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Original Article

Effect of Screen Time on Biogenic Amines, Gross Behavior and Histological Conditions of Rat's Brain

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ABSTRACT

Neurotransmitters and hormones work together in a complex way in the body to control mental and physical processes. **Objective:** To focus on dopamine, a crucial neurotransmitter produced by mesencephalic neurons in both the brain and peripheral organs. **Methods:** The study was conducted on albino rats weighing 180-200 gm. The rats were introduced into the new apparatus designed with the measurements of 40 x 40 cm in length, 25 x 25 cm in breadth, and 30 cm in height on all four sides. All sides were painted black except one mounted with (Light Emitted Diode) LED display. Rats were shown the screen for 1 hour daily for 30 minutes with high pixel resolutions and bright colors. The tested group was then compared with the control group on the 30th day on the parameters of gross behavior, biogenic amines of brains, and brain histopathology. **Results:** The results showed anxiety and hyperactive behavior in gross studies. Biogenic amines showed an increase in 2-amino 5-methyl benzoic acid that is the dopamine precursor. The study indicated that low levels of pyrrolidine, which decreased (Gamma Aminobutyric Acid) GABA in the brain, ultimately caused sleep disorders. Histopathological studies also showed the degeneration of neuronal cells in tested brains compared to control. **Conclusions:** The changes found in rats might be useful in determining the drawbacks of using mobiles, tabs, and other screen time.

INTRODUCTION

The human body is a fascinating and complicated entity comprising several interrelated systems and structures. Catecholamines, such as epinephrine, norepinephrine, and dopamine, are essential neurotransmitters and hormones that control several vital biological processes. The primary neurotransmitter on which this investigation will center is dopamine. An amino acid base is transmitted by mesencephalic neurons in the brain and other peripheral organs such as the kidney, pancreas, lungs, and blood vessels [1]. In the central nervous system, dopamine is involved in various vital processes such as movement, memory, pleasurable rewards, behavior and cognition, attention, sleep, inhibition of prolactin production, mood, and learning. However, its role in reward-related behavior receives much attention because of its significant role in causing psychological problems, including addiction, depression, and anxiety [2]. Many things may trigger dopamine release, including past events, stress, and even some medications. Five distinct dopamine receptors are distributed throughout the brain. These receptors are classified into two groups according to their structural and G-protein coupling characteristics [3]. Studies suggest high dopamine levels can lead to addictive behavior towards certain stimuli and reduce dopamine release for other tasks. When the body is subjected to a stimulus of great intensity, such as food [4], the use of sucrose alone

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has been shown to enhance dopamine levels [5]. However, several elements contribute to an unbalanced DA level. An increase in dopamine can lead to excessive movement, psychosis, hyper sexuality and nausea [6]. In contrast, a decrease in dopamine levels may lead to depression and Parkinson's disease [7]. An inability to experience pleasure, Attention Deficit Hyperactivity Disorder (ADHD), procrastination, sleep issues, mood swings, hopelessness, memory loss, and low concentration [8]. Dopamine is not entirely responsible for depression, but it is one of the factors that contribute to it, given all of the harmful effects of low dopamine. Researchers still do not know what exactly triggers depression, but they suspect a combination of hereditary, environmental, and psychological variables. On the other hand, neurotransmitter abnormalities —particularly those affecting dopamine, serotonin, and norepinephrine—are generally believed to have a role in the development of depression [9]. Low dopamine impacts mood, memory, motivation, and behavior; as a result, it can lead to feelings of hopelessness and sleep issues, which are depressive symptoms.

The objective of our current research is centered on the hypothesis that visual stimulation raises dopamine levels in the brain. Dopamine is a crucial player in how we react to visual stimulation, and research has shown that specific colors, such as green, blue, and red, and music can boost this neurotransmitter's release. TV shows, music videos, social media applications, and video games are just a few examples of the various media that have emerged as the world has progressed; some of these media use specific colors and sounds to grab viewers and raise their dopamine levels. Children watching movies, which frequently include vibrant colors and loud music that raises dopamine levels and induces addictive behaviors, raise the specter of this being especially problematic . Children can get anxious and unable to complete other tasks effectively when deprived of this stimulation. In addition to impairing cognitive abilities, screen dependence may lead to psychological problems like ADHD and depression-like symptoms such as insomnia, mood swings, procrastination, cognitive deficit, and low motivation.

METHODS

The study was conducted on albino rats of both genders weighing an average of 180-200gm, obtained from the animal shelter of Dow University of Health Sciences (DUHS) and acclimatized in the animal house of the Institute of Pharmaceutical Sciences Jinnah Sindh Medical University (IPS, JSMU) under the supervision of a trained and well-experienced personnel. The animals were divided into two groups of n=8 rats and assigned numbers 1 to 4.

When handling animals, the methods outlined in the Helsinki Resolution of 1964 were observed. Rats were continuously monitored to ensure that food, water, and all other environmental conditions, such as humidity and temperature, were constant at 25°C and 50–60%, respectively. A 12-hour day/night cycle was also correctly taken into account.

Apparatus Designed

For this experiment, new equipment was created, consisting of a rectangular compartment with measurements of 40 x 40 cm in length, 25 x 25 cm in breadth, and 30 cm in height on all four sides. The box had a visual display mounted on one side, and to prevent any excess light, the polyphenylene material was painted black on three sides and the lid of the apparatus. The equipment was situated in a dark location for better observation and to reduce distractions, while the upper roof was translucent with holes for excellent ventilation.

Model Development

The tested group (n=8) was placed in the experimental apparatus for one hour daily in the morning at a specific time for 30 days. Videos with high-quality pixels and colors were played on the screen, while the control group was kept in their typical habitat in the department's animal house.

Gross Behavior of Rats

Gross behavior is when rats were observed. General behavior, movement patterns, interactions with the environment, and social relationships were all aspects of rodent behavior that were studied. Gross behavior was noted on 30th day in both the control and affected group. The gross behavior was noted by both the groups separately in glass box. Different acts of rats like grooming, writhing, tremors, twitches were observed manually by observer's eye .

Histopathology of Brain

The rats were sacrificed on the 30th day, and their brains were submitted to the Dow laboratory for gross inspection. Slides were made to observe the neuronal changes in the brain.

Liquid Chromatography for Biogenic Amines

Biogenic amines are often separated using liquid chromatography techniques that differentiate these molecules according to their specific chemical characteristics, including polarity, size, and charge. HPLC is a commonly used method for the analysis of biogenic amines. This process utilizes a high-pressure pump to propel a liquid solvent (the mobile phase) containing the sample through a chromatographic column filled with a stationary phase . The various biogenic amines present in the sample exhibited distinct interactions with the stationary phase, resulting in their separation. It is possible to quantify each amine present in the sample by using the area and the area percentage. Larger areas and area

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percentages indicated that the corresponding amines are present in larger concentrations. The characteristics useful to detect biogenic amines are retention time, area and area percentage. Retention time is the duration it takes for a substance to go through the chromatographic column and exit from it. The area refers to the highest point of a compound's chromatographic peak as measured by the detector. It quantifies the quantity of the component in the sample. The greater the magnitude of the region under the peak, the more concentrated the component is in the sample. Area Percentage refers to the proportion of the overall peak area that is occupied by a single compound's peak. It is also known as relative area or relative abundance. The calculation involves dividing the area of the compound's peak by the total area of all peaks in the chromatogram, and then multiplying the result by 100. For the extraction, 5 mL of perchloric acid was used to homogenize the brains. The samples were continuously shaken every ten minutes while being chilled for an hour. The mixture was then centrifuged at 1000 g for 10 min at 4 °C after being filtered using Whatman filter paper (180 m thickness and 11 m particle retention rating at 98% efficiency). The mobile phase acetonitrile of the subsequent solution put into the HPLC: water 42:5

RESULTS

Gross Behavior of Rats

The gross behavior of control and affected rats showed remarkable increase in grooming, rightening reflex, aggression, dizziness, urination and defecation as compare to control group. While it was also noted that there was no evidence of ataxia, staggering gait, writhing, tremors, twitches, nystagmus, ptosis, miosis or mydration and salivation as compare to control.

Table 1: Gross Behavior of Control and Affected Rats

Activities	Control	Test Animal
Effect on CNS		
Grooming	++	++++
Ataxia Gait	-	-
Staggering gait	-	-
Writhing	-	-
Tremor	-	-
Twitches	-	-
Rightening reflex	+	+++
Nystagmus	-	-
Ptosis	-	-
Aggression	-	++++
Dizziness	-	++
Effect of ANS		
Miosis /Mydiasis	-	-
Urination	++	++
Salivation	-	-
Defecation	-	++++

Liquid Chromatography for Biogenic Amines in Control and Affected Brains

The biogenic amines of control and affected brain showed noticeable changes. 2- amino 5-methyl benzoic acid showed low percentage area that is 9.46% as compare to control which shows 20.41%. However, 9-octadecenoic acid showed increase in area percentage 6.29% as compare to control. 5-hydroxydopamine and 2-pyrrolidine showed decrease in area percentage as compare to control.

Table 2: Biogenic Amines of Control Group

Name	Retention time	Area (%)
2- amino 5-methyl benzoic acid	3.683	9760886 (20.41)
9-octadecenoic acid	7.627	569893 (1.19)
5-hydroxydopamine	5.498	112296 (0.23)
2-pyrrolidine	4.425	1309274 (2.74)

Table 3: Biogenic Amines of Affected Brain

Name	Retention time	Area (%)
2- amino 5-methyl benzoic acid	3.585	10360827 (9.46)
9-octadecenoic acid	7.608	5564188 (6.29)
5-hydroxydopamine	5.480	177241 (0.16)
2-pyrrolidine	4.405	1203924 (1.36)

Figure 1 shows the graph of 2- amino 5-methyl benzoic acid with the chemical structure, retention time, area, area percentage and peak value of both the control and affected brain.

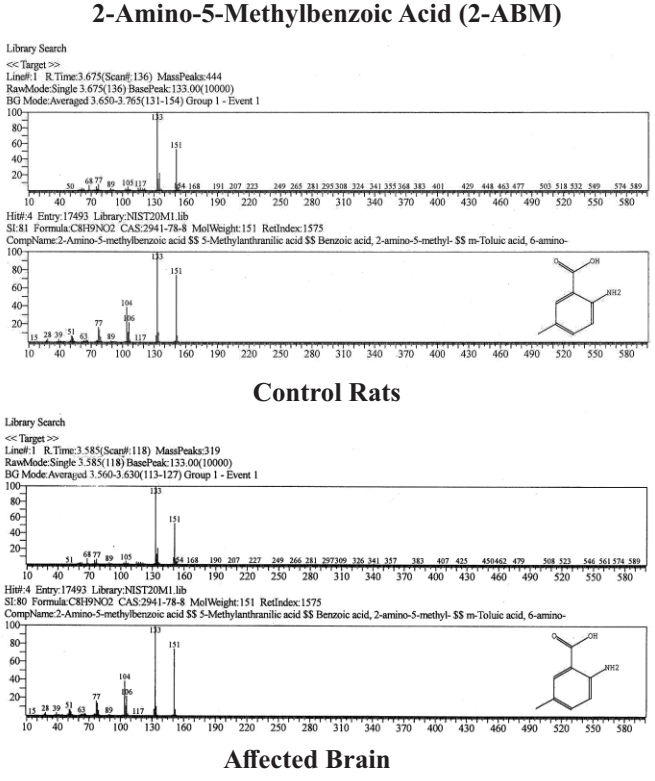

Figure 1: Chromatogram of 2-Amino-5-Methylbenzoic Acid (2-ABM) in Control and Affected Rat's Brain

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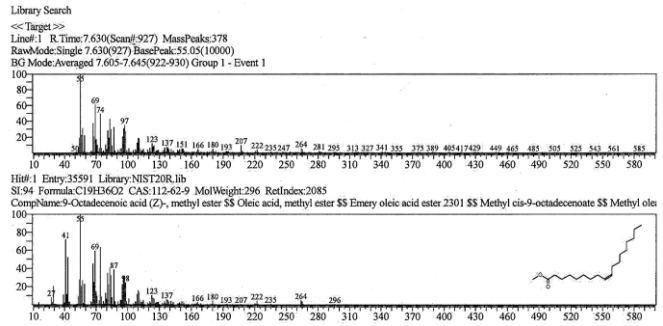
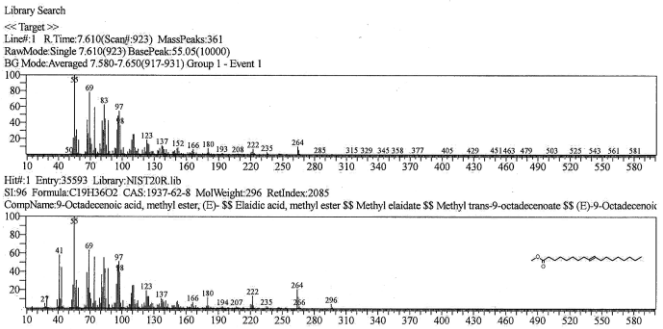
Figure 2 shows the graph of 9-Octadecenoic Acid with the chemical structure, retention time, area, and area percentage with peak value of both the control and affected brain.

9-Octadecenoic Acid (Oleic Acid)



Control Rats

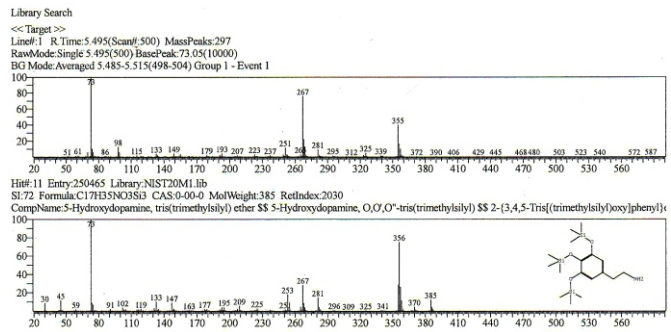


Affected Brain

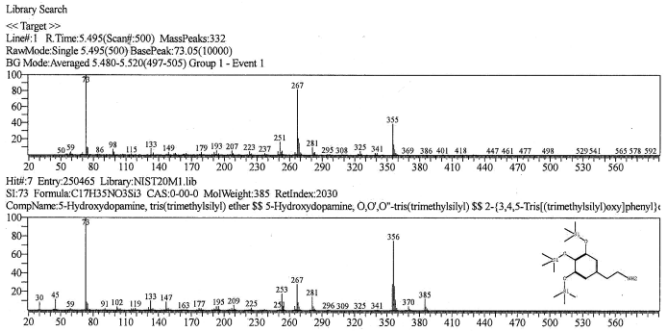
Figure 2: Chromatogram of 9-Octadecenoic Acid (Oleic Acid) Graphs in Control and Affected Rat's Brain

Figure 3 shows the graph of 5-hydroxydopamine with the chemical structure, retention time, area, and area percentage with peak value of both the control and affected brain.

5-Hydroxydopamine (5-OHDA)



Control Rats

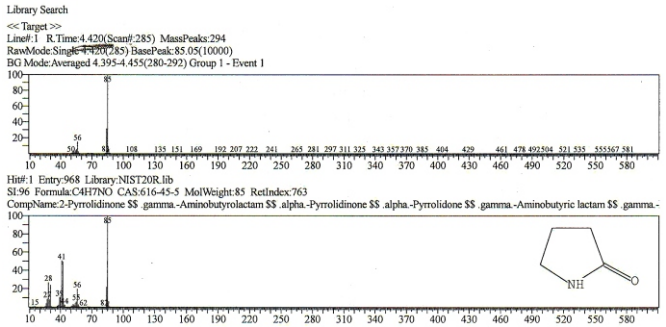


Affected Brain

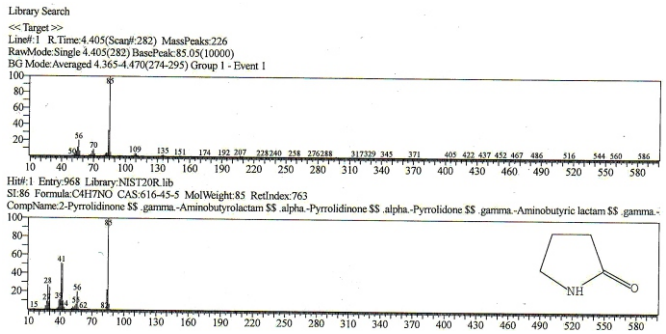
Figure 3: Chromatogram of 5-Hydroxydopamine (5-OHDA) in Control and Affected Rat's Brain

Figure 4 shows the graph of 2 pyrrolidine with the chemical structure, retention time, area, and area percentage with peak value of both the control and affected brain.

2-Pyrrolidine



Control Rats



Affected Brain

Figure 4: Chromatogram of 2 Pyrrolidine in Control and Affected Rat's Brain

Histological Evaluation of Rat's Brain

The histological evaluation of control and affected brain slides exhibited a significant alteration. The degeneration of the nucleus is readily apparent in the affected brain slide. The molecular layer indicating with red arrow is also not apparent in the affected brain. Additionally, it has been shown that the number of apoptotic cells indicating with black arrows is higher compared to the control group.

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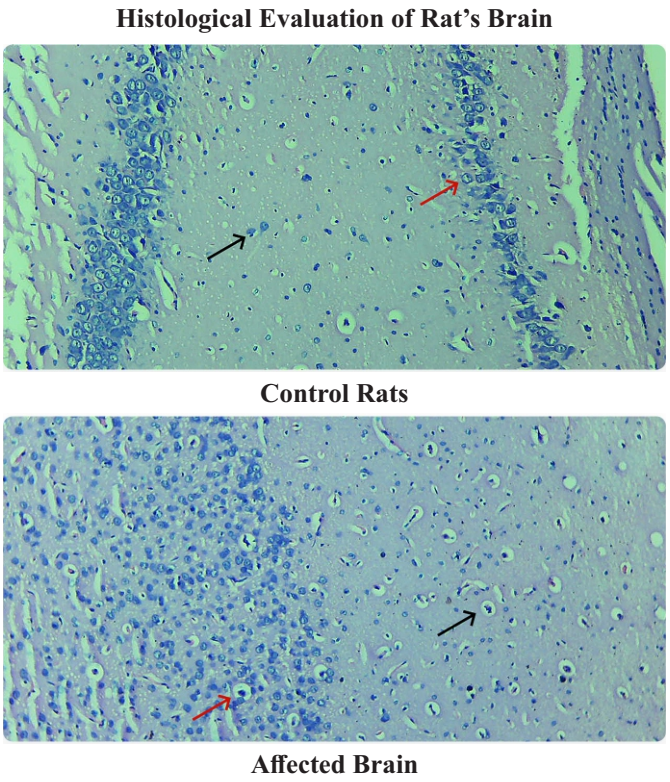

Figure 5: Histological Evaluation of Control and Affected Rat's Brain

DISCUSSION

This study on screen time showed some remarkable results, which indicated that it affects major neurotransmitters in the brain, which results in anxiety and stress and can also lead to depression. There was a decrease in 2-amino-5-methylbenzoic acid (2-ABM) levels in the brains of screen-exposed rats. This is a dopamine precursor. The enzyme aromatic L-amino acid decarboxylase (AAAD) is responsible for converting 2-ABM to dopamine in the brain. Animal studies have shown that 2-ABM raises brain dopamine levels [19]. The screen-affected brains also showed low levels of 2-pyrrolidine. This is responsible for decreased levels of GABA, which causes anxiety, stress, depression, and also problems in learning and memory. GABA low levels also cause sleep disorders, which is also the main problem of children who have high screen time [20]. Another chemical found in our study of the affected brain is 5-hydroxydopamine, which induces the down-regulation of dopamine receptors. 5-OHDA is a chemical that destroys nerve cells that use dopamine as a neurotransmitter. When 5-OHDA is taken up by nerve cells, it is stored in the same vesicles as dopamine [21]. However, when 5-OHDA is released, dopamine receptors do not pick it up and cannot send signals. Instead, it damages the nerve cell and eventually kills it. Reduced brain dopamine levels result from the loss of neurons that produce dopamine. Anxieties, stiffness of the muscles, and slowed movement are symptoms of Parkinson's disease, a neurological ailment that may develop when dopamine levels drop. The degeneration of brain cells that produce dopamine is the underlying cause of Parkinson's disease. Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental condition defined by impulsivity, hyperactivity, and inattention; it is more common in children who spend much time in front of screens [22]. It is also observed in our study that the affected brains have high levels of oleic acid, also known as 9-octadecenoic acid. This increases the dopamine levels in the brain. This high level of dopamine causes aggressive attitudes in both children and adults. Poor impulse control also causes serious mental and physical issues in young and adult people [23]. The gross behavior of rats showed an aggressive attitude, which may be because of the presence of oleic acid in the affected brain. Gross behavior also showed hyperactivity in rodents which is also due to the presence of oleic acid [24]. Histopathological examination revealed degeneration in the nucleus and apoptosis in screening-affected brains, which indicates that neuronal cells may die as a result of prolonged exposure to electronic screens [25]. Thus, results showed that screen time is highly harmful in rats. There is growing data that suggests that excessive screen usage can contribute to anxiety. Long-term exposure to disturbing content, the impact of social media on self-esteem, altered sleep patterns due to blue light emission, and less face-to-face contact can all lead to an elevated sense of anxiety [26].

CONCLUSIONS

This research has determined the detrimental impact of screen time on rats' brains and neurotransmitters, revealing the adverse consequences of screen use in both young individuals and adults. Additional investigations are necessary to strengthen the evidence supporting this study.

Authors Contribution

Conceptualization: HA, KR
Methodology: ZF, RR, JI
Formal analysis: HA
Writing-review and editing: RM, SS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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