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Investigating the Effects of Methamphetamine on the Amygdala of Adult Male Wistar Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Much attention has been drawn to the toxic effect of Methamphetamine in humans. However, it is not clear whether the toxicity is related to vital organs such as the brain. Hence, this work is geared towards unravelling the neurological & histological effects caused by Methamphetamine on the

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amygdala of adult Wistar rats. Twenty-four male Wistar rats were weighed and distributed into 4 groups of 6 animals each. Group A served as the control as they were administered feed & distilled water only; Group B was administered 3mg/kg body weight of Methamphetamine; Group C was administered 5mg/kg body weight of Methamphetamine while Group D was administered 10mg/kg body weight of Methamphetamine. Methamphetamine was administered via oral mode of exposure for 21 days. Twenty-four hours after the last administration, the animals were anaesthetized under chloroform vapour and their skull was dissected by occipitofrontal incision. The brain tissue of some of the animals was prepared for biochemical analysis through the process of homogenization while the remaining brain tissues from some of the animals were harvested and fixed in 10% neutral buffered formalin for 48 hours and grossed to isolate the brain tissue of interest for histological investigation. There was a significant decrease in the body weight of animals in the experimental groups when compared to the control group. Malondialdehyde (MDA) level was significantly higher ($P<0.05$) in the experimental groups when compared to the control group which increased oxidative stress. Whereas Glutathione (GSH) and superoxide dismutase (SOD) levels were significantly lower in the experimental groups when compared to the control group which also resulted in an increase in oxidative stress in the experimental groups. The histological observations showed that following the administration of Methamphetamine, there was moderate to severe degeneration with necrosis, severe aggregate and infiltration of inflammatory cells, severe granular cell hyperplasia and atrophy as well as a focal area of haemorrhage in the experimental groups. The result of this study shows that methamphetamine caused an adverse histological alteration on the amygdala of the Wistar rat. This alteration is dose dependent. Methamphetamine does not support brain health as distortion of brain tissue was revealed.

Keywords: Methamphetamine; oxidative stress; inflammation; amygdala; neurotoxicity.

1. INTRODUCTION

"Methamphetamine, which is a powerful, highly addictive stimulant affects the Central Nervous System. It takes the form of a white, odorless, sour-tasting crystalline powder that easily dissolves in water or alcohol" (Chomcha & Chomchai, 2015). "Methamphetamine is a potent Central Nervous System (CNS) stimulant which is mainly used as a recreational drug and less commonly as a second-line treatment for Attention Deficit Hyperactivity Disorder (ADHD) and Obesity" (Yu et al., 2015). Methamphetamine, discovered in 1893 exists as two enantiomers: Levomethamphetamine and Dextro-Methamphetamine. According to Panenka et al., (2013), "Methamphetamine was developed early in the 20th century from its parent drug; amphetamine, and was used originally in nasal decongestants and bronchial inhalers. Methamphetamine neurotoxicity leads to adverse changes in the structure and function of the brain as evidenced in the reductions in grey matter volume in several brain regions, as well as adverse changes in biomarkers of metabolic integrity" (Krasnova & Cadet, 2009).

"The limbic system, which is responsible for controlling visceral activities, acts as the center of emotions, behavior & memory" (Rajmohan & Mohandas, 2007). "It is also a contributor to the control of reactions to stress, attention & sexual instincts. The amygdala has a primary role in the processing of memory, decision-making, and emotional responses including fear, anxiety, and aggression" (Pabba, 2013). This study is aimed at investigating the effects of methamphetamine on the amygdala of adult male Wistar rats.

2. MATERIALS AND METHODS

2.1 Location of the Study

This study was carried out at the animal house of the College of Health Sciences, Nnamdi Azikiwe University, Nnewi campus, Anambra State Nigeria.

2.2 Materials of the Study

We used twenty-four adult Wistar rats, Iron cages with iron nettings, sawdust (litters), Animal feed (grower and finisher mash), laboratory coat and gloves, dissecting kit, one stopwatch, digital video recorder, measuring cylinder, weighing balance, water bath, sample bottle, 10% Neutral

Buffered Formalin (Sodium Phosphate Monobasic 4.0gm, Sodium Phosphate Dibasic 6.5gm, Formaldehyde 37% 100.0ml, Distilled

Water 900.0ml), Cotton and anaesthesia (chloroform), Graded Alcohol (50%,70%,95% and absolute alcohol), Glass slides and slide rack, Hot plate, Xylene, Paraffin wax, Embedding plate, and pot, Deepex (DPX) Mountant, Hematoxylin and Eosin, Coverslips, Light Microscope, Orbit shake, Diamond pencil, Rotatory microtome, Ethanol for tissue processing, Micropipette, Specimen labels, and bottles, Trays, Paraffin dispenser, Cassette and slide storage, Pipette tips (various sizes), Knife sharpener, Notebook and biro.

2.3 Procurement and Housing of Experimental Animals

Twenty-four (24) adult Wistar rats weighing 180-250kg were procured from Research Enterprise Farm, University of Ibadan, Oyo State. Perspex cages were used to house four (4) groups of six (6) animals each for routine experiments. Each cage had a wire gauze top for cross-ventilation. The animals were allowed for two weeks for acclimatization under normal temperatures (2730^0) at the Animal House of the Basic Medical Sciences, Nnamdi Azikiwe University, Nnewi Campus. They were fed ad libitum with water and grower mesh.

2.4 Procurement of Methamphetamine

Methamphetamine was procured from the locals and authenticated at the Department of Industrial Chemistry, Nnamdi Azikiwe University, Awka, Anambra State.

2.5 Acute Toxicity Test (LD_{50}) of Methamphetamine

The acute toxicity test of Methamphetamine was carried out in the Department of Biochemistry, Faculty of Basic Medical Sciences, Nnamdi Azikiwe University, Nnewi, Anambra State according to the method employed by Dietrich Lorke (1983). In this study, a total number of 13 Wistar rats were used. The test was carried out in two phases. In phase 1, nine adult Wistar rats were used, and they were grouped into three groups of three animals each. Group 1 received 10mg/kg body weight of Methamphetamine, Group 2 received 50mg/kg body weight of Methamphetamine and Group 3 received 100mg/kg body weight of Methamphetamine. The animals were observed for 24 hours for mortality. From the result of phase 1, the second phase was carried out. In phase 2, 4 adult Wistar rats were used, and they were grouped into four groups of one animal each. Group 1 received 200mg/kg body weight of Methamphetamine, group 2 received 300mg/kg body weight of Methamphetamine, group 3 received 400mg/kg body weight of Methamphetamine and Group 4 received 500mg/kg body weight of Methamphetamine. The animals were monitored for another 24 hours for mortality.

LD_{50} was determined by the formula:

$$LD50 = \sqrt{(a \times b)}$$

Where,
A= the lowest dose that brought death
B= the highest dose that did not kill

2.6 Experimental Design

Twenty-four adult male Wistar rats were weighed and allocated into 4 groups of 6 animals each.

Group A served as control (These animals received only distilled water and guinea feed pellets). The test groups were labelled (B, C, D) for methamphetamine.
Group B received 3mg/kg of Methamphetamine (low dose)
Group C received 5mg/kg of Methamphetamine (medium dose)
Group D received 10mg/kg of Methamphetamine (high dose)
Administration of Methamphetamine lasted for 21 days, after which the animals were sacrificed. All administration was done orally with syringes and oral cannula.

2.7 Termination of Treatment

“The behavioral changes were tested across the four groups of animals to identify the animals that had lost their motor function. Twenty-four hours after the last exposure, following the behavioral test, the animals were weighed, then anaesthetized under chloroform vapour, and the animal skull was dissected by occipito-frontal incision. The brain tissues were harvested from the animals and weighed. The brain tissues of some of the animals were prepared for biochemical analysis through the process of homogenization while the remaining tissues of some of the animals were fixed in 10% Neutral Buffered Formalin for 48hrs and grossed to isolate the brain tissue of interest for histological investigations in the histology laboratory of Anatomy Department, Nnamdi Azikiwe University, Nnewi campus” (Pabba, 2013).

3. BEHAVIOURAL TESTS

❖ Morris Water Maze Test

Method of Morris Water Maze Test:

A 36L water maze basin was filled with water at a temperature of about 26ºC. The escape platform was placed at the center of the pool and exposed one inch above the water surface. This teaches the rat that there is a platform and that it is the way to get out of the water. The animals underwent pre-training and water maze testing.

Pre-training test:

- The video camera was turned on and the rat, handled by the tail, was placed at the edge of the basin for a few seconds and was then pushed into the clear water.
- As soon as it enters the water, the timing starts.
- The time until the rat sought safety and stood on top of the escape platform was recorded.
- After this test, the rat was then removed and dried.
- The rats were given an hour to recover before the water maze testing. Water Maze Test:
- The escape platform was then removed, and milk was added to the water to make it opaque and stirred.
- The video camera was turned on and the rat, handled by the tail, was placed at the edge of the basin for a few seconds and was then pushed into the opaque water.
- As soon as it enters the water, the timing starts.
- The time until the rat seek for safety by crossing the midpoint of the water maze basin where the escape platform was situated was recorded.
- The rat was then removed and dried.
- The data for each group was analysed using ANOVA.

3.1 Biochemical Analysis

The brain tissues were taken to the Biochemistry Department for the analysis of Malondialdehyde (MDA), specific antioxidant capacities (GSH, SOD).

Indication: “MDA has been widely used for many years as a convenient biomarker for lipid peroxidation of omega-3 and omega-6 fatty acids because of its facile reaction with thiobarbituric acid. Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acids peroxidation in the cells. An increase in free radicals causes overproduction of MDA. Malondialdehyde level is commonly known as a marker of oxidative stress and the antioxidant status in cancerous patients. When the MDA level goes up in brain disease conditions, the antioxidants are expected to go down (Pabba, 2013). In the normal in-vivo state glucose and oxygen are the two substrates for energy metabolism in the brain but, glucose is the only significant substrate” (Pabba, 2013).

3.2 Homogenization

One gram of the respective organs was weighed and put into 10ml of 0.9% normal saline each and homogenized with a homogenizer at room temperature. After this, each of the samples was centrifuged at 3000rpm for 20 minutes at room temperature. The supernatant was separated and stored in a refrigerator at 2 degrees Celsius for further analysis.

3.3 Lipid Peroxidation

Lipid peroxidation (LPO) was investigated with the method described by Ohkawa et al., (1979), One millilitre (1mL) of 10% chilled (w/v) trichloroacetic acid (TCA) was added to One millilitre (1mL) of 10% homogenate, incubated at 37°C for 10 min and centrifuged at 2,500 rpm for 15 min at room temperature. One millilitre (1mL) of 0.67% thiobarbituric acid (TBA) was added to 1 ml of supernatant and kept in a boiling water bath for 10-15 min. After cooling, 1 ml of distilled water was added to it and absorbance will be taken at 530 nm. The results were expressed as nmol MDA/h/g tissue.

Non-enzymatic antioxidant: Reduced Glutathione (GSH) was investigated with the method described by Ellman (1959). One millilitre of 5% TCA (w/v) was added to 1 ml of 10% homogenate. The suspension was left for 30 min and centrifuged at 2,500 rpm for 15 min. 0.5 ml of supernatant was taken and 2.5 ml of 5'5'dithionitrobenzoic acid (DTNB) was added. The suspension was shaken thoroughly and read at 412 nm. The results were expressed as µmol/g tissue.

3.4 Enzymatic Antioxidants

Superoxide dismutase: Superoxide dismutase (SOD) was investigated with the method

described by Kakkar et al. (1984). A total of 650 µl of sodium pyrophosphate buffer was added to 50 µl of brain supernatant fraction; 50 µl phenazine methosulfate (PMS), 150 µl of nitro blue tetrazolium (NBT), and 100 µl nicotinamide adenine dinucleotide phosphate (NADPH) was added and the mixture vortexed thoroughly. The reaction mixture was incubated for 90 s and 500 µl glacial acetic acid was added to stop the reaction. Two millilitres of n-butanol was added, and vortexed thoroughly. It was kept at room temperature for 10 min. Absorbance was measured at 560 nm. The results were expressed in terms of µmol/min/mg protein.

Tissue processing: For easy study of sections under a microscope, the tissues were passed through several processes of fixation, dehydration, clearing, infiltration, embedding, sectioning, and staining.

Fixation: Fixation was carried out in 10% Neutral Buffered Formalin (Sodium Phosphate Monobasic 4.0gm, Sodium Phosphate Dibasic 6.5gm, Formaldehyde 37% 100.0ml, Distilled Water 900.0ml). The tissues remained in the fluid for 48 hours. After fixation, the tissues were washed overnight under stream tap water to remove any surplus fixatives.

Dehydration: Dehydration of the fixed tissues was done to remove water and other substances. This was carried out in different percentages of alcohol 50%, 70%, and 95% absolute. In each grade of alcohol, tissues were changed twice for two (2) hours and one (1) hour for each change.

Clearing: The tissues were then cleared in two changes of xylene for two hours to remove the absolute alcohol that was used to dehydrate the tissues thereby replacing the absolute alcohol in the tissues with xylene.

Infiltration: The tissues were transferred to two changes of molten paraffin wax for 2 hours each. It was ensured that the amount of wax was 25-50 times the volume of the tissue. Infiltration was carried out to replace xylene in the tissue spaces with molten paraffin wax. The temperature of the paraffin was kept at 60^{o}C.

Embedding: The tissues were embedded by submerging them in two changes of molten paraffin wax contained in cassette metal moulds at a constant temperature of 52-60^{o}C in an oven of paraffin wax for 2 hours each time. The tissues were well-oriented in the moulds to ensure the presentation of the desired parts of the tissues to be examined in the tissue sections.

Sectioning: This is the process by which a thin slice of the tissue of about 4µm thick is made using a rotatory microtome (Leica RM 2125 RST).

Staining (Hematoxylin & Eosin Staining): Sections were dewaxed using xylene for one (1) minute and then rehydrated by alcohol through descending grades of ethyl alcohol and thereafter washed in distilled water. The sections were stained with Hematoxylin for twenty (20) minutes and differentiated with 2% acid alcohol for two (2) seconds. The acid alcohol was washed off with tap water and the sections passed through running tap water for ten (10) minutes to regain the blue colour. The sections were counterstained in 1% aqueous Eosin for thirty (30) seconds and were dehydrated through ascending grades of ethyl alcohol, cleared in xylene, and mounted using DPX. The sections were then viewed under a light microscope.

3.5 Data Analysis

Data was analysed using the SPSS version 27.0.1 software package. Mean and Standard Deviation were obtained, and one-way analysis of variance (ANOVA) was used to compare values between groups. Data was expressed as Mean + Standard Deviation (SD) and then considered statistically significant when $P < 0.05$.

4. RESULTS

4.1 Physical and Behavioral Changes

At the beginning of the experiments, all animals looked healthy and agile. During the two weeks of acclimatization, their stool was normal. On administration of Meth, varying gradations of toxicity were observed.

Generally, the signs of toxicity observed include:

A. Aggressiveness
B. Decreased appetite.
C. Hyperactivity
D. Staggering
E. Weakness
F. Rearing
G. Grooming

4.2 Analysis of Body Weight

Table 1 showing the effect of Methamphetamine on the body weight of the Wistar rats.

Table 1. The effect of Methamphetamine on the body weight of the Wistar rats

Groups	Weight (g)	Mean± SEM	p-value
Group A	Initial	210.05±0.8	0.044
	Final	235.33±1.76	
Group B	Initial	200.33±0.67	0.001
	Final	190.67±0.88	
Group C	Initial	202.33±0.88	0.001
	Final	196.67±1.20	
Group D	Initial	201.33±0.88	0.001
	Final	192.00±2.00	

Data was analysed using Student dependent T-test and values were considered significant at P<0.05

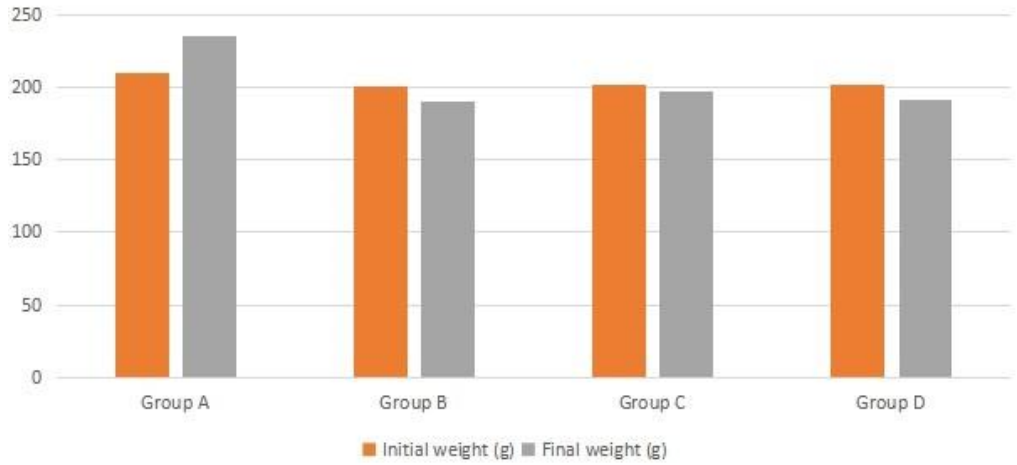

Fig. 1. Effect of Methamphetamine on the body weight

Table 2. The level of oxidative stress that occurred in all 4 groups

	Groups	Mean ± SEM	p-value	F-value
MDA (mm^{-1})	Group A	3.42 ± 0.01		44.160
	Group B	3.5 ± 0.01	0.003	
	Group C	3.64± 0.02	0.000	
	Group D	3.72± 0.06	0.000	
GSH (mm^{-1})	Group A	1.44 ± 0.02		14.246
	Group B	1.40 ± 0.01	0.890	
	Group C	1.30 ± 0.03	0.031	
	Group D	1.25 ± 0.02	0.002	
SOD (mm^{-1})	Group A	8.56 ± 0.02		1336.758
	Group B	7.90± 0.02	0.000	
	Group C	7.54 ± 0.01	0.000	
	Group D	7.33 ± 0.03	0.000	

Data were analysed using One-way ANOVA, followed by Post HOC Fisher's LSD multiple comparisons, and data was considered significant at P<0.05

Table 3. The result of the escape latency time for each group

	Groups	Mean ± SEM	p-value	F-value
Morris Water Maze Test	Group A	16.52±2.93		6.369
Escape latency (Seconds)	Group B	27.20±4.54	0.341	
	Group C	40.25±3.84	0.044*	
	Group D	43.50±11.23	0.002*	

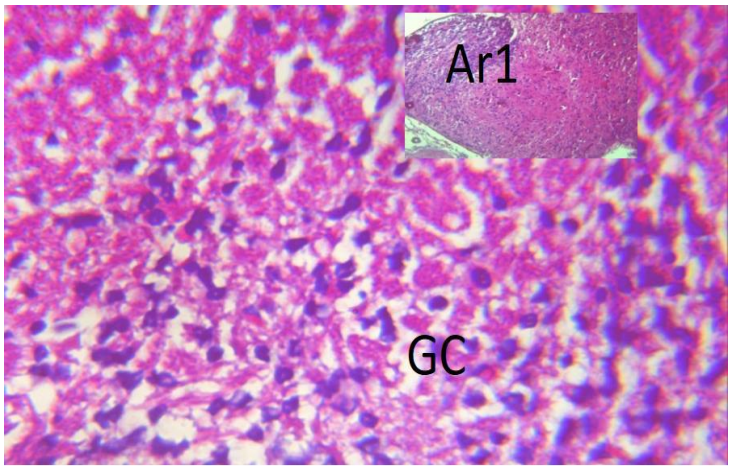

Fig. 2. Photomicrograph of Group A r1 section of amydala

Photomicrograph of group A r1 section of amydala (x100 X400/(H/E) shows numerous aggregate of granular cells and other neuronal cell that are normal.

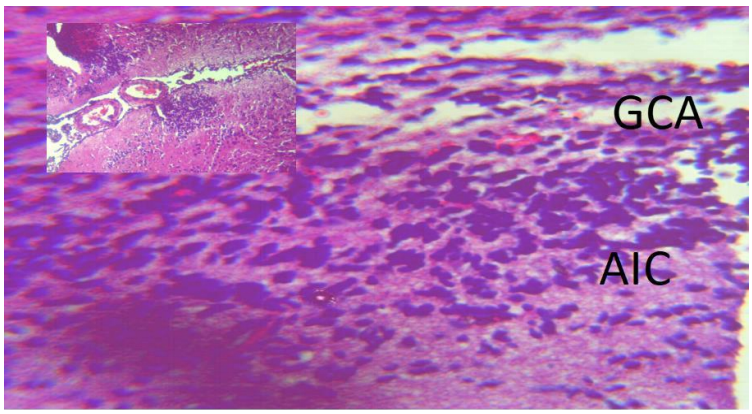

Fig. 3. Photomicrograph of group B section on amydela induced with 3mgkg metamphetanine

Photomicrograph of group B section of amydela indused with 3 mgkg metamphetanine only (x100 x400/(H / E) shows severe degeneration with sever aggregate of inflammatory (AIC) and granular cell attrophy (GCA)

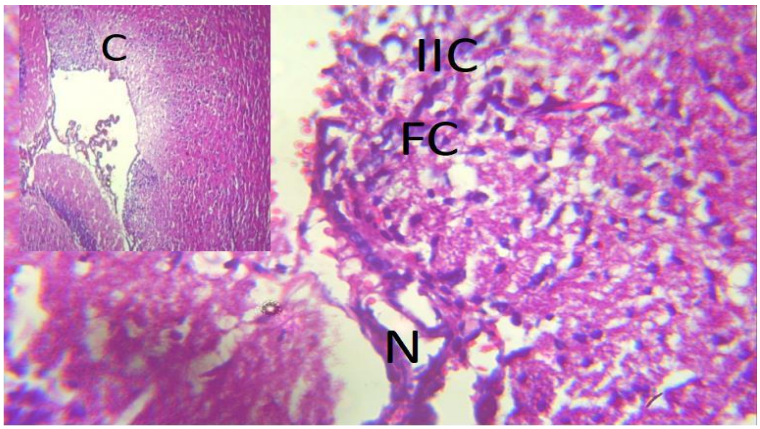

Fig. 4. Photomicrograph of group c section of amydela induced with 5mgkg metaphetanine

Photomicrograph of group C section of amydela inused with 5mgkg metamphetanine only (x100 X400/(H/E) shows moderate to severe degeneration with necrosis (N), moderate fatty change (FC) and infilteration of inflammatory (IIC)

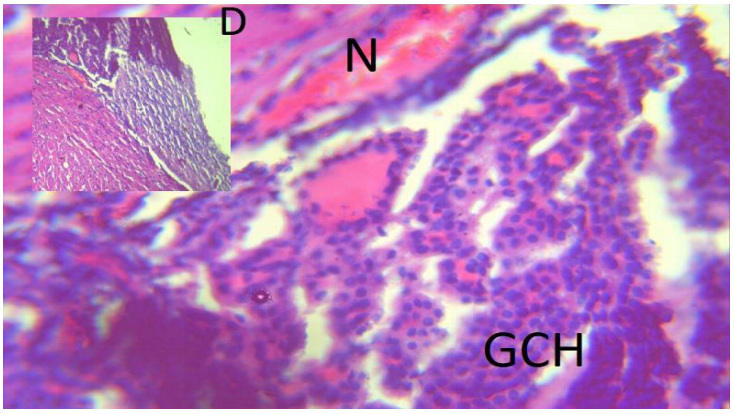

Fig. 5. Photomicrograph of Group D section of amygdala which received 10mgkg methamphetamine

Photomicrograph of Group D section of amygdala which received 10mgkg methamphetamine only (x100 X400/(H/E) shows severe degeneration with severe granular cells hyperplasia (GCH) and focal area of haemorrhage (H)

4.3 Morris Water Maze Test Result

Table 3 showing the result of the escape latency time for each group.

4.4 Acute Toxicity Test (LD_{50}) Result of Methamphetamine

The acute toxicity test of methamphetamine showed varying gradations of toxicity which includes aggressiveness, decreased appetite, staggering, weakness, and activeness, and mortality was also observed. Thus, the LD_{50} is 141.42mg/kg body weight of adult Wistar rats.

5. DISCUSSION

"Methamphetamine has been reported to cause increased activity and talkativeness, decreased appetite and a pleasurable sense of well-being or euphoria. However, Methamphetamine differs from amphetamine in that, at comparable doses, a much greater amount of the drug gets into the brain, making it a more potent stimulant. It also has longer lasted and more harmful effects on the CNS" (Panenka et al., 2013). In this study, observation of body weight difference revealed a significant increase in the body weight of the animals in Group A. "This could be physiological because the only substance they were exposed to was feed and water. A significant body weight decrease was observed in experimental Groups B, C & D when compared to Group A. This could be because methamphetamine have been documented to cause weight loss which is attributed to a few different reasons" (Jaafari-Sheybani et al., 2021).

"Methamphetamine is a stimulant that increases energy levels. When people binge use this drug to avoid the unwanted side effects, it may lead to days without quality sleep. Alongside this constant activity, methamphetamine is also believed to suppress appetite. Regular users may go days without a full meal" (Pabba, 2013).

"There is also evidence to suggest that long-term drug abuse can impact the body's metabolism and ability to store fat, but this discovery still needs further review. Over time, all these factors can lead to drastic weight loss as well as malnutrition from a poor diet when users do eat. As a stimulant, meth makes the body work harder, increasing your heart rate and speeding up your metabolism. At the same time, it suppresses the appetite, turning off the body's hunger response. You lose interest in eating and rapidly lose body mass. The size of your stomach shrinks, further limiting your intake of the nutrients necessary for maintaining good health. Meth also seem to affect triglycerides (where unused calories that provide energy are stored) and glycogen (stored glucose that the body uses for energy). The brain and body work together to ensure one gets enough food automatically. When the body needs fuel (food), it prompts with hunger sensations, which are tied to the brain's reward center. Healthy activities, like eating a nutritious meal, release dopamine, train your brain to remember they made you feel good, and prompt you to repeat them. When taken, meth releases high levels of dopamine into the brain. The flood of dopamine overrides your natural hunger signals causing you to lose your appetite. Meth can also cause dry mouth

and nausea, adding to the disinterest in eating" (Pabba, 2013).

The relative organ weight of Groups B, C & D with Methamphetamine was similar to the relative organ weight of the control Group A. The above report corroborates the fact that there was no pathology detected in the histology of the Wistar rat's amygdala, before the administration of meth within the stipulated period.

The oxidative stress result shows that, there was an increase in Malondialdehyde (MDA) biomarker level in the body which means that there was an increase in pro-oxidants when compared to antioxidants (reactive oxygen species) thus, resulting in an increased level of oxidative stress in experimental Group B (3.53 ± 0.01), Group C (3.64 ± 0.01) and Group D (3.72 ± 0.06) when compared to control Group A (3.42 ± 0.01).

This result shows that there was a disruption in the normal function of the brain cells and their molecular system during the experimental period. This result is in line with the study carried out by Horner et al., (2011) who reported that "treatment with multiple high doses of methamphetamine can induce oxidative damage, including dopamine (DA)-mediated reactive oxygen species (ROS) formation, which may contribute to the neurotoxic damage of monoamine neurons and long-term depletion of DA in the caudate putamen (CPu) and substantia nigra pars compacta (SNpc). Malondialdehyde (MDA), a product of lipid peroxidation by ROS, is commonly used as a marker of oxidative damage and treatment with multiple high doses of METH increases MDA reactivity in the CPu of humans and experimental animals".

For the glutathione (GSH) biomarker, the result shows that there was a significant decrease in glutathione biomarker level in the body which simply means that there was an increased generation of reactive oxygen species with methamphetamine exposure thus, increasing oxidative stress in experimental Group B (1.40 ± 0.01), Group C (1.30 ± 0.03) and Group D (1.25 ± 0.02) when compared to Group A (1.44 ± 0.02). This shows that there was a disruption in the normal function of the brain cells and their molecular system during the experimental period. This is in line with the work of Asensi et al., (1999) who reported that "Methamphetamine interferes with dopamine reuptake, which results in increased dopamine oxidation that creates oxidative stress, which can lead to degeneration of dopaminergic terminals. Previous studies have shown that the trace element selenium protects against methamphetamine toxicity. However, the specific selenoproteins responsible for protection have not been elucidated. According to Imam et al., (1999), 100µm meth decreases GPX1 & GPX4 protein levels, and Glutathione peroxidases 1 and 4 (GPx1 and GPx4) are known for incorporating selenium into the amino acid selenocysteine, and their known antioxidant functions makes them good candidates for protection from methamphetamine-induced oxidative damage. Hence, a reduction in GSH level will result in increased oxidative stress except in cases of increased selenium intake".

For the Superoxide mutase (SOD) biomarker, the result shows that there was a significant decrease in the level of superoxide dismutase biomarker thereby increasing oxidative stress in experimental Group B (7.90 ± 0.02), Group C (7.54 ± 0.01) and Group D (7.33 ± 0.03) when compared to Group A (8.56 ± 0.02). This shows that there was a disruption in the normal function of the brain cells and their molecular system during the experimental period and this is because, the potent antioxidant contained in Superoxide mutase (SOD), which protects the body against oxidative stress was suppressed by meth. According to Imam et al., (1999), 100µm of meth decreases protein levels which serves as an antioxidant that protects the brain against methamphetamine-induced oxidative damage.

The histopathological findings revealed that the Wistar rats representing the control group, administered only feed and water for the period of 3 weeks, showed a control section of the amygdala with normal neuronal and granular cells well represented. Experimental groups B, C & D represent groups administered with low (3mg/kg), moderate (5mg/kg) and high dose (10mg/kg) of meth. The experimental Group B section of the amygdala revealed that there was severe degeneration with severe aggregate of inflammatory and granular cell atrophy.

Experimental Group C section of amygdala revealed that there was moderate to severe degeneration with necrosis, moderate fatty change and infiltration of inflammatory cell. Experimental Group D section of the amygdala revealed that there was severe degeneration with severe granular cell hyperplasia and focal area of hemorrhage. This is in line with a study conducted by Cadet & Krasnova, (2009), who

affirmed that “Methamphetamine (METH) has the potential to disrupt the activities of neurotransmitters in the Central Nervous System (CNS) and cause neurotoxicity through various pathways. These pathways include increased production of reactive nitrogen and oxygen species, hypothermia, and induction of mitochondrial apoptosis. In this study, the long term effects of METH addiction on the structural changes in the amygdala of postmortem human brains was conducted and this finding revealed that METH was found to induce inflammation and neurodegeneration in the amygdala. The continuous use of METH eventually leads to drug addiction and causes serious health complications, including attention deficit, memory loss and cognitive decline. These neurological complications are strongly associated with METH-induced neurotoxicity and neuro-inflammation, which leads to neuronal cell death”. “The current review investigates the molecular mechanisms underlying METH-mediated neuronal damages. Our analysis demonstrates that the process of neuronal impairment by METH is closely related to oxidative stress, transcription factor activation, DNA damage excitatory toxicity and various apoptosis pathways. Thus, we reach the conclusion here that METH-induced neuronal damages are attributed to the neurotoxic and neuro-inflammatory effect of the drug. With all the reported health hazard caused by Methamphetamine, in association with the pathological effect it has on the brain histology as reviewed by this study, it can be stated that there is now a histological proof that further solidifies the findings credited to the negative effect of Methamphetamine on the brain's health” (Chomchai & Chomchai, 2015).

6. CONCLUSION

Methamphetamine caused an adverse histological alteration in the amygdala of the rats at varying dosages employed. This study, in agreement with other works, has been able to reveal that Methamphetamine does not support brain health because distortion in brain tissue was revealed.

7. RECOMMENDATION

This study has helped to establish a neurological and histological standpoint on the effect of Methamphetamine on the amygdala. We hereby recommend that other research should be carried out where methamphetamine is combined with an antioxidant such as ginseng because research has shown that ginseng components have the potential to treat some cognitive deficits and could reduce oxidative stress leading to an enhancement in cognitive function.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval was obtained from the ethical committee, Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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