**Toxicological Examination of Dopamine's Involvement in Substance Abuse: An Overview**

# *Abstract*

*Dopamine is an organic chemical of the catecholamine. It shows the reward action and regulation in brain. it show the repeat pleasurable activities .The release of dopamine in the brain (striatum, accumbens etc.) as neurotransmitter and it absorb through the receptor by neurone . We summarise the dopamine release and its role .We also discuss the side effects of drug abuse and some treatment (for the control of dopamine release). The objective of this review is to overcome the action of dopamine and its releasing sites. Also show the dopamine role in drug abuse. the incensement of rate of dopamine also produce the reinforcing effect of drug abuse .*

**Key words: -** reward , reinforce , dopamine, receptor, drug.

# Introduction:-

 Dopamine is the neurotransmitter.it has been classically associated with reinforcing effect of drug abuse. Addictive use of drug for non medicinal purpose , and show the behavioral changes due to release of dopamine[1][2][3]. Dopaminergic neurones in human brain synthesize and release the neurotransmitter dopamine[4].Dopamine D2 receptor are the auto receptor.It is also known as the target of antipsychotic drug[5,6,7,8,9].The increasement of rate of dopamine is responsible for the reinforcing effect of drug abuse it regulate the function of dopamine neurones. This receptor also present in central nervous system, kidney, vascultarate and pituitary gland. It mainly regulates the neuroendossive secretion.[10,11,12,13,14] The production of dopamine takes place in the ventral tagemental area.Dopamine D2 receptor are ligand sensitive.When rate of dopamine increase occurs to conditioned stimulation in human subject addiction.In some addiction, the inhibition of dopamine therapeutically beneficial e. g. addiction of cocaine drug. dopamine cells fire in response to silent stimuli and their activation by drugs will be experienced as highly silent[15,16,17,18]. The degeneration of dopamine and its imbalance in the striatum .It has been directly related to the clinical akinesia of this disease.The activation of D2 receptor has opposite effect on these striatal neurones and consequently dopamine function Psycho stimulant increase the availability of dopamine it support transient hyper activation as unifying hypothesis of abused drug dopamine and CAMP regulated phosphoprotein Mr.32kDs ( DARPP-32) is a key modulator of drug abuse.The high dopamine state or level to initiate the reinforcing effect of drug abuse Implications of dopamine receptor in numerous physiological functions produces unwanted effects Drug abuse hijack the reward system by increasing the dopamine concentration in the striatum but especially in the accumbens[18,19] addictive drug modulates the properties of dopamine neuron , it alters the dopamine dependent behaviors related to the drug abuse .

 The development of dopamine cell bodies in the VTA to limbic structure such as the amygdala ventral pallidum, hippocampus and nucleus accumbens and cortical areas these are play different role in different addiction Drug abuse having different categories like narcotics, cannabinoids, depressants stimulants, hallucinogens Wise proved in1996 an enhancement in meso- corticolimbic dopamine activity is the one of the common feature of drug abuse All addictive drug produces an enhancement of extracellular DA level in nucleus accumbens[20,21,22]. Dopamine must consistently linked to cocaine abuse related effects Cocaine, heroin, methamphetamine, marijuana, alcohol, nicotine, amphithetamine , opioids these are substance include in drug abuse[23,24,25].

**Pharmacology of dopamine in drug of abuse:-**Dopamine are the chemical , it transmit the neurone. The actual function of addictive drug - used ever develop compulsive drive to taking the drug . Reduction of D2 receptor as well as the decresement of dopamine release in dorsal striatum, decrease the natural reinforce. The liberation of dopamine within the dorsal striatum and nucleus accumbens it produces the reinforce effect.[26]

The synaptic incresement of dopamine occur during intoxication in drug abuse. Dopamine also modulates the activity of hippocampus, which are region implicated in memory, conditioning, and habit formation. dopamine involved with prediction of reward [2728,29,30,31].

# Action of dopamine in brain for the drug of abuse :-

1. Drug abuse cause the release of dopamine in ventral striatum the activation of D2 receptor inhibits the reward system
2. In the dorsal striatum release of dopamine through the d2 receptor increase the neurotransmission in limbic area and neuronal accumbens
3. The increasement of dopamine in nucleus accumbens show the reinforcing effect of drug abuse
4. The movement of dopamine level in the dorsal striatum it shows the affect the activation behaviour.[32]

# Drug and its action:-

* 1. Methanol drug enhancing the effect on nicotine induced dopamine release in the nucleus accumbens it change midbrain dopamine function by altering DARPP-S2 signalling in this could reverse drug abuse.
	2. N- acetylcysteine which decrease DLC dependent cue- controlled cocaine seeking habits also disrupts the heroin seeking habits
	3. Benzodiazepines and barbiturates increases the dopaminergic neuron firing the VTA which underlies their reinforcing effects .[33]
	4. Morphine, heroine and fentanyl increasing the dopamine in nucleus accumbens , which underlies their reinforcing effects.[34]

# Side effects due to drug abuse:-

Drug abuse is dangerous to human. Cause dopamine to flood the reward pathway. It also cause following common side effects.

* Heart attack
* Vomiting
* Incresement of heart rate and blood pressure
* Anxiety and agitation
* Health problem ( include mental health)

# Conclusion: -

Dopamine, a neurotransmitter, plays a subtle yet crucial role in the realm of drug abuse. While its presence may not be as pronounced as other neurotransmitters, such as serotonin or norepinephrine, it exhibits a reinforcing effect that contributes significantly to the addictive nature of substances. Understanding this role is essential for fostering informed decision-making among citizens.

Proper dissemination of information regarding dopamine's involvement in drug abuse is paramount. Citizens need to be educated about the intricate interplay between neurotransmitters and addictive substances, shedding light on the neural mechanisms that underlie the reinforcing effects. This knowledge empowers individuals to make informed choices and better comprehend the potential consequences of substance abuse.

The prohibition of drugs of abuse becomes imperative when considering their detrimental impact on health. Substance abuse not only perturbs the delicate balance of neurotransmitters like dopamine but can lead to severe physical and mental health consequences. Prohibiting these substances is a preventive measure aimed at safeguarding public well-being and curbing the societal burden of addiction-related issues.

In conclusion, recognizing the nuanced but vital role of dopamine in drug abuse underscores the importance of comprehensive public education. Empowering citizens with accurate information enables them to make informed decisions and contributes to the broader effort to mitigate the adverse effects of substance abuse on individual and public health. Prohibition serves as a necessary step in preserving the well-being of society at large

# References

1. ."Dopamine in Drug Abuse and Addiction: Results of Imaging Studies and Treatment I[mplications | Psychiatry and Behavioural Health,JAMA](https://jamanetwork.com/journals/jamaneurology/fullarticle/794743) [Neurology](https://jamanetwork.com/journals/jamaneurology/fullarticle/794743)

[JAMA](https://jamanetwork.com/journals/jamaneurology/fullarticle/794743) Network " https://jamanetwork.com/journals/jamaneurology/fullarticle/794743

1. . Methamphetamine abuse disturbs the dopaminergic system to impair hippocampal- based learning and memory: An overview of animal and human investigations
2. ." The Role of Dopamine and Its Dysfunction as a Consequence of Oxidative Stress Hugo Juárez Olguín, 1 , 2 , \* David Calderón Guzmán, 3 Ernestina Hernández García, 1 and Gerardo Barragán Mejía 3 Author information Article notes Copyright and License information PMC Disclaimer
3. ."Drugs, Brains, and Behaviour: The Science of Addiction: Drugs and the Brain | NIDA" [https://nida.nih.gov/publications/drugs-brains-behavior-](https://nida.nih.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain) [science-](https://nida.nih.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain) [addiction/drugs-brain](https://nida.nih.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain)
4. . The tonic/phasic model of dopamine system regulation and its implications for understanding alcohol and psychostimulant craving A Grace 1
5. . The neurocircuitry of addiction: an overview .M W Ellenstein 1, R E See
6. . Heroin seeking becomes dependent on dorsal striatal dopaminergic mechanisms and can be decreased by N-acetylcysteine Ritchy Hode Bourg 1, Jennifer E Murray 2, Maxime Fouy ssac 3, Mickaël Puaud 3, Barry J Everitt 3, David Belin 3
7. . National Institute on Drug Abuse (NIDA)
8. . Phasic Dopamine Release in Appetitive Behaviours and Drug Addiction Authors: Wanat, Matthew J.; Willuhn, Ingo; Clark, Jeremy J.; Phillips, Paul E.M. Source: Current Drug Abuse Reviews, Volume 2, Number 2, 2009, pp. 195-213(19) Publisher: Bentham Science Publisher
9. Illicit dopamine transients: Reconciling actions of abused drugs Trends in Neurosciences April 2014Dan P. Covey Mitchell F. Roitman Paul A. Garris
10. Molecular insights into GPCR mechanisms for drugs of abuse Journal of Biological Chemistry18 August 2023Omar B. Sanchez-ReyesGregory ZilbergDaniel Wacker
11. Human Immunodeficiency Virus (HIV) Infection of Human Macrophages Is Increased by Dopamine: A Bridge between HIV-Associated Neurologic Disorders and Drug Abuse The American Journal of PathologySeptember 2009 Peter J. GaskillTina M.

CalderonJoan W. Berman

1. Methamphetamine abuse disturbs the dopaminergic system to impair hippocampal-based learning and memory: An overview of animal and human investigations Neuroscience C Biobehavioural Reviews1 October 2021 Mayuri Shukla Bruno Vincent
2. Alteration of dopamine receptors subtypes in the brain of opioid abusers: A postmortem study in Iran Neuroscience Letters20 November 2018 Mitra-Sadat Sadat- ShiraziMohammad-Reza Zarrindast Nasim Voussoir
3. Role of dopamine in drug reinforcement and addiction in humans: results from imaging studies ND Volkow, JS Fowler, GJ Wang - Behavioural pharmacology, 2002 - journals.lww.com
4. Imaging dopamine's role in drug abuse and addiction ND Volkow, JS Fowler, GJ Wang, R Baler, F Telang - Neuropharmacology, 2009 – Elsevier
5. Dopamine receptor 1 neurons in the dorsal striatum regulate food anticipatory circadian activity rhythms in miceChristian M Gallardo1†, Martin Darvas2†, Mia Oviatt1, Chris H Chang3, Mateusz Michalik4, Timothy F Huddy5, Emily E Meyer3, Scott A Shuster1, Antonio Aguayo5, Elizabeth M Hill5, Karun Kiani3, Jonathan Ikpeazu1, Johan S Martinez1, Mari Purpura3, Andrea N Smit4, Danica F Patton4‡ Ralph E Mistlberger4, Richard D Palmiter6, Andrew D Steele1,5\*
6. PATHOPHYSIOLOGICAL BASIS OF VULNERABILITY TO DRUG ABUSE: Role of an Interaction Between Stress, Glucocorticoids, and Dopaminergic Neurons Pier Vincenzo Piazza and Michel Le Moa1 Psych des Comprtements Adaptifs, INSERM U259, Universid de Bordeaux 11, Domaine de Carreire, Rue Camille Saint-Saens, 33077 Bordeaux Cedex, France
7. Dopamine Release in the Dorsal Striatum during Cocaine-Seeking Behaviour under the Control of a Drug-Associated Cue Rutsuko Ito, Jeffrey W. Dalley, Trevor W. Robbins, and Barry J. Everitt Department of Experimental Psychology, University of Cambridge, Cambridge, CB2 3EB, United Kingdom
8. Cocaine Cues and Dopamine in Dorsal Striatum: Mechanism of Craving in Cocaine Addiction Nora D. Volkow,1 Gene-Jack Wang,2 Frank Telang,1 Joanna S. Fowler,3 Jean Logan,3 Anna-Rose Childress,4 Millard Jayne,1 Yeming Ma,1 and Christopher Wong3
9. Dopamine and alcoholism: neurobiological basis of ethanol abuse Erkki Tupalaa,b,\*, Jari Tiihonena,c aDepartment of Forensic Psychiatry, University of Kuopio, Niuvanniemi Hospital, FIN-70240 Kuopio, Finland bDepartment of Pharmacology and Toxicology, University of Kuopio, Finland cDepartment of Clinical Physiology, Kuopio
10. Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rat
11. (amphetamine/cocaine/ethanol/nicotine/opiate) GAETANO Di CHIARA AND ASSUNTA IMPERATO Institute of Experimental Pharmacology and Toxicology,

University of Cagliari, Viale A. Diaz, 182, 09100 Cagliari, Italy Communicated by Louis Sokoloff, February 17, 1988

1. Dopamine in drug abuse and addiction: results from imaging studies and treatment implications N D Volkow, J S Fowler, G-J Wang C J M Swanson Molecular Psychiatry volume 9, pages557–569 (2004).
2. Dopamine and Addiction Annual Review of Psychology Vol. 71:79-106 (Volume publication date January 2020)
3. Homologies and Differences in the Action of Drugs of Abuse and a Conventional Reinforcer (Food) on Dopamine Transmission: An Interpretative Framework of the Mechanism of Drug Dependence Author links open overlay panelGaetano Di Chiara, Gianluigi Tanda, Cristina Cadoni, Elio Acquas, Valentina Bassareo, Ezio Caronboni
4. Substance use disorders: a comprehensive update of classification, epidemiology, neurobiology, clinical aspects, treatment and prevention Nora D. Volkow, Carlos Blanco
5. Mechanisms and regulation of dopamine release Changliang Liu and Pascal S. Kaeser\*
6. The Role of Dopamine and Its Dysfunction as a Consequence of Oxidative Stress Hugo Juárez Olguín, 1 , 2 , \* David Calderón Guzmán, 3 Ernestina
7. Hernández García, 1 and Gerardo Barragán Mejía 3 .Author information Article notes Copyright and License information PMC Disclaimer
8. Homologies and Differences in the Action of Drugs of Abuse and a Conventional Reinforcer (Food) on Dopamine Transmission: An Interpretative Framework of the
9. Mechanism of Drug Dependence Author links open overlay panelGaetano Di Chiara, Gianluigi Tanda, Cristina Cadoni, Elio Acquas, Valentina Bassareo, Ezio Caronboni
10. Volkow ND, Wang GJ, Fowler JS, et al. Brain DA D2 receptors predict reinforcing effects of stimulants in humans: replication study. Synapse. 2002c;46:79–82. [PubMed] [Google Scholar]
11. Schultz W. Getting formal with dopamine and reward. Neuron. 2002;36:241–

263. [PubMed] [Google Schol