EFFECTS OF CHRONIC PROMETHAZINE AND HALOPERIDOL INGESTION ON FEEDING BEHAVIOUR IN MALE ALBINO RATS: SEPARATE AND COMBINED ANALYSIS

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ABSTRACT: Following the concern about gender differences in the effect of haloperidol and promethazine, separately and in combination, on feeding behaviour, as presented by Balogun et al. (2025) with female rats, the present study investigated the same phenomena using male rats this time around. Using 24 male albino rats, divided into four groups of six rats each, Combined drug, haloperidol group, promethazine group and saline group, their feeding behaviour was observed after ingestion of the drugs. It was observed that male rats gained more weight and ate more in all the groups, demonstrating the effect of the drugs on feeding behaviour. The implications of these findings for drug consumption and food intake, especially for those concerned with body weight gain/loss were emphasised and discussed.

Keywords: Separate And Combined Ingestion, Haloperidol, Promethazine, Feeding Behaviour, Male Rats

INTRODUCTION/BACKGROUND OF THE STUDY

As the interrogation of substance abuse continues to grow especially when it concerns the use/abuse of cocktails of drugs, Balogun et al (2025) investigated separate and combined effects of chronic ingestion of Haloperidol and Promethazine on the feeding behaviour of female albino rats. During the discussion of the study at a forum, the question was asked that "why the choice of only female rats, why not male or both males and females (rats in general)" The answer given was that because of the high fecundity rate of these rats, keeping them together may bring in other extraneous variables that were not planned for in the study. However, the import of gender concern of the audience did not go unnoticed, particularly, when we know that gender reactions to drugs in behavioural and physiological compositions do exist (Dunne, et.al, 1993). For example, Frezza et.al (1990) observed that women become intoxicated after drinking smaller quantities of alcohol than men because of physiological differences between the genders (women have less total body water than men).

Balogun et al. (2025) observed that combining drugs, especially psychoactive drugs, does have its physiological, physical and psychological consequences, and this is worrisome enough to warrant continuous interrogation by every stakeholder in human health. This is because certain behavioural

reactions to substance use can become habitual (addictive), tending towards compulsive-obsessive, as observed by Grant et al. (2010). Several behaviours, besides psychoactive substance ingestion, produce short-term rewards that may engender persistent behaviour, despite knowledge of adverse consequences, i.e., diminished control over the behaviour. Such can be found in the way we eat (food consumption and its various dynamics); some people have eating disorders that may lead to weight loss or obesity. Balogun et al. (2025) observed that weight gain and food intake differentials exist when haloperidol and or promethazine were ingested separately and in combination with one another, especially among female participants in the study. Would the same observation be made, given gender differentials, in the present study?

As earlier stated, the concern in the present study, as a follow-up to Balogun et al. (2025), was to establish gender differences in reaction to feeding behaviour using haloperidol and promethazine. "Research indicates that women and men can experience different reactions to substance abuse, with women often reporting greater impairment and a higher risk of relapse, even though men generally have higher rates of substance use overall (NIDA< 2020). These differences can be attributed to biological factors like hormone fluctuations, as well as social and environmental influences impacting how women access and utilise substances compared to men. Men are more likely than women to use almost all types of illicit drugs," (NIDA, 2020), but women may be light users of drugs, especially alcohol, and so be a binge drinker, but suffer more psychiatric disorders (Grant, et.al., 2010; Dunne, et.al. 1993; Brady & Randall, 1988, Frezza, et. al, 1990)

What haloperidol and promethazine are in terms of chemical compositions and effects on human behaviour has been given elsewhere (Balogun et al. 2025). The referenced study well documented their inhibiting or stimulating effects, particularly when feeding behaviour is the concern. It would, therefore, not be appropriate to repeat this in the present study again as it would amount to self-plagiarism.

Statement of the Problem

Drug use and abuse is a common phenomenon among students and adolescence these days, and the practice of drug salad (synergism), which is a process in which more than one drugs are combined and taken, is on the increase (Tallarida, 2011) The risk associated with both Haloperidol and Promethazine include addiction and physical dependence, as well as liver and kidney damage, even death when overdosed (Tallarida, 2011) The drug, Haloperidol is an antipsychotic and Promethazine is known as an opiate, and both alter brain activity. This is known as one of the side effects of some other kinds of drugs as well. The question is, however, can the intake of these drugs, Haloperidol and Promethazine, lead to a change in food consumption patterns, especially among males?

Thus, the following questions were raised:

- 1. Can the persistent ingestion of Haloperidol lead to a change in the food consumption behaviour of male albino rats?
- 2. Can the persistent ingestion of Promethazine lead to a change in the food consumption behaviour of male albino rats?

3. Can the persistent ingestion of Haloperidol and Promethazine, combined together, lead to a change in the food consumption behaviour of male albino rats?

Purpose of Study

This study is being carried out to see if a change in consumption pattern behaviour can be said to be a side effect of the ingestion of Haloperidol and Promethazine. A long list of side effects associated with the intake of this antipsychotic and opiates has been verified. The purpose of this study is to find out if a change in consumption pattern behaviour can be added to this long list of side effects. In addition, the study was designed to establish feeding behaviour differentials in reaction to Balogun et al. (2025), who used the same drugs on female rats.

Hypotheses

- 1. There will be a significant effect of promethazine on eating behaviour among male albino rats
- 2. There will be a significant effect of Haloperidol on eating behaviour among male albino rats.
- 3. There will be a significant effect of both Promethazine and Haloperidol on eating behaviour among male albino rats.
- 4. There will be a significant effect of Promethazine on weight gain among male albino rats.
- 5. There will be significant effects of Haloperidol on weight gain among male albino rats
- 6. There will be a significant effect of both Haloperidol and Promethazine on weight gain among male albino rats.

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METHODOLOGY

Research Design

The design to be used for this research is randomized experimental design, using simple ANOVA approach. The independent variables are the chronic administration of Haloperidol, Promethazine and the combination of both in the male albino rats, while the dependent variable is consumption pattern or behaviour displayed or exhibited by the male albino rats.

Participants

A total population of 24 male albino rats were used for this study. The randomisation technique was used to select and assign the rats into the different groups with a sample size of six (6), that

is, 6 rats in the control group, 6 rats in the Haloperidol group, 6 rats in the Promethazine group and 6 rats in the Haloperidol and Promethazine combined group. The study commenced after two (2) weeks of the rats getting acclimatized to the rat lab (their cages), which they were housed in. They were properly fed and given adequate water, until they grew to the appropriate body size. The different drugs were administered to the rats according to their body weights. Rats in the control group were given saline (distilled water).

Setting

The psychology laboratory unit of the Department of Psychology, University of Ibadan.

Instruments Used

- 0. Recording sheets.
- 1. Laboratory coat.
- 2. Oral cannula (metal /plastic)
- 3. Laboratory hand Gloves.
- 4. A blue, black and red marker for easy identification of male albino rats from, the control and experimental rats.
- 5. Distilled water
- 6. Weighing balance –for the daily weighing of rats.
- 7. Experimental cages
- 8. Stopwatch /Timer for timekeeping and recording
- 9. Two 1ml /5ml disposable syringes
- 10. Mouse cubes Rat feed
- 11. Promethazine capsule (powder in capsule diluted with distilled water)
- 12. Haloperidol capsules (powder in capsule diluted with distilled water)
- 13. Disinfectants (Dettol/ Iza1)

Drug Preparation and Concentration

1.1mg per kg was the dosage used for administering Promethazine to the rats, while 1mg per kg was the dosage used in administering Haloperidol to the rats, and this dosage was calculated and given based on the individual weight of each rat. For the combined group, a mixture of Promethazine and Haloperidol was given with the same doses above; then there was the control group that was given only water, which was about 0.5ml of distilled water per rat.

Procedure

The rats were housed in cages at the laboratory and acclimatised for 21 days before starting the experiment. During this period, food and water were freely available and given without any form of deprivation. After the orientation period, there was an eight (8) day baseline period before treatment commenced; this was undertaken so as to erase any plausible explanation for the outcome of the experiment, i.e. extraneous variables. They were divided into four (4) groups: the control group, the Promethazine group, the Haloperidol group and the Promethazine and

Haloperidol group; each group consisted of 6 rats. 28 male rats were used for the study, and 4 extra in case of mortality. The study took 28 days, in which the rats in the experimental groups were exposed to treatment and were injected with the use of an oral cannula, a solution containing Promethazine, Haloperidol and a combination of both drugs throughout the period of the experiment, the control group were not exposed to Promethazine or Haloperidol but were treated with distilled water solution (placebo).

The volume of Promethazine, Haloperidol, and a combination of both drugs administered to the rats was dependent on their body weight. However, after treating the rats according to their groups each day, 30 minutes was allowed for the drug to be properly and effectively ingested or assimilated into their system before introducing them to food and water. This condition was applied throughout the experimental period.

Data were recorded after 24 hours from the previous administration. The quantity of food intake was determined by subtracting the weight of the food remaining and spillage from the food given from the previous day. On the other hand, the weight gained was obtained by subtracting the weight of the rat the previous day before administration from the weight of the rat on the new day after administration.

Each day at the expiration of the 24-hour period, the following operations were carried out

- 0. Weighing of each rat
- 1. Removal of water containers from cages
- 2. Removal of feed containers which contain remaining feeds from cages
- 3. Removal and keeping of food spilt by each rat
- 4. Injection of saline, separate and combined Promethazine and Haloperidol into the control and experimental groups, respectively

Statistical Analysis

Simple Analysis of Variance (ANOVA) was used to analyse data collected from the experiment

RESULTS

The data collected was analysed using Randomised Block Analysis of Variance (ANOVA), descriptive statistics of mean and standard deviation, and graphical representation.

Hypothesis I

Promethazine and Haloperidol ingestion will jointly interact to affect the weight gain of male Albino rats exposed to the drugs. This hypothesis was tested using the Randomized Block ANOVA, and the result is presented in Table 1a.

Table 1a: Summary Randomized Block ANOVA table showing the influence of exposure to acute intake of anti-psychotic (Haloperidol & Promethazine) on weight gain of male Albino rats.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial η ²
Block	1093.806	1	1093.806	2.414	.121	.007
Treatment	13680.762	1	13680.762	30.193	.000	.083
Error	150886.670	333	453.113			
Corrected Total	165661.238	335				

The result from Table 1a reveals that exposure to chronic intake of anti-psychotic (Haloperidol & Promethazine) significantly impacted the weight gain among Albino Rats F (1, 333) = 30.19, p < 0.01, $\eta^2 = .08$. The result demonstrated that weight gain increased by 8% with exposure to chronic acute intake of anti-psychotic (Haloperidol and Promethazine) compared to the control group. Further analysis of the mean differences was carried out with an LSD post hoc multiple comparison Test, and the result is presented in Table 1b.

Table 1b: Summary of descriptive statistics and LSD post hoc comparison on the mean difference between rats exposed to chronic intake of anti-psychotics (Haloperidol & Promethazine) and those not exposed (Control).

	Mean	S.E.M	LSD POST HOC	Sig.
Combined (Haloperidol + Promethazine)	111.262 ^a	1.642	12.76*	.000
Control	98.500 ^a	1.642	12.70*	.000

*. The mean difference is significant at the .05 level.

a. Covariates appearing in the model are evaluated at the following values: Day = 14.5000.

From the analysis, mean differences showed that rats in the control ($\bar{x} = 98.50$) significantly lesser weight gain compared to rats ingested with Haloperidol + Promethazine ($\bar{x} = 111.26$). The mean differences were significant. Based on this, the hypothesis that there will be a significant difference in weight gain among male Albino rats ingested with different drugs is thus accepted.

Hypothesis II

Haloperidol ingestion will significantly affect the weight gain of male albino rats exposed to the drugs. This hypothesis was tested using the Randomized Block ANOVA, and the result is presented in Table 2aFrom the analysis, mean differences showed that rats in the control ($\bar{x} = 98.50$) significantly lesser weight gain compared to rats ingested with Haloperidol + Promethazine ($\bar{x} = 111.26$). The mean differences were significant. Based on this, hypothesis which states that

there will be a significant difference in weight gain among male Albino rats ingested with different drugs is thus accepted.

 Table 2a: Summary Randomized Block ANOVA table showing the influence exposure to chronic intake of anti-psychotic (Haloperidol) on weight gain.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial η^2
Block	4035.433	1	4035.433	3.787	.053	.011
Treatment	403.048	1	403.048	.378	.539	.001
Error	354882.472	333	1065.713			
Corrected Total	359320.952	335				

The result from Table 2a shows that exposure to chronic intake of anti-psychotic (Haloperidol) did not significantly influence the weight gain among Albino Rats F (1, 136) = .38, p > 0.05, η^2 = .00. The result demonstrated that weight gain increased by 0% with exposure to chronic intake of antipsychotic (Haloperidol) compared to the control group. Further analysis of the mean differences was carried out with an LSD post hoc multiple comparison Test, and the result is presented in Table 2b.

Table 2b: Summary of descriptive statistics and LSD post hoc comparison analysis showing the mean difference in weight gain between rats exposed to chronic intake of anti-psychotic (Haloperidol) and those exposed to Normal saline.

	Mean	S.E.M	LSD POST HOC	Sig.
Haloperidol	100.690 ^a	2.519	2 10	51
Control	98.500^{a}	2.519	2.19	.54

*. The mean difference is significant at the .05 level.

a. Covariates appearing in the model are evaluated at the following values: Day

= 14.5000

From the analysis, mean differences showed that rats in the control ($\bar{x} = 98.50$) significantly displayed lesser weight gain compared to rats ingested with Haloperidol ($\bar{x} = 100.69$). The mean differences were not significant. Based on this, the hypothesis that states that there will be a significant difference in weight gain among male rats that ingested different drugs is thus rejected.

Hypothesis III

Promethazine ingestion will significantly affect the weight gain of male albino rats exposed to the drugs. This hypothesis was tested using the Randomized Block ANOVA, and the result is presented in Table 3a.

 Table 3a: Summary Randomized Block ANOVA table showing the influence of exposure to chronic intake of anti-psychotic (Promethazine) on weight gain.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial η ²
Block	2432.002	1	2432.002	5.127	.024	.015
Treatment	13170.039	1	13170.039	27.764	.000	.077
Error	157961.281	333	474.358			
Corrected Total	173563.321	335				

The result from Table 3a shows that exposure to chronic intake of anti-psychotic (Promethazine) significantly caused weight gain among male Albino Rats F (1, 136) = 27.76, p < 0.001, η^2 = .08. The result demonstrated that weight gain increased by 8% with exposure to acute intake of anti-psychotic (Promethazine) compared to the control group. Further analysis of the mean differences was carried out with LSD post hoc multiple comparison test, and the result is presented in Table 3b.

Table 3b: Summary of descriptive statistics and LSD post hoc comparison analysis showing the mean difference in weight between rats exposed to chronic intake of anti-psychotic (Promethazine) and those exposed to Normal saline.

			LSD POST	Sig.
	Mean	S.E.M	HOC	_
Promethazine	111.021 ^a	1.680	10.50*	000
Control	98.500 ^a	1.680	12.52*	.000

*. The mean difference is significant at the .05 level.

a. Covariates appearing in the model are evaluated at the following values:

WEIGHT = 3.1490, Days = 7.5000.

From the analysis, mean differences showed that rats in the control ($\bar{x} = 98.50$) significantly gained more weight compared to rats ingested with Promethazine ($\bar{x} = 111.02$). The mean differences were significant. Based on this, hypothesis three, which stated that there would be a significant difference in weight gain among male rats, is thus accepted.

Hypothesis IV

Promethazine and Haloperidol ingestion will jointly interact to affect the food consumption of male Albino rats exposed to the drugs. This hypothesis was tested using the Randomized Block ANOVA, and the result is presented in Table 4a.

Table 4a: Summary Randomized Block ANOVA table showing the influence of exposure to chronic intake of anti-psychotic (Haloperidol and Promethazine) on food consumption of male Albino rats.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial η ²
Block	1093.806	1	1093.806	2.414	.121	.007
Treatment	13680.762	1	13680.762	30.193	.000	.083
Error	150886.670	333	453.113			
Corrected Total	165661.238	335				

The result from Table 4a. reveals that exposure to acute intake of anti-psychotic (Haloperidol & Promethazine) significantly impacted food consumption among Albino Rats F (1, 333) = 30.19, p < 0.01, $\eta^2 = .08$. The result demonstrated that food consumption increased by 40% with exposure to acute intake of anti-psychotic (Haloperidol and Promethazine) compared to the control group. Further analysis of the mean differences was carried out with descriptive statistics and LSD post hoc multiple comparison Test, and the result is presented in Table 4b.

Table 4b: Summary of descriptive statistics and LSD post hoc comparison of the mean difference between rats exposed to acute intake of anti-psychotic (Haloperidol & Promethazine) and those not exposed (Control).

	Mean	S.E.M	LSD POST HOC	Sig.
Combined (Haloperidol + Promethazine)	111.262 ^a	1.642	12.76*	.000
Control	98.500 ^a	1.642	12.70*	.000

*. The mean difference is significant at the .05 level.

a. Covariates appearing in the model are evaluated at the following values: Day = 14.5000.

From the analysis, mean differences showed that rats in the control ($\bar{x} = 98.50$) significantly lesser food consumption compared to rats ingested with Haloperidol + Promethazine ($\bar{x} = 111.26$). The mean differences were significant. Based on this, the hypothesis that there will be a significant difference in food consumption among male Albino rats ingested with different drugs is thus accepted

Hypothesis V

Haloperidol ingestion will significantly affect the food consumption of male albino rats exposed to the drugs. This hypothesis was tested using the Randomized Block ANOVA, and the result is presented in Table 5a.

Table 5a: Summary Randomized Block ANOVA table showing the influence of exposure to chronic intake of antipsychotics (Haloperidol) on food consumption.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial η ²
Block	1001326.832	1	1001326.832	600.288	.000	.643
Treatment	22946.616	1	22946.616	13.756	.000	.040
Error	555469.542	333	1668.077			
Corrected Total	1579742.990	335				

The result from Table 5a shows that exposure to chronic intake of anti-psychotic (Haloperidol) significantly influenced food consumption among Albino Rats F (1, 333) = 13.76, p < 0.0, η^2 = .04. The result demonstrated that food consumption decreased by 4% among rats exposed to chronic intake of anti-psychotic (Haloperidol) compared to the control group. Further analysis of the mean differences was carried out with an LSD post hoc multiple comparison Test, and the result is presented in Table 5b.

Table 5b: Summary of descriptive statistics and LSD post hoc comparison analysis showing the mean difference in food consumption between rats exposed to acute intake of anti-psychotic (Haloperidol) and those exposed to Normal saline.

	Mean	S.E.M	LSD POST HOC	Sig.
Haloperidol	103.136 ^a	3.151	16.50	000
Control	119.664 ^a	3.151	16.52	.000

*. The mean difference is significant at the .05 level.

a. Covariates appearing in the model are evaluated at the following values: Day

= 14.5000

From the analysis, mean differences showed that rats in the control ($\bar{x} = 119.66$) significantly displayed more food consumption compared to rats ingested with Haloperidol ($\bar{x} = 103.14$). The mean differences were significant. Based on this, the hypothesis that there will be a significant difference in food consumption among male rats ingested with different drugs is thus rejected.

Hypothesis VI

Promethazine ingestion will significantly affect the food consumption of male albino rats exposed to the drugs. This hypothesis was tested using the Randomized Block ANOVA and the result presented in Table 6a.

 Table 6a: Summary Randomized Block ANOVA table showing the influence of exposure to

 Acute intake of anti-psychotic (Promethazine) on food consumption.

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial η ²
Block	1062642.865	1	1062642.865	1209.195	.000	.784
Treatment	3228.960	1	3228.960	3.674	.05	.04
Error	292640.972	333	878.802			
Corrected Total	1358512.797	335				

The result from Table 4.11 shows that exposure to chronic intake of anti-psychotic (Promethazine) significantly affects food consumption among male Albino Rats F (1, 333) = 3.67, p < 0.05, η^2 = .04. The result demonstrated that food consumption increased by 4% with exposure to acute intake of anti-psychotic (Promethazine) compared to the control group. Further analysis of the mean differences was carried out with descriptive statistics and LSD post hoc multiple comparison Test, and the result is presented in Table 6b.

Table 6b: Summary of descriptive statistics and LSD post hoc comparison analysis showing the mean difference in food consumption between rats exposed to acute intake of anti-psychotic (Promethazine) and those exposed to Normal saline.

	Mean	S.E.M	LSD POST HOC	Sig.
Promethazine	113.464	2.203	< 0 0*	05
Control	119.664	2.203	6.20*	.05

*. The mean difference is significant at the .05 level.

a. Covariates appearing in the model are evaluated at the following values: Day

= 14.5000

From the analysis, mean differences showed that rats in the control ($\bar{x} = 119.66$) significantly consumed more food compared to rats ingested with Promethazine ($\bar{x} = 113.02$). The mean differences were significant. Based on this, hypothesis stated that there will be a significant difference in food consumption among males' rats ingested compare to thus accepted.

DISCUSSION

On whether a combined intake of the two drugs (Haloperidol and promethazine) would have effect on one measure (weight gain) of feeding behaviour, it was observed that a slight gain of 8% was recorded. This goes to confirm that drugs, especially in combination, increase weight gain, as attested to by Balogun et al. (2025) and others. This was equally supported by Schankweiler et al. (2023) and Bonder and Davis C (2022) when they talked about binge eating behaviour and more so for university students as observed by Gan et al. (2011). This observation goes to show that

males gain more weight than females (Balogun et al. ,2025). It was further observed that the food intake of the male rats was significantly influenced by the combined drugs (up to 40%), and this may be responsible for the increased body weight gain by the male rats. While female rats in Balogun et al. (2025) were not eating much, the contrary was the case in the present study. Females were discovered to be binge eaters, believing that drugs can further suppress appetite for food; males eat more, and this could be attributable to biological composition differences.

On singular drug intake, it was observed that there was no significant weight gain (almost 0%) when the rats were ingested with haloperidol, even when compared with the control group in the study. However, food intake increased by as much as 4%. This suggests that even if individuals eat much, there is no gain in the eating as it does not contribute significantly to weight gain in the male rats.

On the effect of promethazine, it was observed that there was a significant increase in food consumption was recorded (about 4%), just as it was observed with haloperidol. This is to establish that anti-psychotic drugs like haloperidol and promethazine contribute (individually) to increased food intake. It was equally observed that a significant increase occurred among rats that were ingested with promethazine. The conclusion from this observation is that people concerned with weight loss (especially males) should avoid consumption of drugs, especially haloperidol and haloperidol, either singularly or in combination. Doing otherwise would not make them achieve their goals.

Conclusion

Justification for embarking on gender differences in the effects of separate and combined ingestion of drugs on food intake has been established in this study. Contrary to the observations of Balogun et al. (2025) study with female rats, the present study observed that male rats gained more weight and ate more food, be it with separate and or combined ingestion of haloperidol and promethazine. Males were more affected than females in their feeding behaviour when ingested with haloperidol and/or promethazine. Whether this is "good news" or not is a matter of debate in the future, as the effects of drug consumption on human beings continue.

Limitations

The conclusion arising from this paper should be taken cautiously because human beings were not directly used in the study (ethical considerations). Different results may be obtained when human beings are direct participants in the study. Second, the chemical, physiological and anatomical compositions of the drugs were not determined, and this may make it difficult to conclude the definite effects of the drugs either individually or in combined form.

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