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Letter to the Editor

Targeting neuroinflammation: a critical opportunity in the evolving landscape of neuropharmacology

Sir,

Neurodegenerative disorders such as Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and frontotemporal dementia continue to impose an escalating global health burden, yet therapeutic progress has remained disappointingly slow. For decades, neuropharmacology has been dominated by symptomatic approaches-cholinergic modulation, dopaminergic replacement, or glutamatergic stabilization-offering only transient relief without modifying disease trajectory. However, emerging evidence indicates that neuroinflammation is a central, unifying pathological mechanism across neurodegenerative diseases. This paradigm shift has catalyzed a new wave of drug development targeting microglial activation, inflammasomes, complement pathways, and neuroimmune signalling. There is now a compelling need to accelerate translational efforts in this domain, particularly in low-and middle-income countries where the incidence of neurodegenerative disorders is rapidly rising.

Neuroinflammation, once considered a bystander phenomenon, is now recognized as a driver of neurodegeneration. Microglia and astrocytes-traditionally viewed as supportive glial cells-play decisive roles in synaptic pruning, clearance of misfolded proteins, and maintenance of neural homeostasis. Dysregulated glial activation results in chronic cytokine release, complement-mediated synapse loss, oxidative stress, and propagation of misfolded proteins such as amyloid-β, tau, and α-synuclein. Accumulating evidence from human post-mortem studies, CSF biomarkers, PET imaging, and genome-wide association studies underscores the centrality of neuroimmune mechanisms, particularly pathways involving TREM2, C1q complement, and the NLRP3 inflammasome.[1-3]

In this context, several promising neuroinflammation-modulating therapies have entered early-phase clinical trials. NLRP3 inhibitors, such as dapansutrile and novel blood-brain barrier-penetrant small molecules, have shown the ability to reduce microglial activation and downstream IL-1β signalling.[4] Preclinical studies demonstrate attenuation of amyloid plaque burden, improved synaptic density, and cognitive rescue in AD models, offering a mechanistic rationale for clinical translation.

Similarly, TREM2 agonists-including monoclonal antibodies (e.g., AL002)-aim to enhance microglial phagocytic function and promote a disease-resolving microglial phenotype.[5] Early-phase trials have demonstrated biomarker modulation and acceptable safety profiles. Complement inhibition represents another promising avenue: blocking C1q has been shown to prevent aberrant synaptic elimination in AD and Huntington's disease models.[6] A phase I trial of ANX005, a humanized anti-C1q antibody, has already shown favourable tolerability and preliminary biological activity.[7]

Yet, despite the excitement surrounding these targets, major translational gaps persist. Many neuroinflammatory pathways are context-dependent-protective in early disease but deleterious in chronic states. Microglia themselves exist on a functional continuum rather than the simplistic M1/M2 dichotomy; blanket suppression of inflammation risks impairing innate immune functions crucial for debris clearance and tissue repair.[8,9] Moreover, patient heterogeneity-genetic, metabolic, and environmental-poses significant challenges for predicting therapeutic response. Biomarkers capable of stratifying patients into the neuroinflammatory endotypes remain limited in the availability, particularly in resource-limited settings.

For countries like India, which are expected to witness exponential growth in neurodegenerative disease burden due to demographic shifts, urbanization, metabolic risk factors, and air pollution, this field demands urgent attention. The majority of Indian clinical centres still lack PET imaging for microglial markers (e.g., TSPO-PET), facilities for CSF biomarker testing, or advanced neuroimmunology laboratories. Without infrastructure, early access to neuroinflammation-targeting therapeutics will be severely restricted. The recent WHO report highlighting the massive global burden of neurological disorders further underscores the urgency for national strategies to strengthen neurology research and care ecosystems.

I wish to emphasize three immediate priorities:

INVESTMENT IN TRANSLATIONAL NEURO-IMMUNOLOGY RESEARCH

Government and institutional funding must support laboratories focusing on microglial biology, inflammasome pharmacology, and biomarker discovery. Regional centres of excellence in neuroimmunology should be established.

INTEGRATION OF NEUROINFLAMMATORY BIOMARKERS INTO CLINICAL PRACTICE

Standardized protocols for CSF inflammatory markers, blood-based cytokine panels, and advanced neuroimaging should be implemented to stratify patients and monitor treatment response.

FACILITATION OF CLINICAL TRIALS IN LMIC POPULATIONS

Representation of Indian and other LMIC populations in global neuroinflammation drug trials is critically low. Given genetic and environmental differences, inclusion is essential for generalizable results.

Neuroinflammation offers a rare convergence of mechanistic clarity, therapeutic promise, and cross-disease applicability. With multiple agents entering phase I/II trials, this is a pivotal moment in neuropharmacology. If we act now to build scientific capacity, clinical infrastructure, and trial readiness, countries like India can not only adopt but also contribute meaningfully to breakthroughs in neurodegenerative disease treatment. The window of opportunity is narrow but decisive.

Soham Sinha*

Department of Pharmacology, RCSM Medical College and CPR Hospital, Kolhapur, Maharashtra, India

***Correspondence to**
Dr. Soham Sinha,
E-mail: sohamsinha1217@gmail.com

REFERENCES

1. Heneka MT, Carson MJ, El Khoury J, Landreth GE, Brosseron F, Feinstein DL, et al. Neuroinflammation in Alzheimer's disease. Lancet Neurol. 2015;14(4):388-405.
2. Keren-Shaul H, Spinrad A, Weiner A, Matcovitch-Natan O, Dvir-Szternfeld R, Ulland TK, et al. A unique microglia type associated with restricting development of Alzheimer's disease. Cell. 2017;169(7):1276-1290.e17.
3. Guerreiro R, Wojtas A, Bras J, Carrasquillo M, Rogaeva E, Majounie E, et al. TREM2 variants in Alzheimer's disease. N Engl J Med. 2013;368(2):117-27.
4. Anderson FL, Biggs KE, Rankin BE, Havrda MC. NLRP3 inflammasome in neurodegenerative disease. Transl Res. 2023;252:21-33.
5. Wang S, Mustafa M, Yuede CM, Salazar SV, Kong P, Long H, et al. Anti-human TREM2 induces microglia proliferation and reduces pathology in an Alzheimer's disease model. J Exp Med. 2020;217:9.
6. Dejanovic B, Wu T, Tsai M-C, Graykowski D, Gandham VD, Rose CM, et al. Complement C1q-dependent excitatory and inhibitory synapse elimination by astrocytes and microglia in Alzheimer's disease mouse models. Nat Aging. 2022;2(9):837-50.
7. Lansita JA, Mease KM, Qiu H, Yednock T, Sankaranarayanan S, Kramer S. Nonclinical development of ANX005: A humanized anti-C1q antibody for treatment of autoimmune and neurodegenerative diseases. Int J Toxicol. 2017;36(6):449-62.
8. Paolicelli RC, Sierra A, Stevens B, Tremblay M-E, Aguzzi A, Ajami B, et al. Microglia states and nomenclature: A field at its crossroads. Neuron. 2022;110(21):3458-83.
9. Gao C, Jiang J, Tan Y, Chen S. Microglia in neurodegenerative diseases: mechanism and potential therapeutic targets. Signal Transduct Target Ther. 2023;8(1):359.

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