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ASSESSMENT OF THE EFFECTS OF CANNABIS INGESTION ON LATERAL GENICULATE BODY AND SUPERIOR COLLICULUS OF WISTAR RATS

Desalu A.B.O., *Owolabi J.O., Adeyemo F.O., Olanrewaju A.J. and Olatunji S.Y.

Department of Anatomy, Ben Carson School of Medicine, Babcock University, Nigeria.

***Corresponding Author: Owolabi J.O.**

Department of Anatomy, Ben Carson School of Medicine, Babcock University, Nigeria.

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ABSTRACT

Cannabis is a recreational drug often abused, especially by young people. It is however, classified illegal in many countries of the world. It is worth paying attention to cannabis use among young people because several behavioural and emotional aberrations have been associated with cannabis use. Such effects also vary with dosage, frequency of use and the longevity of the period of use. The current investigation considered the effects of cannabis ingestion on the lateral geniculate body and the superior colliculs in experimental animals- adult Wistar rats. These structures are vital components of the visual pathway; understanding the effects of cannabis ingestion on them might help to understand the possible effects of this psychoactive substance on vision and its pathway especially at its various levels. Twenty-four (24) adolescent Wistar rats were randomly divided into four groups of six rats each labelled A, B, C, and D. Group A animals served as the standard control; Group B animals were adminstered the low dose of cannabis [150mg/kg body weight] Group C were administered the medium dose of cannabis [250mg/kg body weight] while Group D were administered the high cannabis dose [500mg/kg body weight]. All animals were fed *ad libitum* on standard rat pellets throughout the duration of treatment that lasted 21 days. At the end treatment, the animals were sacrificed by cervical dislocation and the brain tissue specimens were excised, fixed in formal saline and processed using the Haematoxylin & Eosin and the Luxol Fast Blue techniques. Cannabis produced observable effects on Superior Colliculus and the Lateral Geniculate Body as reported in this study. The effects were specificically on neuronal morphology, spatial distribution of neurons and glia and neuropil integrity.

KEYWORDS: Cannabis, Lateral Geniculate Body, Superior Colliculus, Wistar Rats, Effects.

INTRODUCTION

Cannabis is used both for recreational and medicinal purposes. Cannabis sativa is commonly called Indian hemp or Cannabis sativa and is popularly known as “Igbo” in Yoruba language.[1] It acts almost entirely on the higher nerve centers.[2] Delta-9-THC is the substance in the plant that produces the "high," feeling of intoxication that users crave.[3]

A lot of studies have shown the effects of cannabis on the major parts of the brain- frontal cortex, hippocampus and cerebellum[4-7] but very few have studied its effects on the visual pathway. The regular use or intake of cannabis causes both psychological and morphological damage on the brain and related organs.[8] These may be presented as prolonged functional disturbance of the visual pathways and this has also been reported after the use of hallucinogenic drugs.[8] Cannabis was reported to have produced toxic effects on the neurons of the visual cortex in rats[9] and modulated sensory or perceptual function in the visual pathway.[10] Previous studies showed that C. sativa has a complex effect on the brain;[11,12] and could affect the visual cortex.[9] Caffeine affects perception senses including visual.[8,13] The specific effects of cannabis on the visual pathway structural integrity is yet to be established;[14] however, it is believed that cannabis could interact with the structures of the visual pathway- including the lateral geniculate body and superior colliculus- because the active ingredients in cannabis include the cannabinoid receptors which are present throughout the visual pathway.[15]

The lateral geniculate body (LGB) and the superior colliculus (SC) are vital components of the visual pathway. The visual or optic pathway is the nervous pathway that transmits impulses from the retina visual center in the cerebral cortex. The visual pathway consists mainly of these components: 1. Optic nerve 2. Optic Chiasma 3. Optic tract 4. Lateral Geniculate Body 5. Superior Colliculus 6. Optic radiation 7. Visual Cortex. The peripheral receptors of light are situated in the retina, a layer of cells at the back of the eye. Nerve fibers arising in the retina constitute the optic nerve. The right and left optic nerves join to form the optic chiasma, in

which many of the fibers decussate to the opposite side. The uncrossed fibers of the optic nerve, along with the fibers that decussated form the optic tract.[16] The optic tract then wraps around the midbrain to get to the lateral geniculate nucleus, where all the axons must synapse. The visual cortex (VC), lateral geniculate body (LGB) and superior colliculus (SC) constitute the intracranial visual relay centers. In mammals, the two strongest pathways linking the eye to the brain are those projecting to the LGB, and to the SC.[17] The primary visual cortex surrounds the calcarine fissure and each primary visual cortex receives information directly from its ipsilateral lateral geniculate body and transmits information to two primary pathways called dorsal and ventral streams.[18] The visual cortex detects the orientation of lines and borders.[19]

It is therefore important to evaluate the effects of cannabis active substances on the various components of the visual cortex towards validating the overall effects on vision. Furthermore, the brain is believed to be more vulnerable to psychoactive agents influences using the developmental stages; especially the juvenile stage of development. The current study is primarily aimed at assessing the histological effects of *Cannabis sativa* on the visual pathway structures- Lateral Geniculate Body, Superior Colliculus of adolescent Wistar rats. It has potential to contribute significantly to knowledge by examining the LGB and SC in the juvenile animal models.

MATERIALS AND METHOD

A total of 24 adolescent Wistar albino rats of both sexes were used for the experiment. They were procured and housed in the animal house of Babcock University, Nigeria. Average weight of rats was 86g. Dried *Cannabis sativa* leaf was obtained from the National Drug Law Enforcement Agency. The leaves were blended using dry blender and used to prepare aqueous extract.[20,21] Regimen was designed based on the literature reviewed and previous pilot studies findings- to modulate human scenarios of cannabis use as low, medium and high doses. Experimental; animals were housed in plastic cages in four groups of six each and given food and water *ad libitum*. Group A (6) Animals were given standard rat chow and clean water; Group B (6) Animals were given 150mg/kg body weight of cannabis sativa; Group C (6) Animals were given 250mg/kg body weight of cannabis sativa and Group D (6) Animals were given 500mg/kg body weight of cannabis sativa. The rats were administered their respective doses of Cannabis sativa using an oral cannula for 21 days. At the end of a 21-day administration, the rats were sacrificed by cervical dislocation. All protocols and ethical practices were duly observed and adequate precautions were taken. The animals were then dissected to excise the brain tissues. The excised organs were immediately fixed in formal saline to preserve and prepare them for tissue processing and slide preparation. Tissues were sectioned and demonstrated using the Haematoxylin and Eosin staining technique[22] and the Luxol Fast Blue[23] techniques. Photomicrographs were obtained using the Accuscope Photomicrographic Set and results were interpreted using qualitative histological principles.[24]

RESULTS

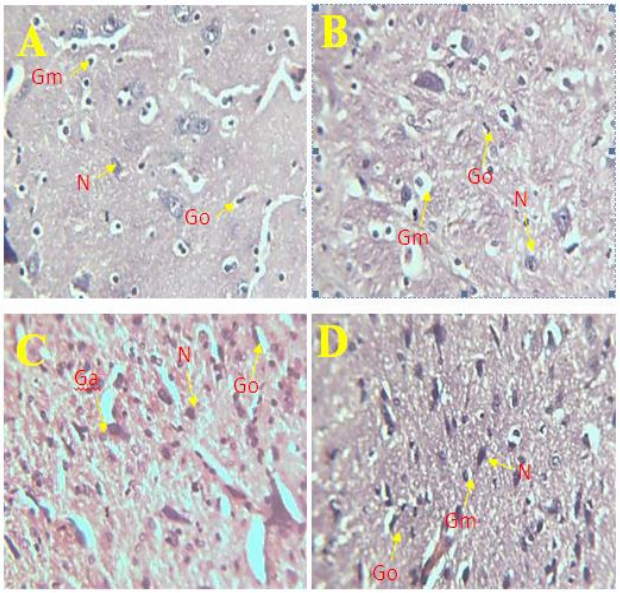

Figure 1: Photomicrographs of the lateral geniculate body of the Animal Groups demonstrating the cortical cells [H&E]. Tissue histoarchitecture is largely preserved; neurons appear morphologically heterogeneous particularly in the Group D that were administered high cannabis dosage. [N= Neurons; Ga= Glia- Astrocyte; Gm= Glia- Microglia; Go= Glia- Oligodendroglia].

Group A animals served as the standard control; Group B animals were adminstered the low dose of cannabis [150mg/kg body weight] Group C were administered the medium dose of cannabis [250mg/kg body weight] while Group D were administered the high cannabis dose [500mg/kg body weight].

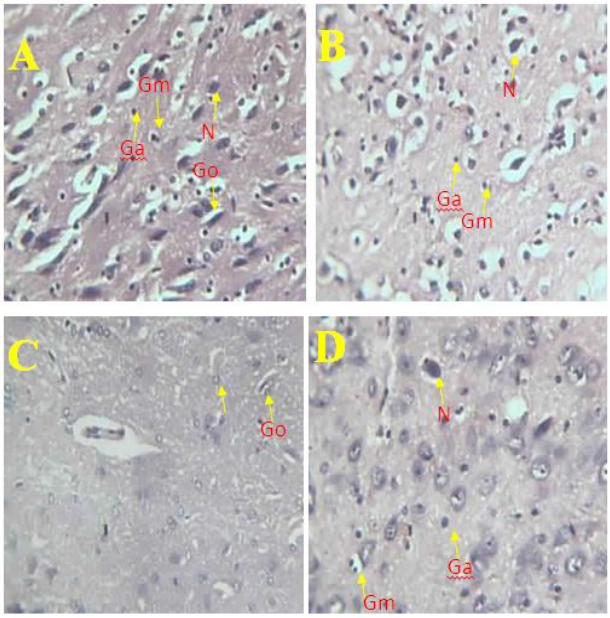

Figure 2: Photomicrographs of the superior colliculus of the Animal Groups demonstrating the cells and neuropil [H&E]. Cortical histoarchitecture is largely preserved; but neurons are ,morphologically heterogeneous in the treated groups. [N= Neurons; Ga= Glia- Astrocyte; Gm= Glia- Microglia; Go= Glia- Oligodendroglia].

Group A animals served as the standard control; Group B animals were administered the low dose of cannabis [150mg/kg body weight] Group C were administered the medium dose of cannabis [250mg/kg body weight] while Group D were administered the high cannabis dose [500mg/kg body weight].

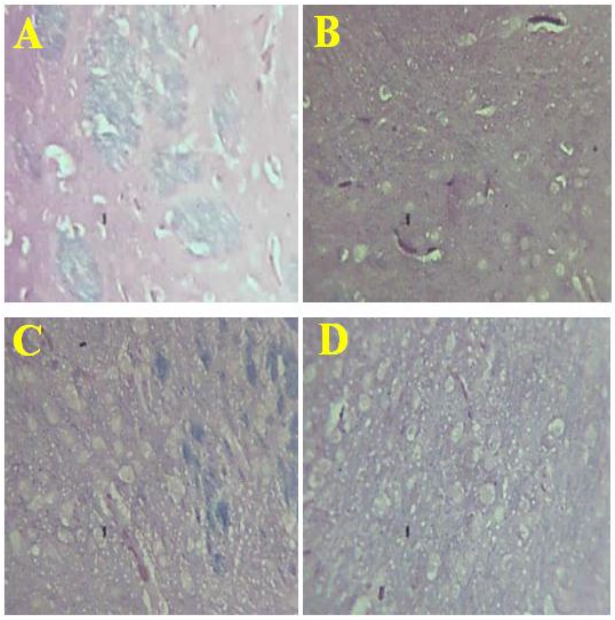

Figure 3: Photomicrographs of the lateral geniculate body of the experimental animal groups [Luxol Fast Blue]. Neuropil is properly demonstrated and there are no signs of extensive damage or disruption. [A, B, C and D are photomicrographs of the lateral geniculate body of the Groups A, B, C and D animals].

Group A animals served as the standard control; Group B animals were administered the low dose of cannabis [150mg/kg body weight] Group C were administered the medium dose of cannabis [250mg/kg body weight] while Group D were administered the high cannabis dose [500mg/kg body weight].

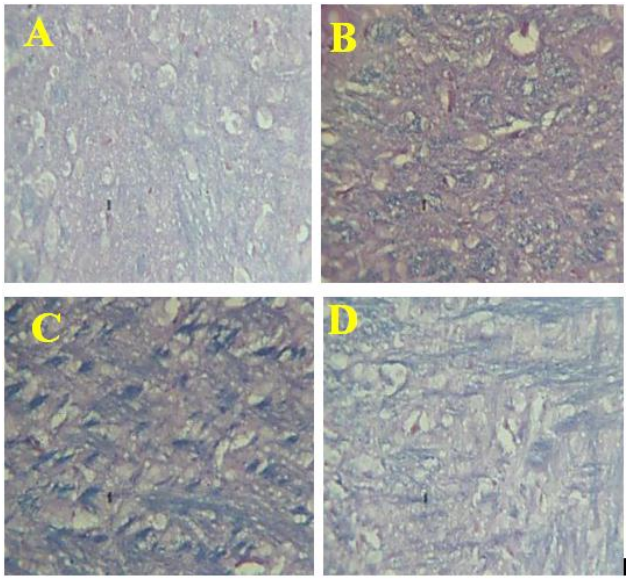

Figure 4: Photomicrographs of the superior colliculus of the Animal Groups [Luxol Fast Blue]. Fibre myelination pattern is largely preserved across the groups without extensive disruption. [A, B, C and D are photomicrographs of the lateral geniculate body of the Groups A, B, C and D animals].

Group A animals served as the standard control; Group B animals were administered the low dose of cannabis [150mg/kg body weight] Group C were administered the medium dose of cannabis [250mg/kg body weight] while Group D were administered the high cannabis dose [500mg/kg body weight].

DISCUSSION

Lateral Geniculate Body Histoarchitecture; Cellular and Myelin Integrity

The histological demonstration of the LGB of the experimental animals is presented in Figure 1. Relative to the normal control group A tissue, the Lateral Geniculate Body of the group B animals appears relatively normal. A few cells show signs of distortion in group C and similar observation is made in group D. This suggests that cannabis administration at higher dose affected cell morphology.

Cannabis as used in this investigation does not grossly alter the histo architecture of the LGB and neurons are relatively preserved without major disrupting to the neuropil. What is however clearly observable is the fact that the morphologies of the cells are affected by cannabis exposure at the higher doses. LGB neurons that are exposed to the highest dose of cannabis are intensely stained and they are morphologically different from the

control Group. This implies that the neurons express morphological heterogeneity. It also therefore implies that high dose cannabis exposure could later neuronal morphologies without necessarily causing cell death or general tissue disruption. It is naturally expected that this effect would also influence the interactions and patterns of communication between the functionally connected cells. More so, this morphological alteration is not a positive sign of neuronal health, and as such could only influence the process of visioning negatively.

Using the Luxol Fast Blue technique to demonstrate myelin integrity of the Lateral Geniculate Body across the experimental animal groups; there is no extensive damage or disruption to the neuropil or pattern of myelination. However, the neuropil is less intact in group C and especially group D when higher doses of cannabis were used. It is logical, therefore, to infer that higher cannabis dose could alter neuropil or myelin integrity though mildly. The highest dose caused reduction in myelination integrity by observing myelin sheath relative abundance as demonstrated. This observation correlates with the morphological results being reported and complements the observations. A primary consequence of the cellular morphological distortions that caused heterogeneity will be poor myelination in this group. This further emphasised the fact that neuronal communication would be limited in this animal group. This is a negative sign about visual pathway integrity at the level of LGB.

Superior Colliculus Histoarchitecture; Cellular and Myelin Integrity

The histoarchitecture of the superior colliculus across the superior colliculus across the animal groups (Fgure 3) also shows that the effects of cannabis on this structure is also dose-dependent. While a few cells appear heterogenous in group B with large pericellular spaces. Many are also poorly demonstrated in group C and neurons are typically heterogenous in group D. Altogether, cannabis influences neuronal morphologies and spatial distribution in the Superior Colliculus.

Cannabis at the higher doses [Groups C and D] had negative effects on neuronal morphology. It is observable that neurons are less prominently demonstrated when the medium and high doses of cannabis were administered to the animals. This observation also suggests that cannabis exposure also alters neuronal morphology in the SC with the possibility of causing localized neuronal death. High dose cannabis is therefore unhealthy for the visual pathway especially at the level of the SC. This result showed that cannabis has the potential to cause neuronal cum structural integrity compromises at the higher centers of the visual pathway. Taken, altogether, high dose cannabis exposure is deleterious to the SC by causing morphological distortions of the cells and instances of localized cell or tissue damage.

Cannabis high dosage caused reduction in myelin integrity demonstration relative to the control. Cannabis treatment therefore negatively affected the integrity and abundance of myelination in the SC. Consequently, this would affect the transmission of impulses along the nerve fibre and could negatively affect the quality of sight or mechanism of visioning.

Cannabis has been previously reported to affect vision and vision-related structures. Cannabinoids have been reported to have potentials to modulate, influence or even alter visual processes.[15] Cannabis ingestion reportedly caused degeneration of the neurons of occipital cortex, right lateral geniculate nucleus and right superior colliculus of Wistar rats.[1] These current findings are in line with these previous reports. The results also confirm the previous work of Schwitzer *et al.*, 2014,[15] that cannabis affects structures of the visual pathway.

CONCLUSION AND RECOMMENDATION

Cannabis produced observable effects on the Superior Colliculus and the Lateral Geniculate Body as reported in this study. The effects are specifically on neuronal morphology, spatial distribution of neurons and glia and neuropil integrity. The effects are dose-dependent, however, not generally extensive. It is therefore recommended that further investigation should be conducted to examine the roles of dosage variation relative to cannabis use and consequently its effects and safety.

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