-Hill Medical Publishing Division.
4. Rochester, J. R. (2013). Bisphenol A and human health: A review of the literature. *Reproductive Toxicology*, *42*, 132–155.
5. Susiarjo, M., Sasson, I., Mesaros, C., and Bartolomei, M. S. (2013). Bisphenol A exposure disrupts genomic imprinting in the mouse. *PLoS Genetics*, *9*(4), e1003401.
6. Albus, U. (2012). Guide for the care and use of laboratory animals (8th ed.). SAGE Publications.
7. Abraham G.E. (1981) The application of natural steroid radioimmunoassay to gynecologic endocrinology. In: Abraham GE, editor. Radioassay Systems in Clinical Endocrinology, Basel: Marcel Dekker,: 475-529.
8. Matsumoto, J., Yokota, H. and Yuasa, A. (2022). Developmental increases in rat hepatic microsomal UDP-glucurono-syltransferase activities toward xenoestrogens and decreases during pregnancy. *Environ Health Perspect.* 110:193–196.
9. Walker DM, Gore AC. (2017). Transgenerational neuroendocrine disruption of reproduction. *Nature Reviews Endocrinology*, 13(9):540–556.
10. Manikkam M, Tracey R, Guerrero-Bosagna C, Skinner MK. (2013). Plastics derived endocrine disruptors (BPA, DEHP, DBP) induce epigenetic transgenerational inheritance of obesity, reproductive disease and sperm epimutations. *PLoS One*, 8(1):e55387.
11. Wolstenholme, J. T., Taylor, J. A., Shetty, S. R., Edwards, M., Connelly, J.J., Rissman, E. F. (2011). Gestational exposure to low dose bisphenol A alters social behavior in juvenile mice. *Plos One*, *6*(9):25448.
12. Susiarjo M, Xin F, Bartolomei MS. (2013). Epigenetic effects of endocrine disruptors on reproduction and development. *Reproductive Toxicology*, 42:109–118.

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