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V-Discover

THE STUDENTS DIGITAL MAGAZINE

THEME : NEUROPHARMACOLOGY

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NEUROPHARMACOLOGY

FOUNDATIONS OF NEUROPHARMACOLOGY

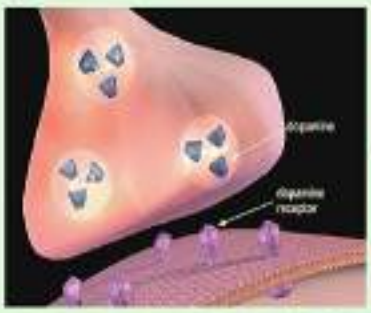
Neuropharmacology is the branch of science that studies how drugs influence the nervous system and, in turn, behaviour. It encompasses two interlinked fields:

Behavioural Neuropharmacology:
Examines how drugs affect mood, cognition, addiction, and mental health.

Molecular Neuropharmacology:
Focuses on the cellular interactions between drugs and neural components like neurotransmitters and receptors.

NEUROTRANSMITTERS: CHEMICAL MESSENGERS OF THE BRAIN

Neurotransmitters are chemicals that transmit signals from one nerve cell (neuron) to another across a tiny gap called the synapse. They are crucial for communication in the nervous system and play a key role in regulating mood, memory, behaviour, and body functions.



MILESTONE IN NEUROPHARMACOLOGY...

From prehistoric use of natural psychoactives (~3000 BCE) to the 20th century discovery of neurotransmitters, anesthetics, antidepressants, and antipsychotics, neuropharmacology evolved into a scientific discipline with modern drug classes.

Between 2001–2025, the field advanced with novel mechanisms (NMDA, orexin, psychedelics), digital & precision medicine, gene therapies, and disease-modifying treatments for brain disorders.

YEAR / PERIOD	MILESTONE IN NEUROPHARMACOLOGY
Prehistoric (~3000 BCE)	Use of natural psychoactive substances (e.g., opium, coca leaves, cannabis) for pain relief and rituals.

2013	Launch of two major brain research initiatives: Human Brain Project (Europe) and BRAIN Initiative (USA) - focusing on neuroscience and drug discovery.
2015	FDA approvals of new atypical antipsychotics: brexpiprazole (Rexulti) and cariprazine (Vraylar).
2016	Approval of pimavanserin (Nuplazid) - first drug specifically for Parkinson's disease psychosis.
2017	Approval of Abilify MyCite, the first "digital pill" with an ingestible sensor to track adherence.
2018	FDA approval of cannabidiol (Epidiolex) - first cannabis-derived drug for epilepsy.
2019	FDA approval of esketamine (Spravato) - a nasal spray for treatment-resistant depression.
2020	Psychedelics (psilocybin, MDMA) enter late-stage clinical trials for depression and PTSD.
2021	FDA approval of aducanumab (Aduhelm) - controversial, but first anti-amyloid Alzheimer's therapy.
2022	Approval of daridorexant (Quviviq) - orexin receptor antagonist for insomnia.
2023	FDA approval of lecanemab (Leqembi) - second-generation Alzheimer's drug targeting amyloid.
2024 – 2025	Growth of gene therapy, CRISPR, AI-based drug discovery, and digital neurotherapeutics. Psychedelic - based therapies expected to gain approval in some regions.

NEUROPHARMACOLOGY STATISTICS REPORT

Market and Research Trends :

Global neuropharmacology market (all CNS drugs) was estimated at ~USD 80–90 billion in 2020, expected to grow at 4–5% CAGR, reaching ~USD 120–130 billion by 2030.

Main drivers: aging population, rise in Alzheimer's, depression, Parkinson's, and precision medicine demand.

Key segments:

Antidepressants & antipsychotics: ~30% share
Neurodegenerative (Alzheimer's, Parkinson's): ~25%
Epilepsy & seizure drugs: ~15%
Sleep disorders, ADHD, others: ~30%

Research & Innovation Highlights

Over 800+ ongoing clinical trials for CNS-related new drugs worldwide.

Psychedelics research funding grew by ~200% between 2019–2024.

Alzheimer's research dominates R&D spend (~40% of neuropharma pipelines).

REGIONAL INSIGHTS

North America: largest market (~45%), due to high prevalence & healthcare spending.

THERAPEUTIC DRUG CLASSES AND CLINICAL RELEVANCE

Antidepressants: Mechanisms & Clinical Use Antidepressants improve mood by increasingneurotransmitter levels (serotonin, norepinephrine, dopamine). Though primarily used for depression, many are effective for anxiety, chronic pain, and sleep disorders.	SSRIs (e.g., Fluoxetine): Block serotonin reuptake. SNRIs (e.g., Duloxetine): Inhibit serotonin and norepinephrine reuptake. TCAs (e.g., Amitriptyline): Reuptake inhibition + histaminic, muscarinic blockade. MAOIs (e.g., Phenelzine): Inhibit monoamine oxidase to increase neurotransmitters. Atypical Antidepressants (e.g., Bupropion): Various mechanisms including dopamine reuptake inhibition.
Antipsychotics & Schizophrenia Management Antipsychotics are central to treating schizophrenia by altering dopamine and serotonin activity.	Typical (1st Gen): Block D_2 receptors (e.g., Haloperidol). Atypical (2nd Gen): Block D_2 & 5-HT_2A receptors (e.g., Risperidone). 3rd Gen (Partial D_2 Agonists): Modulate dopamine (e.g., Aripiprazole). Muscarinic Agonists: Target M1/M4 to reduce dopamine indirectly (e.g., Xanomeline + Trospium).
Opioids & the Pain Crisis Opioids act on μ-opioid receptors to relieve pain but carry high risk of addiction.	Morphine: Full MOR agonist, classic pain relief. Morphine: Full MOR agonist, classic pain relief. Fentanyl: Highly potent, rapid onset. Buprenorphine: Partial MOR agonist, safer ceiling effect for respiratory depression.
Psychedelics in Mental Health Therapy Psychedelics	(e.g., psilocybin, LSD, MDMA, ketamine) show promise in depression, PTSD, and anxiety. Most act on 5-HT_2A receptors, enhancing emotional openness and disrupting negative thought patterns

DRUG INDUCED NEUROTOXICITY

Refers to damage to the central or peripheral nervous system caused by medications such as antibiotics, chemotherapeutics, or psychotropics. Symptoms vary from mild tremors or confusion to severe outcomes like seizures or irreversible neuropathy. Mechanisms involve neurotransmitter imbalance, oxidative stress, mitochondrial damage, and neuroinflammation. Early detection and targeted, supportive care are key. Future approaches focus on biomarker monitoring, neuroprotection, and personalized dosing.

CATEGORY	KEY INSIGHTS
Affected Systems	**CNS**: Encephalopathy, seizures, sedation, extrapyramidal symptoms **PNS**: Peripheral/optic neuropathy, neuropathic pain
Notable Agents	**CNS**: Metronidazole, lithium, methotrexate, opioids, antipsychotics **PNS**: Cisplatin, vincristine, bortezomib, isoniazid, linezolid
Mechanisms	GABA inhibition, oxidative stress, mitochondrial dysfunction, ion channel disruption, proteasome inhibition
Current Approach	Symptom monitoring, drug cessation, dose adjustment, antidotes (e.g., leucovorin for methotrexate, pyridoxine for isoniazid), supportive care (hydration, seizure control)
Future Focus	Biomarker-guided detection, neuroprotective adjuvants, pharmacogenomics, adaptive/personalized dosing, early intervention strategies

FRONTIERS IN NEUROPHARMACOLOGICAL RESEARCH

Neuropharmacology of Sleep

Sleep is a neuro-regulated state crucial for brain repair and emotional balance.

Sleep-Modulating Drugs:

a. Benzodiazepines (e.g., Diazepam)
b. Z-drugs (e.g., Zolpidem)
c. Melatonin & agonists
d. Antidepressants (e.g., Trazodone)

Common Sleep Disorders:

Insomnia: Treated with GABAergic agents or melatonin.

Narcolepsy: Managed with stimulants andREM blockers.

RLS: Treated with dopamine agonists or gabapentin.

AI & Personalized Sleep: EEG-based staging + ML enhances treatment precision.Optogenetics: Circuit-targeted sleep regulation using light and gene editing.

Histamine H_3 Targets: New wakefulness modulators in arousal-related conditions.

Gut-Brain Axis: Gut microbiota impacts insomnia and sleep apnea; probiotics under study.

Metabolic Links: Ketones affect sleep–wake transitions; potential for metabolic sleep treatments

Chronotherapy: Tailoring drug timing to circadian rhythms for enhanced efficacy

Epigenetic Insights: Sleep loss affects gene expression; HDAC inhibitors show cognitive promise.

Orexin Antagonists: Target sleep and neurodegenerative symptoms (e.g., Suvorexant for Alzheimer's-related tau)

NEUROPLASTICITY & PHARMACOLOGICAL MODULATION

Neuroplasticity

The ability of the nervous system to reorganize its structure, function, and connections inresponse tointernal or external stimuli is knownas neuroplasticity.

Neuroplasticity-Boosting Drugs

Class	Drug Example	How It Works: Application area
SSRIs	Fluoxetine	Stimulates hippocampal neurogenesis: Depression, Stroke Recovery
NMDA Modulators	D-Cycloserine	Enhances long-term potentiation: PTSD, Phobias, Cognitive Training
BDNF Enhancers	Ampakines	Raises brain-derived neurotrophic factor: Alzheimer's, Cognitive Decline

GENE THERAPY FOR NEUROLOGICAL CONDITIONS

A promising treatment option for several neurological conditions, many of which are brought on by genetic abnormalities or involve faulty cellular pathways, is gene therapy.Gene therapy involves inserting genes into cells(via vectors like AAV or lentiviruses) to corrector silence faulty genes.

Gene Therapy for Nervous Conditions

SMA:*Zolgensma* (AAV9) restores SMN1 gene → better survival, motor skills.
Parkinson's: AAV2-AADC gene therapy boosts dopamine → improves motor function
LCA:*Luxturna* (AAV2) fixes RPE65 mutation → restores vision.
Huntington's: Gene silencing reduces mutant HTT protein → early trial success.

EMERGING TECHNOLOGIES & INNOVATIONS
AI IN DRUG DISCOVERY

Artificial Intelligence is revolutionizing how brain-targeted drugs are discovered, optimized, and brought to market - reducing time, cost, and clinical failure rates.

Gene Therapy for Nervous Conditions

AI-Powered Mapping of Disease Pathways:ModernAI models integrate genomics, proteomics, transcriptomics, and metabolomics to decode complex brain diseases and discover "undruggable" targets.
Machine Learning Advancements: Graph Neural Networks (GNNs) and transformer-based models outperform classical models in predicting target relevance.Platforms like GraphCast (by DeepMind) use network biology to reveal hidden drug-disease links.

AI in Protein Structure & Binding Analysis

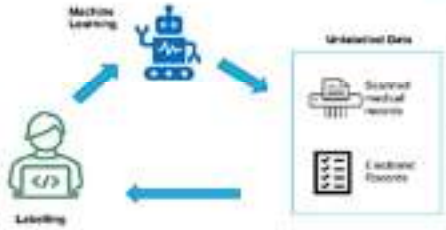
AlphaFold3 & RoseTTAFold2:Predict full protein structures including dynamic changes, RNA-protein complexes, and multi-protein assemblies, which aid neurodegenerative drug design. Beyond the Surface:Detect allosteric and cryptic binding sites (not seen in static structures).Early quantum ML models accelerate folding and binding affinity simulations - even for ultra-large neuro targets.

Drug Repurposing with AI

LLMs like GPT-5 & Med-PaLM-3:Scan EHRs, trial registries, and global literature to generate hypotheses for new uses of old drugs.

Knowledge Graphs:Tools like Google Pathways link genes, diseases, and drugs into interactive networks that reveal overlooked connections.

NLP & Biomedical Literature Mining



Next-Gen NLP Models : Multilingual and domain-specific models mine data from preprints, patents, and regulatory filings, flagging emerging risks and novel targets.
Automated Meta-Analyses:AI performs systematic reviews in hours instead of months- streamlining clinical guidelines and regulatory submissions.

AI ACHIEVEMENTS IN DRUG DISCOVERY

HALICIN
Deep learning discovered halicin, a new antibiotic active against resistant bacteria.

RAPID AI-DESIGNED DRUGS
DSP-0038 (Alzheimer's psychosis) and Insilico medicine's fibrosis candidate reached clinical trials in record time.

PRECISION ONCOLOGY
Exscientia's AI-driven cancer trials improved patient response rates by over 50%.

AI-FIRST BIOTECH IPOs
Several AI-native biotech firms have gone public, reflecting industry-wide confidence in AI-driven pipelines.

Compound Design & Virtual Screening

Generative AI:
Diffusion models and GNNs now design novel, synthesizable molecules with ideal ADME-Tox profiles (absorption, distribution, metabolism, excretion, toxicity).

Self-Driving Labs:
AI+robotic labs automate design → → synthesize → test cycles - enabling rapid brain-drug candidate discovery

Federated Learning:
Allows companies to collaborate securely on drug screening without sharing private data.

Smarter Clinical Trials & Preclinical Models

Digital Twins:
Simulated patient avatars help test drug responses, adjust dosing, and design personalized trials – especially useful in CNS disorders.

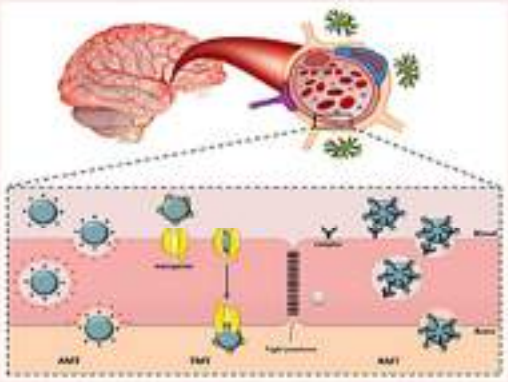
Synthetic Control Arms:
AI creates placebo-free cohorts from real-world data, cutting costs and timelines.

Wearable Integration:
AI interprets biosensor data (e.g. EEG, actigraphy), giving real-time insights into sleep, seizure, or mood biomarkers

ADVANCED DRUG DELIVERY SYSTEM

Crossing the blood-brain barrier (BBB) is one of the biggest challenges in treating neurological diseases. These cutting-edge delivery systems offer precision, speed, and fewer side effects.

Nanoparticles: Targeted Brain Delivery at the Nanoscale
Nanoparticles (1–100 nm) are engineered carriers that can cross the BBB to deliver drugs directly into the brain.
Increases drug stability and target specificity
Reduces systemic side effects
Allows sustained release and improved absorption
Applications: Used in treatment of Parkinson's, Alzheimer's, glioblastoma, and other brain tumors.



Intranasal Delivery: The Shortcut to the Brain
Medications are administered through the nose, reaching the brain via the olfactory and trigeminal nerves, bypassing the BBB entirely.
Non-invasive, needle-free, and fast
Requires lower doses
Minimizes peripheral toxicity
Applications: Ideal for acute conditions like stroke, seizures, and neurodegenerative diseases like Alzheimer's.

Exosomes: Nature's Nanocarriers
Exosomes are tiny extracellular vesicles secreted by cells, capable of carrying proteins, RNA, and therapeutic molecules.
Naturally crosses the BBB
Biocompatible and low immunogenicity
Can be engineered for targeted therapy
Applications:Emerging therapies for Parkinson's, brain cancers, and gene delivery in neurodegenerative disorders.

Did You Know???The same receptor (CCR5) that allows HIV to infect immune cells also plays a role in brain inflammation, memory, andneuroplasticity- makingHIV drugs a candidate for Alzheimer's treatment

Kappa Opioid Receptor Blockers: A New Era in DopamineRegulation

Kappa opioid receptors (KORs) play a key role in regulating stress, mood, motivation, and addiction by modulating dopamine (DA) neurons. Their targeting offers promising treatments for neuropsychiatric disorders.

Normalizing Dopamine Signaling

KORs regulate dopamine release and clearance via the dopamine transporter (DAT).

In DAT dysfunction (e.g., DAT Val559 mutation), dopamine leaks continuously, creating "dopamine noise" that blunts normal brain signaling.

This contributes to ADHD, bipolar disorder, autism, schizophrenia, and addiction.

Long-acting KOR blockers reduce mutant DAT on neuron surfaces, preventing dopamine leakage without disrupting healthy signaling

Experimental Insights

FROM THE BLAKELY MOUSE MODEL

Mice with DAT Val559 mutation show cognitive rigidity, compulsive behaviors, and sex-dependent effects.

KOR antagonists restore dopamine balance and reverse behavioral issues without affecting healthy mice, indicating high therapeutic precision

Enhancing Dopamine Naturally:For those with dopamine-related motivation or mood challenges (e.g., ADHD), structured lifestyle approaches can boost dopamine function:
Engage in meaningful, goal-directed activities, Regular physical exercise (walking, yoga), Exposure to music, novelty, social interaction, and learning, Avoid overstimulation (limit excessive screen time) to prevent receptor fatigue.

EVOLVING HORIZONS IN NEUROPHARMACOLOGY

Brain–Computer Interfaces (BCIs): Merging Mind and Machine
A Brain–Computer Interface (BCI) is a system that translates brain signals into digital commands to control external devices - from robotic arms to communication software.

Core Components
Signal Acquisition: EEG, fMRI, fNIRS, ECoG, or intracortical implants
Preprocessing & Classification: Filters, extracts, and decodes brain activity
Output Control: Converts signals into actions (e.g., typing, movement, speech

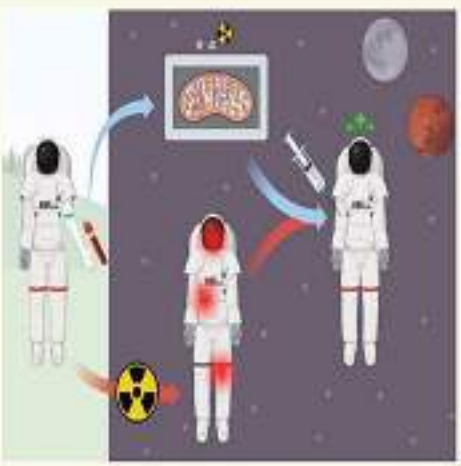
TYPES	FEATURES	LIMITATIONS
Non-invasive	EEG-based (safe, widely used)	Lower precision, more noise
Invasive	ECoG or intracortical implants	High precision, requires brain surgery

NEUROPHARMACOLOGY OF SPACE TRAVEL

Neural Resilience in Space Missions
Long-duration space missions expose the brain to microgravity, radiation, isolation, and circadian disruption-affecting mood, cognition, sleep, and motor control.

Neuropharmacology plays a vital role in managing these effects using CNS-active drugs for sleep, anxiety, motion sickness, and cognitive function. However, space alters drug absorption and metabolism, requiring precise dosing and delivery for safe, effective treatment beyond Earth.

CNS Structural & Functional Changes
Neuroplasticity shifts: altered gene expression in dopamine/serotonin systems impacts cognition and motor control.
Blood-brain barrier (BBB) compromised by radiation/microgravity → oxidative damage, inflammation, increased permeability
Radiation neurotoxicity: neutron/GCR exposure causes neuroinflammation, oxidative stress, DNA damage.



VIVEKANANDHA EDUCATIONAL INSTITUTIONS

TIRUCHENGODE CAMPUS

- SWAMY VIVEKANANDHA MEDICAL COLLEGE HOSPITAL AND RESEARCH INSTITUTE
- VIVEKANANDHA DENTAL COLLEGE FOR WOMEN
- SWAMY VIVEKANANDHA COLLEGE OF PHARMACY
- VIVEKANANDHA COLLEGE OF NURSING
- VIVEKANANDHA SCHOOL OF ANM
- SWAMY VIVEKANANDHA PHYSIOTHERAPY COLLEGE
- VIVEKANANDHA ALLIED HEALTH SCIENCE COLLEGE (Co-Ed)
- KRISHNA INSTITUTE OF OPTOMETRY AND RESEARCH
- VIVEKANANDHA INSTITUTE OF HEALTH SCIENCE & RESEARCH (Boys)
- KRISHNA INSTITUTE OF HEALTH SCIENCE (Boys)
- VIVEKANANDHA COLLEGE OF ENGINEERING FOR WOMEN (AUTONOMOUS)
- VIVEKANANDHA COLLEGE OF TECHNOLOGY FOR WOMEN
- VIVEKANANDHA INSTITUTE OF INFORMATION AND MANAGEMENT STUDIES
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- KRISHNA COLLEGE OF EDUCATION FOR WOMEN
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- THIRU BALAJI SCAN CENTER
- ALLWIN GROUP OF COMPANIES
- M.K.G. FOODS AND FEEDS
- M.K.G. ENTERPRISES

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