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Review Article

A Review on Neuropharmacology: Mechanisms, Drug Classes, and Clinical Applications

***Asha D. Thakor*, Rakshit M Dharajiya, Misbah Z. Shaikh, Amar M. Raval**

Sharda School of Pharmacy, Pethapur, Gandhinagar, Gujarat, India

A B S T R A C T

Background: Neuropharmacology is a vital branch of pharmacology that focuses on the interaction of drugs with the nervous system, particularly the central and peripheral nervous systems. It plays a crucial role in understanding neurotransmission and in the treatment of neurological, psychiatric, and neurodegenerative disorders such as depression, schizophrenia, epilepsy, Parkinson's disease, and Alzheimer's disease.

Methods: This review was conducted through a comprehensive analysis of existing experimental and clinical literature on neuropharmacology. Key areas reviewed include the organization of the nervous system, major neurotransmitters, synaptic transmission mechanisms, mechanisms of drug action, classification of neuropharmacological agents, and their clinical applications. Special emphasis was placed on drug–receptor interactions, neurotransmitter modulation, and challenges in central nervous system drug delivery, including blood–brain barrier limitations.

Results: The review highlights that neuropharmacological drugs exert their effects primarily by modulating neurotransmitter release, receptor activation or blockade, reuptake inhibition, and enzyme inhibition. Major drug classes such as antidepressants, antipsychotics, anxiolytics, antiepileptics, analgesics, and antiparkinsonian agents have shown significant clinical benefits. However, adverse effects, drug dependence, tolerance, and limited brain penetration remain major concerns. Emerging strategies such as nanocarriers, receptor-mediated transport, and intranasal delivery show promise in overcoming current therapeutic limitation

Keywords: Nervous System, Neurotransmitters, Synaptic Mechanism SNARE, Drug Mechanisms, Antidepressants.

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*Address for Correspondence:

Asha D. Thakor, Sharda School of Pharmacy, Pethapur, Gandhinagar, Gujarat, India

INTRODUCTION

Neuropharmacology is referred to by two interrelated terms. Pharmacology is the scientific study of drugs, while the prefix "neuro" denotes the involvement of neurons and the nervous system. Neuropharmacology specifically investigates neurotransmitters and their effects on the central nervous system, particularly the brain and spinal cord [1].This discipline is extremely broad, encompassing topics ranging from the modulation of individual neurons to the regulation of entire brain regions, the spinal cord, and peripheral nerves.

Neuropharmacology is critically important due to its role in understanding and treating neurological and psychiatric disorders. By studying how various drugs interact with the nervous system, researchers and clinicians can develop novel therapeutic agents for conditions such as Parkinson's disease, schizophrenia, epilepsy, depression, and anxiety [2]. In addition, understanding drug mechanisms of action helps improve the safety and efficacy of existing medications[4].

Neuropharmacological research also contributes to elucidating the molecular and cellular mechanisms underlying neurological and psychiatric disorders and supports the development of targeted therapies with fewer adverse effects.Despite significant advances, substantial knowledge gaps remain regarding the complex interactions between drugs and the nervous system, particularly concerning incomplete understanding of mechanisms and long-term adverse effects.Therefore, comprehensive review articles are essential to summarize current evidence, identify

emerging trends, and highlight unresolved research questions. This review focuses on recent developments in neuropharmacological mechanisms, neuropharmacological agents and their actions, novel therapeutic approaches, and supporting clinical and experimental evidence[5].

Organization of Nervous System:

The nervous system is broadly divided into two main parts: the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS includes the brain and spinal cord, which serve as the body's main control centers. The brain is safely enclosed within the skull, while the spinal cord runs through the vertebral canal of the spine. In contrast, the PNS consists of nerves and ganglia, which are groups of neurons located outside the CNS. These nerves act like communication cables, carrying signals between the CNS and the rest of the body[6].

A simple way to understand this division is to think of the CNS as everything inside the skull and spinal column, and the PNS as everything outside. However, this is a slight oversimplification. In reality, some components of the peripheral nervous system are found within the cranial and vertebral cavities. The term peripheral reflects the role of this system—it extends beyond the brain and spinal cord to connect them with muscles, organs, and sensory structures. Because of this complexity, the boundary between the central and peripheral nervous systems is not always sharply defined [7].

Table 1: Major Divisions of the Nervous System [8]

DIVISON	COMPONENT	DRUG RELEVANT FEATURE
CNS	Brain, spinal cord	Targets for psychotric and neurologic drugs
PNS	Somatic and autonomic nerve	Autonomic drugs act (Sympathetic and parasympathetic) here
ANS	Sympathetic and parasympathetic	Site of action for cholinergic and adrenergic drug

NEUROTRANSMITTERS:

a) Acetylcholine (ACh)

Acetylcholine was the first neurotransmitter discovered and plays roles in muscle activation, attention, memory, and plasticity. This is described in educational neurobiology resources that note ACh's action at neuromuscular junctions and in cognitive brain circuits.

A review in Acetylcholine as a neuromodulator explains that ACh influences synaptic plasticity and modulates attention and learning processes in the central nervous system[9].

b) **Dopamine (DA)**

Dopamine, or DA for short, is also called the 'pleasure chemical' because, as soon as mammals get their reward for their actions, the chemical is released, and this reward could be the form of food, drugs, or sex. Dopamine is one of the most researched chemical components of the nervous system, simply because of its multifaceted functions in human behaviors and cognition[10].Dopamine's roles in reward, motivation, movement, attention, and learning, as well as its involvement in Parkinson's disease, addiction, and schizophrenia, are well documented in comprehensive neurotransmitter overviews.

c) **Glutamate**

Glutamate is the primary excitatory neurotransmitter in the brain and a major mediator of synaptic plasticity and learning. Excess glutamate leads to excitotoxicity, contributing to neuronal death in stroke and ALS.

On a negative note, a negative electrical current or inhibitory signal comes from GABA. On a positive note, however, the excitatory function of GLU cannot be overemphasized in the process of acquiring a new experience and storing a new memory through LTP[11].

d) **Serotonin (5-HT)**

Serotonin's role in mood modulation, sleep, appetite, and memory is described in comprehensive neurotransmitter function overviews. Insufficiencies of 5HT have been associated with depressive and neuropsychiatric disorders.

The role of 5HT, however, extends into more areas and has also come into function in regulating appetite, sleep, and memory and, most recently, decision-making[12].

MECHANISM OF ACTION:

Nerve impulse (Action Potential) arrives at presynaptic nerve terminal

↓

Opening of voltage-gated calcium (Ca^{2+}) channels

↓

Calcium ions enter the presynaptic terminal

↓

Calcium activates the "active zones" on the presynaptic membrane

↓

Neurotransmitter-filled synaptic vesicles move to the active zone

↓

SNARE proteins are activated

Syntaxin-1 (on presynaptic membrane) & SNAP-25 (on presynaptic membrane)

Synaptobrevin-2 (on vesicle membrane)

↓

Formation of SNARE complex

↓

Fusion of synaptic vesicle with presynaptic membrane

↓

Calcium-triggered exocytosis occurs

↓

Neurotransmitters are released into the synaptic cleft

↓

Neurotransmitters bind to receptors on the postsynaptic neuron

↓

Signal is transmitted to the next neuron . (12)

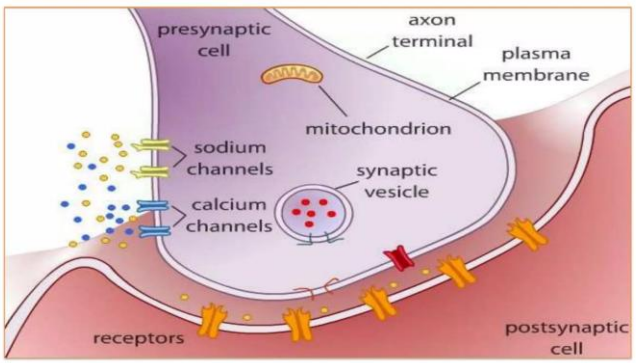
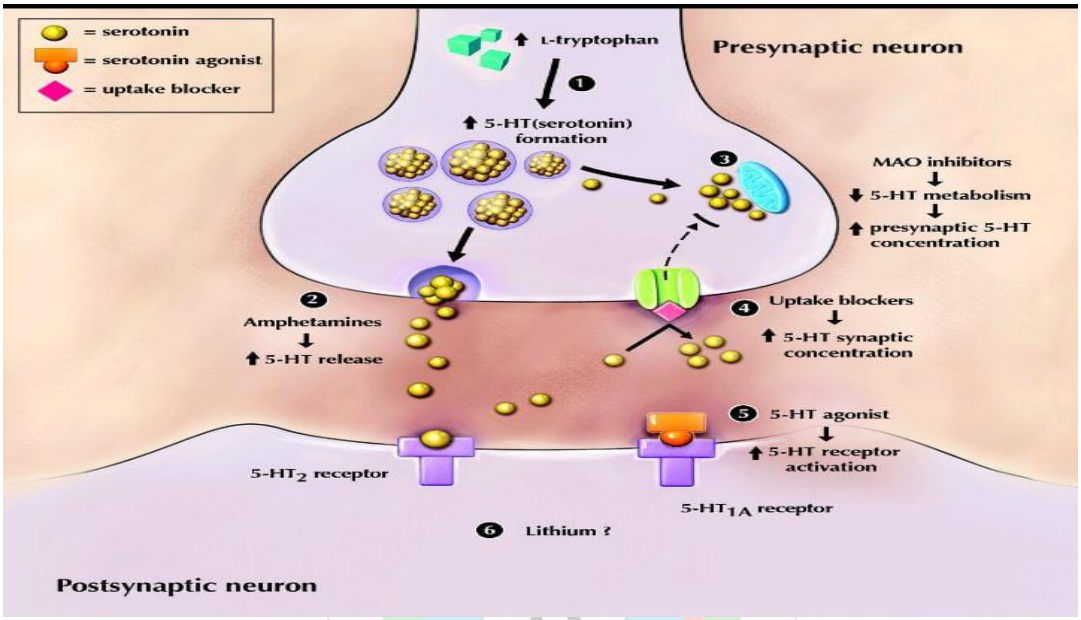


Table 2: Drug Mechanisms in Neuropharmacology [13]

Drug Class	Mechanism of Action	Therapeutic Use
Dopamine Agonists	Stimulate dopamine receptors	Parkinson's Disease
SSRI (Selective Serotonin Reuptake	Inhibit serotonin reuptake	Depression, Anxiety
NMDA Receptor Antagonists	Block NMDA receptors	Alzheimer's, Epilepsy
Benzodiazepines	Enhance GABA-A receptor activity	Anxiety, Seizures



Mechanisms of Drug Action in Neuropharmacology

1. **Modulation of Neurotransmitter Release:-**

   Some drugs promote release (e.g., amphetamine increases catecholamines). Others inhibit release, such as botulinum toxin blocking acetylcholine exocytosis**[14].**

2. **Receptor Agonism and Antagonism:-**

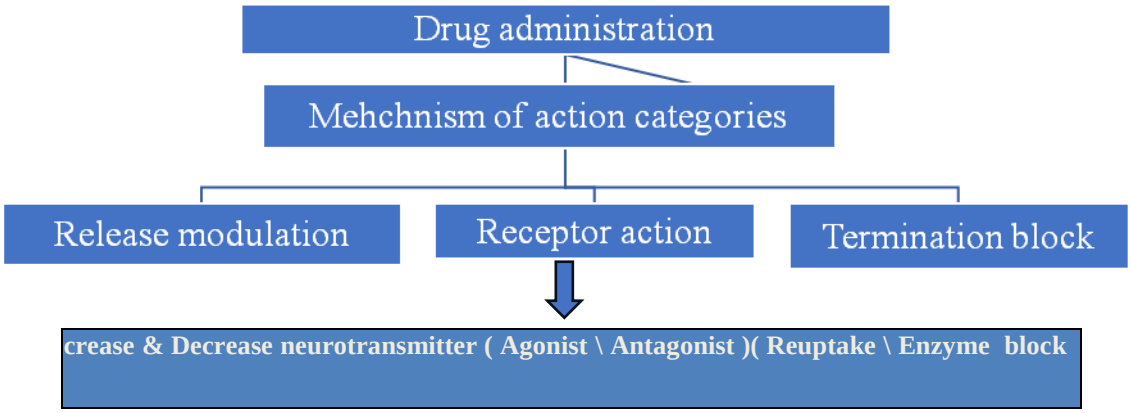
   Drugs may mimic natural neurotransmitters (agonists) or block their receptors (antagonists). For example, morphine acts as a μ-opioid receptor agonist**[15]**.

3. **Inhibition of Reuptake Transporters:-**

   SSRIs increase serotonin availability by inhibiting its reuptake. Similarly, cocaine blocks dopamine and norepinephrine transporters **[16]**.

4. **Enzyme Inhibition:-**

   MAO inhibitors block monoamine breakdown, enhancing neurotransmitter levels. Acetylcholinesterase inhibitors prolong acetylcholine activity in Alzheimer's therapy



Flowchart: Drug Mechanisms Affecting Synaptic Transmission

Major Drug Classes in Neuropharmacology

Neuropharmacological drugs are agents that modify neuronal function by acting on specific neurotransmitters, receptors, ion channels, or signaling pathways within the central nervous system. These drugs are classified into therapeutic categories based on their mechanisms of action and clinical uses[17].

- **Antidepressants:** SSRIs, SNRIs, TCAs, MAOIs.
- **Antipsychotics:** Typical (1st Gen) & Atypical (2nd Gen).
- **Anxiolytics/Sedatives/Hypnotics:** Benzodiazepines, Barbiturates.
- **Analgesics:** Opioids, NSAIDs (COX-2 Inhibitors).
- **Anticonvulsants (Anti-epileptics):** Valproate, Topiramate, Gabapentin, etc..
- **Antiparkinsonian Agents:** Dopamine agonists, anticholinergics

1. Antidepressants

Depression is a complex mood disorder associated with altered monoamine neurotransmission, particularly involving serotonin (5-HT), norepinephrine (NE), and dopamine (DA). Antidepressant drugs act by increasing the availability of these neurotransmitters in the synaptic cleft[18].

a. Selective Serotonin Reuptake Inhibitors (SSRIs)

SSRIs selectively inhibit the serotonin transporter (SERT), preventing reuptake of serotonin into presynaptic neurons and thereby enhancing serotonergic neurotransmission.

Examples: Sertraline, Fluoxetine

Pharmacological effects:

- Increased synaptic serotonin levels
- Improvement in mood, sleep, and emotional regulation

Adverse effects:

- Nausea, headache
- Sexual dysfunction
- Insomnia or anxiety in early treatment

SSRIs are considered first-line therapy for major depressive disorder due to their efficacy and tolerability.

b. Tricyclic Antidepressants (TCAs)

TCAs inhibit the reuptake of both norepinephrine and serotonin by blocking NET and SERT transporters. They also interact with muscarinic, histaminergic, and α-adrenergic receptors.

Examples: Amitriptyline, Imipramine

Pharmacological effects:

- Enhanced monoaminergic neurotransmission
- Sedative and anxiolytic effects

Adverse effects:

- Anticholinergic effects (dry mouth, blurred vision, constipation)
- Orthostatic hypotension
- Cardiac arrhythmias (especially in overdose)

Due to their side-effect profile, TCAs are now mainly used when newer antidepressants are ineffective[19].

c. Monoamine Oxidase Inhibitors (MAOIs)

MAOIs inhibit monoamine oxidase enzymes (MAO-A and MAO-B), which are responsible for the breakdown of serotonin, norepinephrine, and dopamine.

Pharmacological effects:

- Increased levels of monoamines in the brain

Limitations:

- Dietary restrictions (tyramine-containing foods)
- Risk of hypertensive crisis
- Significant drug interactions

Because of these limitations, MAOIs are reserved for treatment-resistant depression[20].

2. Antipsychotics

Antipsychotic drugs are used in the treatment of schizophrenia and other psychotic disorders. Their therapeutic effects are primarily mediated through modulation of dopaminergic pathways in the brain.

a. Typical (First-Generation) Antipsychotics

Typical antipsychotics primarily block dopamine D_2 receptors in the mesolimbic pathway.

Example: Haloperidol

Therapeutic effects:

- Reduction of positive symptoms such as hallucinations and delusions

Adverse effects:

- Extrapyramidal symptoms (EPS)
- Tardive dyskinesia
- Hyperprolactinemia

b. Atypical (Second-Generation) Antipsychotics[20]

Atypical antipsychotics block both dopamine D_2 and serotonin 5-HT_2A receptors.

Example: Risperidone

Adverse effects:

- Weight gain
- Metabolic syndrome (varies among agents)

3. Anxiolytics and Sedative–Hypnotics

These drugs are used to relieve anxiety and induce or maintain sleep by enhancing inhibitory neurotransmission.

a. Benzodiazepines

Benzodiazepines enhance the effect of gamma-aminobutyric acid (GABA) by increasing the frequency of chloride channel opening at the GABA_A receptor.

Example: Diazepam

Clinical uses:

- Acute anxiety

- Status epilepticus
- Muscle relaxation

Limitations:

- Sedation
- Tolerance and dependence with long-term use

b. Non-Benzodiazepine Hypnotics

These drugs selectively act on specific GABA_A receptor subtypes involved in sleep regulation.

Example: Zolpidem

Primarily used for short-term management of insomnia.

4. Antiepileptic Drugs

Epilepsy is characterized by abnormal, excessive neuronal firing. Antiepileptic drugs aim to suppress seizure activity by stabilizing neuronal membranes or enhancing inhibitory transmission [20].

Table 3: Major Mechanisms of Action

Class :	Example :	Action
1.Sodium Channel Blockade	Carbamazepine	Reduces repetitive neuronal firing by prolonging the inactivated state of sodium channels.
2.Enhancement of GABAergic Transmission	Valproate	Increases GABA levels and inhibits excitatory neurotransmission.
3.CalciumChannel Modulation	Ethosuximide	Blocks T-type calcium channels, particularly effective in absence seizures.

7. Drugs for Neurodegenerative Diseases:-

1. Alzheimer's disease (AD):

Alzheimer's disease (AD), a progressive neurodegenerative disease, is the most frequent cause of dementia. AD initially presents with forgetfulness, learning problems, followed by language, judgment, and activity limitations. Pathologically, AD shows amyloid β plaque deposition outside the neuron, while the neuron shows neurofibrillary tangle deposits, associated with loss of function.

Cholinergic dysfunction, characterized by reduced acetylcholine receptors, represents the marked neurochemical change, which occurs early in the disease. By now, symptomatic management, primarily involving the cholinergic system, continues, but the search for a modifying drug continues**[21].**

2. Parkinson's disease

Parkinson's disease (PD) is a progressive, chronic, and degenerative movement disorder consisting of a substantial loss of dopaminergic neuronal cells within the substantia nigra, an area of the brain responsible for managing movements.

However, this loss of dopaminergic neurons contributes to characteristic motor symptoms of PD, which include rest tremor, rigidity, bradykinesia, and postural instability. apart from motor symptoms, a patient can also experience a range of non-motor symptoms, which include sleep problems, mood alteration, dementia, and autonomic function problems. Although there is no confirmed remedy, current management is aimed at symptom control, which includes replacing and imitating the function of dopamines**[22]**.

3. Schizophrenia

schizophreniais a seriously chronic and severe psychological condition involving issues concerning thought, perception, emotions, and behavior. It has also been linked to imbalances of dopamine transmission, including overactive dopamine expression in the frontal parts of the brain.

Some symptoms of the condition include psychoses like hallucinations, delusions, thought disorder, and damage to intellectual functioning. It is usually treated with antipsychotic drugs, whose function is to counteract (block) dopamine receptors and thus provide a way of dealing with the condition by lessening the psychoses of the affected individuals**[23]**.

8. Neuropharmacology of Pain Management: -

Neuropathic pain management. Changes in the nervous system, leading to dysfunctional pain pathways, give rise to neuropathic pain.

Pathophysiology: Neuropathic pain consists of dysfunctional nociceptive pathways, central sensitization, ion channel disorders, or altered neurotransmitter levels within the central or peripheral nervous systems.

1. Opioid Analgesics

Morphine, a type of opioid analgesic, interacts with μ-opioid receptors to modulate pain transmission but is hampered by tolerance, addiction, and safety issues.

"Non-Opioid Analgesics": NSAIDs inhibit the synthesis of prostaglandins and are more effective in inflammatory pain conditions, while having very little effect on "pure" neuropathic.

Adjuvant Analgesics: The role played by antidepressants, such as duloxetine, and anticonvulsants, such as gabapentin, is highlighted as they make excellent adjuvants because of their efficacy in neurotrans[24].

2. Diabetic Neuropathy

Diabetic neuropathy is a common complication of long-standing diabetes, most often presenting as distal symmetric

polyneuropathy with sensory loss in a stocking–glove pattern, pain, and possible autonomic dysfunction. Nearly 50% of diabetic patients are affected, with better glycemic control slowing progression mainly in type 1 diabetes.

Risk increases with longer disease duration, poor glucose control, aging, obesity, hypertension, and dyslipidemia. The condition develops due to metabolic injury, oxidative stress, mitochondrial dysfunction, nerve ischemia, and abnormal nerve signaling.

Symptoms range from numbness and tingling to severe neuropathic pain and weakness. Treatment mainly aims at pain relief, as disease-modifying therapies are still under research[25].

9. Blood–Brain Barrier and Drug Delivery Challenges:-

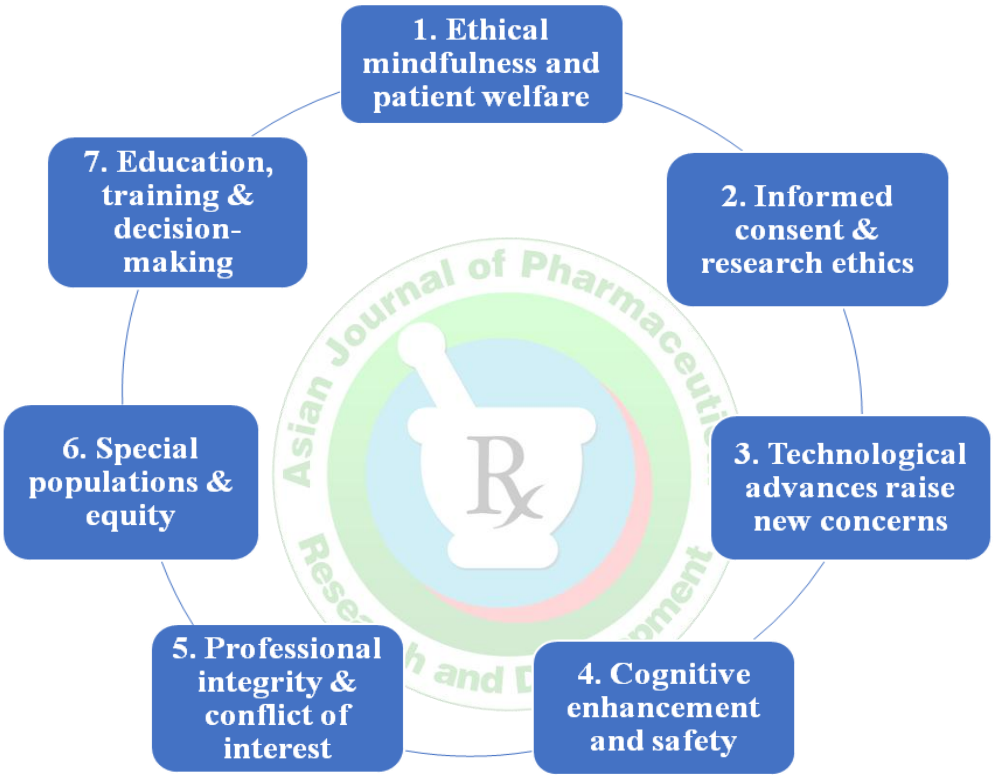
The blood–brain barrier (BBB) restricts passage of large or hydrophilic molecules .

Only lipid-soluble drugs or those with specific transport systems can effectively enter the CNS.

Strategies to overcome BBB limitations include[26]**:**

- Drug nanocarriers (liposomes)
- Receptor-mediated transcytosis
- Intranasal delivery routes

10 . Safety, Dependence, and Ethical Considerations[27]



CONCLUSION:

Neuropharmacology is a crucial and evolving discipline that integrates neuroscience and pharmacology to understand and treat disorders of the nervous system. By elucidating neurotransmitters, synaptic mechanisms, and drug actions, it supports the rational development of therapies for neurological and psychiatric diseases. Although current drugs are effective, challenges such as adverse effects, dependence, and blood–brain barrier limitations remain. Ongoing research and advanced drug-delivery strategies are essential for developing safer, more targeted, and disease-modifying treatments, ultimately improving patient care and clinical outcomes.

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