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Extracorporeal hemoadsorption and neurological disorders: A challenging perspective

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ABSTRACT

Extracorporeal hemoadsorption is a promising therapeutic strategy for neurological complications associated with chronic kidney disease and acute kidney injury. Neurological disorders—including cognitive impairment, Parkinson disease, and dementia—are more prevalent in individuals with renal dysfunction due to shared inflammatory pathways and the accumulation of protein-bound uremic toxins (PBUTs), such as advanced glycation end products (AGEs), indoxyl sulfate, and p-Cresol. PBUTs exacerbate neurological conditions by promoting neuroinflammation and neurodegeneration. They are inadequately removed *via* conventional dialysis, necessitating alternative solutions. Hemoadsorption has shown potential in reducing systemic inflammation and eliminating PBUTs, offering neuroprotective and disease-modifying effects. Preclinical studies have demonstrated significant reductions in AGEs, indoxyl sulfate, and amyloid-beta peptides in models of Alzheimer's disease (AD) and other conditions, improving outcomes. In clinical trials involving inflammatory disorders such as Guillain-Barré syndrome, hemoadsorption reduced cytokines—including tumor necrosis factor alpha, interleukin-17 (IL-17), and IL-22—correlating with enhanced recovery and reduced ventilation requirements. While evidence supports its efficacy, further research is needed to standardize protocols, evaluate long-term outcomes, and explore its potential in broader populations. Hemoadsorption could transform the management of individuals with renal and neurological disorders, improving disease outcomes and quality of life.

Key words: hemoadsorption, neurological disorders, chronic kidney disease, protein-bound uremic toxins, neuroinflammation, advanced glycation end products, indoxyl sulfate

INTRODUCTION

Neurological abnormalities commonly occur in individuals with chronic kidney disease (CKD) and acute kidney injury (AKI). These relationships are considered secondary, as the brain and kidney engage in complex crosstalk to maintain homeostasis. Consequently, AKI and CKD can induce anatomical, functional, and biochemical changes in the brain, including alterations in neurotransmitter and cytokine concentrations, acid-base homeostasis, drug metabolism, and the accumulation of uremic toxins.[1,2] In addition, the incidence of neurological disorders has increased considerably in recent years, with greater risk observed in association with CKD. Indeed, individuals at all stages of CKD have a higher likelihood of developing cognitive disorders, Parkinson disease (PD), dementia, and neuropsychiatric conditions such as depression and anxiety.[3,4] Although the etiologies of these neurological disorders differ and are multifactorial and complex, inflammation appears to be a common denominator.[4,5]

EPIDEMIOLOGY OF NEUROLOGICAL DISEASES AND KIDNEY FUNCTION

Epidemiologic data suggest that impaired renal function is strongly associated with an increased risk of cerebrovascular disease. Individuals undergoing hemodialysis exhibit an exceptionally high incidence of cerebral microhemorrhages and a greater prevalence of silent strokes.[3,4] In the general population, the risk of fatal or nonfatal ischemic and hemorrhagic stroke increases when the estimated glomerular filtration rate (eGFR) falls below 60 mL/min/1.73 m^2,[6] rises linearly with further eGFR decline, and is even higher in the presence of albuminuria.[7]

CKD is also associated with a higher risk of cognitive disorders, including a 30%-60% prevalence of cognitive impairment in executive functions—with the prevalence increasing by 11% for every 10 mL/min/1.73 m^2 decrease in eGFR.[8-10] Some studies have reported improved cognitive performance following a hemodialysis session, suggesting a possible link to the reduction of uremic toxins.[11]

Other conditions associated with an eGFR decline are

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movement disorders, especially PD [Table 1]. Reduced eGFR and proteinuria have been identified as independent risk factors for the development of PD, with a hazard ratio (95% confidence interval) of 1.74 (1.32-1.63) for an eGFR < 30 mL/min/1.73 m^2.[18,20] This relationship may be explained by shared pathophysiologic mechanisms, such as oxidative stress, protein-bound uremic toxins (PBUTs), and hypertension.[22,23]

Furthermore, the accumulation of uremic toxins—each following molecule-specific trajectories during CKD progression—may contribute to neurological dysfunction. For instance, molecules implicated in the kidney-brain axis, such as parathyroid hormone and beta 2 microglobulin (β2M), begin to rise as early as CKD Stage 3.[24] Levels of asymmetrical dimethylarginine, a known neurovascular toxin, approximately double by the time end-stage kidney disease is reached. Notably, parathyroid hormone may begin to increase even within the normal range from CKD Stage 2,[24-26] suggesting that subtle metabolic disturbances emerge early and may affect brain health over time. Additionally, the accumulation of PBUTs, such as p-Cresol and indoxyl sulfate (IS), typically begins at CKD Stage 4, further contributing to systemic and neurological toxicity [Figure 1].[27,28]

Table 1

Epidemiological evidence linking kidney dysfunction to neurodegenerative outcomes

Diseases	Author (original Study)	Year	Study population	Sample size (n)	Study design	Main findings
Cognitive impairment and dementia	Kjaergaard *et al.*,[12]	2023	Danish national registry cohort comparing individuals with kidney disease vs. matched general population without kidney disease or dementia	82,690 (CKD)/413,405 (controls)	Retrospective population-based cohort	Kidney disease associated with modestly increased risk of dementia, primarily vascular dementia
	Stocker *et al.*,[13]	2023	German population-based cohort aged 50-75 years, followed for 17 years	9940	Prospective cohort study	No statistically significant association between impaired kidney function and dementia, AD or vascular dementia
	Li *et al.*,[14]	2024	U.S. adults ≥ 60 years from NHANES 2011-14	2234	Cross-sectional analysis	CKD stages 3-5 were significantly associated with worse cognitive performance (CERAD: OR 0.70; Animal Fluency: OR 0.64; DSST: OR 0.60). Lower eGFR linked to poor cognition. Nonlinear dose-response for DSST and Animal Fluency; linear for CERAD. Cognitive decline also seen in early CKD. Authors recommend cognitive screening in all CKD patients
	Chu *et al.*,[15]	2022	Adults ≥ 60 years from NHANES (USA)	3223	Cross-sectional study	CKD stages G4-G5 were associated with worse global and domain-specific cognitive function (especially executive function, verbal fluency, and immediate recall), but only among those with low physical activity. No association for delayed recall or self-perceived memory decline. Physical activity mitigated cognitive impairment risk in CKD. Objective cognitive tests were more sensitive than subjective measures
	Shang *et al.*,[16]	2024	Chinese adults ≥ 45 years old without baseline CI	16,515	Prospective cohort (CHARLS)	CKD was associated with a higher incidence of cognitive impairment (HR 1.56; 95% CI: 1.19-2.04) and earlier CI onset by 1.24 years. Risk was higher in 45-54 age group. CKD also associated with increased mortality (HR 1.25; 95% CI: 1.03-1.51), but not statistically significant in Laplace analysis
PD	Peng *et al.*,[17]	2024	General population aged 39-72 years from UK Biobank	400,571	Prospective cohort study	Decreased kidney function (eGFR < 30 mL/min/1.73 m^2) is significantly associated with increased risk of PD. The study also found a nonlinear relationship between eGFR and PD risk, and identified changes in brain gray matter volumes in low eGFR groups
	Nam *et al.*,[18]	2019	South Korean adults > 65 years	3,580,435	Nationwide retrospective cohort	Chronic renal dysfunction and proteinuria (≥ 1+ in dipstick test) were independently associated with increased risk of developing PD. Risk increased progressively with lower eGFR and higher proteinuria. Coexistence of CKD and proteinuria conferred the highest risk (HR 1.33).
	Wang *et al.*,[19]	2017	Korean adult aged 60-80 years from NHIS-Senior cohort	506,089	Retrospective cohort study	Advanced CKD (eGFR <15 mL/min/1.73 m^2) was significantly associated with increased risk of PD, especially in men (HR 3.71). No significant association was found in earlier CKD stages or in women.
	Wang *et al.*,[20]	2014	Taiwanese adults with ESRD compared to a general population without kidney disease or PD	8325 ESRD patients vs. 33,382 controls	Retrospective cohort study	ESRD was associated with a 1.73-fold increased risk of PD. The risk was higher in women, younger patients, and during the first year after ESRD diagnosis. Risk was further elevated in those with diabetes and cardiovascular disease.
	Kwon *et al.*,[21]	2023	Korean cohort of individuals aged ≥ 40 years with matched controls	16,559 (CKD)/66,236 (controls)	Observational retrospective cohort	No significant overall association between CKD and PD, except in specific subgroups (*e.g.*, rural residents)

CKD, chronic kidney disease; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; DSST, digit symbol substitution test; NHIS, National Health Insurance Service; eGFR, estimated glomerular filtration rate; PD, Parkinson diseases; AD, Alzheimer's Disease; NHANES, National Health and Nutrition Examination Surveys; OR, odds ratio; CI, cognitive impairment; HR, hazard ratio; 95% CI, 95% confidence interval; CHARLS, China Health and Retirement Longitudinal Study; ESRD, end-stage renal disease.

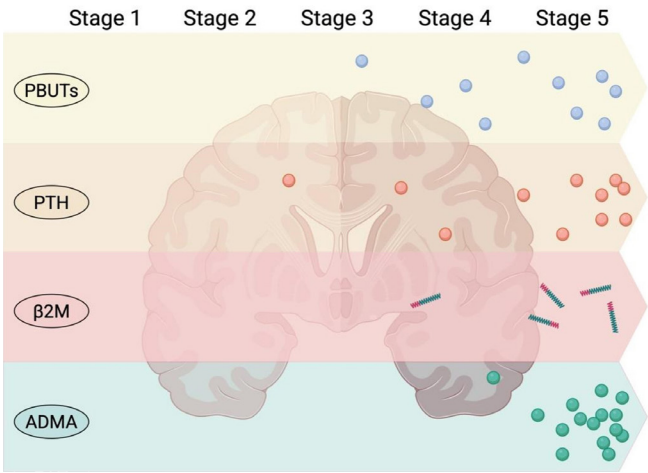

Figure 1. Trajectory of uremic toxins and neurotoxic mediators across chronic kidney disease progression. PBUTs, protein-bound uremic toxins; PTHl, parathyroid hormone; β2M, beta 2 microglobulin; ADMA, asymmetric dimethylarginine. Created in BioRender. Ramirez, G. (2025) https://BioRender.com/m0xhy3i

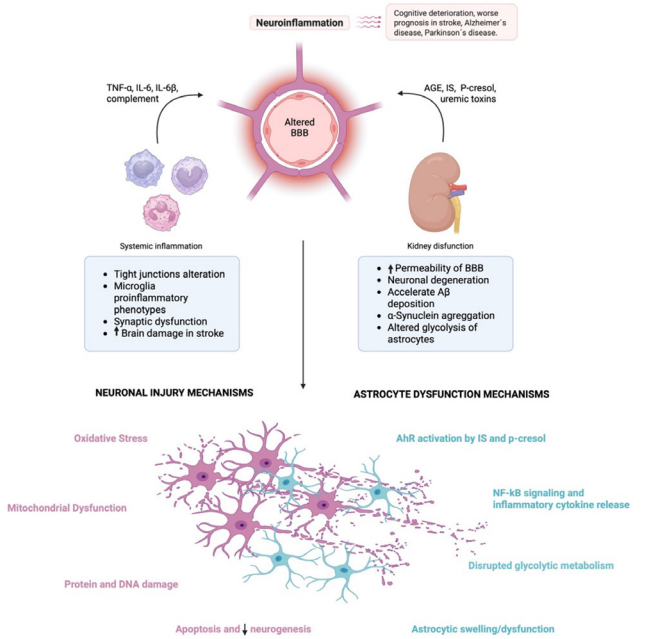

Figure 2. Mechanisms of neuroinflammation and astrocyte dysfunction induced by uremic toxins and systemic inflammation. TNF-α,tumor necrosis factor alpha; IL-6, interleukin-6; AGE, dvanced glycation end product; IS, indoxyl sulfate; BBB, blood-brain barrier; NF-κB, nuclear factor kappa-B. Created in BioRender. Ramirez, G. (2025) https://BioRender.com/smkw6l7

The complex interplay between the brain and the kidney can be partially explained by the susceptibility of both organs to vascular lesions and, consequently, to traditional cardiovascular risk factors. However, other mechanisms may also be involved, such as chronic inflammation and direct neuronal toxicity induced by uremia.[3]

ROLE OF INFLAMMATION AND ACCUMULATION OF UREMIC TOXINS IN NEUROLOGICAL CONDITIONS

Inflammation and neurological damage

The blood-brain barrier (BBB) is a highly selective, nonfenestrated system separating the brain parenchyma from the blood and protects the brain from circulating neurotoxic compounds. Its disruption has been implicated in neurodegenerative conditions such as neurocognitive impairment, Alzheimer's disease (AD), and PD.[29,30]

Rodent and human models of CKD have exhibited increased BBB permeability and associated cognitive impairment.[31,32] Studies have demonstrated that pro-inflammatory cytokines—including tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), and IL-1β—can damage the BBB and thus alter its permeability by destroying the tight junctions of the neurovascular unit.[33,34] These cytokines can also change the phenotype of the microglia toward a pro-inflammatory state, characterized by the secretion of more TNF-α, IL-1α, and complement component 1q, which interact with astrocytes to propagate neuroinflammation.[35] In individuals with CKD, the levels of these cytokines are frequently elevated due to reduced renal clearance, the inherent chronic inflammatory state of the disease, and dialysis-related factors.[36] Consequently, CKD may contribute to BBB disruption and increase the brain's vulnerability to neuroinflammation.

Neuroinflammation contributes to cellular impairment in various domains, such as synaptic dysfunction, inhibition of neurogenesis, microglial priming, apoptosis, and alterations in CNS proteins—ultimately accelerating brain aging and cognitive decline [Figure 2].[37] Furthermore, the cascade inflammatory response is a central mediator in the course of stroke. Elevated levels of these cytokines in the cerebrospinal fluid (CSF) and blood of stroke patients are associated with clinical prognosis. In preclinical studies, TNF-α receptor inhibitors have been shown to reduce brain damage in a model of ischemic stroke.[38]

Forming another group of pathologies mediated by inflammation are peripheral nervous system diseases, which include Guillain-Barré syndrome (GBS). GBS is an acute inflammatory demyelinating polyradiculopathy characterized by nerve edema, perivenular lymphocytic infiltrates, and macrophage-mediated demyelination, accompanied by the production of IFN-γ, TNF-α, IL-1, and IL-10, which exacerbates nerve damage and promotes myelin phagocytosis.[39] Additionally, analysis of the CSF of individuals with GBS has revealed increased concentrations of the pro-inflammatory cytokines IL-8, IL-1, IL-17, IL-22 and of chemokines compared to healthy controls.[39,40] This upregulation of pro-inflammatory cytokines correlates with the clinical severity of GBS, whereas increased concentrations of the anti-inflammatory cytokines IL-4, IL-10, and TGF-β are associated with recovery.[39,41] Moreover, one of the treatment options for GBS, intravenous immunoglobulin, has been shown to reduce circulating levels of the pro-inflammatory cytokines TNF-α and IL-1β, with clinical improvement linked to the reduction of TNF-α levels.[39]

Beyond inflammatory mediators, another pathophysiological pathway involves the accumulation of PBUTs, which aggravate neurological dysfunction through distinct but complementary mechanisms.

Protein-bound uremic toxins and neurological damage

The accumulation of uremic toxins is considered a nontradi-

tional risk factor for the development of neurological disorders in CKD.[3] Among the persistently retained molecules are advanced glycation end products (AGEs) and other classical PBUTs.[3] These metabolites are ineffectively removed through conventional dialysis due to their strong affinity for plasma proteins, leading to their systemic accumulation in individuals undergoing this treatment.[3,42,43]

AGEs are formed through nonenzymatic reactions between sugars and proteins or lipids—a process accelerated by oxidative stress and altered metabolism, as observed in CKD.[44] Their accumulation contributes to endothelial oxidative damage, disrupting cell barriers *via* oxidant species such as hydroxyl, carbonate, and thiyl radicals. The accumulation of reactive oxygen species *via* the AGEs-receptor for AGEs (RAGE) signaling pathway increases the BBB's paracellular permeability by downregulating actin depolymerizing factor expression, thereby promoting neuronal degeneration and cell membrane damage through lipid peroxidation, changes in protein structure and function, protein oxidation, and structural DNA damage [Figure 2].[45,46]

In AD, RAGE facilitates transport of the RAGE-bound Aβ across the endothelial cell membrane of the BBB *via* transcytosis. Additionally, RAGE expression is markedly elevated in regions of Aβ accumulation.[47,48] N-carboxymethyl-lysine—one of the best-characterized AGEs and a marker of AGE accumulation in several tissues—has been identified in intracellular protein deposits within neurofibrillary tangles and in the CSF of individuals with AD.[22] Moreover, increased dietary AGEs have been associated with poorer spatial learning, accelerated Aβ deposition in mice, and faster cognitive decline in adults.[22]

Another disease affected by AGEs is PD. AGEs may contribute to Lewy body crosslinking and intracellular oxidative stress *via* RAGE activation.[49] Consequently, AGEs are directly implicated in microglia-mediated neuroinflammation and α-synuclein aggregation, potentiating PD degeneration and progression.[22]

Classical PBUTs originate primarily from the gut microbial metabolism of dietary components. In individuals with end-stage kidney disease, enzymatic alterations in the gut microbiota increase the production of uremic toxin precursors, which are subsequently conjugated with sulfate ions in the liver to form PBUTs. These toxins accumulate as a result of impaired renal excretion and bind to the aryl hydrocarbon receptor (AhR), contributing to systemic intracellular signaling pathways implicated in uremic toxicity.[43]

One of the most extensively studied PBUTs is IS, which induces free radical production and amplifies the inflammatory response in LPS-stimulated macrophages. IS can also directly damage neurons and activate AhR in astrocytes, triggering oxidative stress, nuclear factor kappa-B (NF-κB) signaling, and the release of pro-inflammatory cytokines.[46] Additionally, in rodent models of CKD, AhR activation by IS accumulation is linked to BBB disruption, impaired cognitive performance, and neuroinflammation. Moreover, IS affects glycolysis in astrocytes not only dose-dependently but also time-dependently. The significance of aerobic glycolysis in astrocytes has been extensively documented in metabolic brain disorders such as AD and PD.[31,46,50,51]

Another PBUT linked to neurological manifestations is p-Cresol. Elevated p-Cresol levels reportedly altered brain dopamine metabolism, reducing the excitability of dopaminergic neurons in the ventral tegmental area and exacerbating neurological disorders in experimental animals, including progressive neurodegeneration characteristic of PD.[52] Individuals with PD experiencing motor fluctuations had been found to have higher plasma p-Cresol levels and increased concentrations in the CSF.[53]

In summary, the accumulation of PBUTs in CKD plays a critical role in driving oxidative stress, endothelial dysfunction, and neuroinflammation. Their limited clearance by conventional dialysis and their ability to activate pro-inflammatory and oxidative signaling pathways—such as RAGE and AhR—highlight their contribution to the pathogenesis of neurodegenerative diseases, including AD and PD. Understanding these mechanisms underscores the need for more effective detoxification strategies and therapeutic interventions to mitigate their systemic and neurological effects.

ROLE OF HEMOADSORPTION IN NEUROLOGICAL CONDITIONS

Anti-inflammatory and immune-modulating agents are attracting growing interest as therapeutic candidates for neurodegenerative diseases. However, current therapeutic strategies remain inadequate in mitigating inflammatory pathways and eliminating toxic molecules in neurological diseases. Epidemiological studies on the effects of NSAIDs on PD progression have yielded inconsistent results. Nonetheless, alternative drugs with anti-inflammatory properties are being tested in preclinical and clinical trials.[54] Conventional dialysis is not only unable to remove adequate amounts of inflammatory mediators but also of PBUTs.[55] To address these limitations, hemoadsorption has emerged as a potential strategy for removing soluble mediators of inflammation and PBUTs through their sorbent-based mass separation from blood or plasma in both acute and chronic clinical settings.[56]

Extracorporeal hemoadsorption offers an additional approach to blood purification, either independently or in conjunction with other renal replacement therapies. It addresses limitations of prevailing dialysis techniques that rely on diffusion and convection, particularly those related to membrane permeability. The adsorption of solutes onto porous surfaces is ultimately governed by the pore density and diameter of the sorbent structure (typically 20-500 A), as well as the solute concentration. Although forces such as van der Waals and ionic bonds are involved, the hydrophobic affinity of the sorbent with the targeted solutes is the principal mechanism for solute removal in currently available sorbent cartridges.[57]

In this context, the efficacy and safety of extracorporeal hemoadsorption largely depend on the characteristics of the adsorbent material [Table 2]. Uncoated activated charcoal, one of the earliest materials used, demonstrates strong adsorption capacity but is associated with adverse effects such as platelet activation and thrombocytopenia, which limit its clinical use. In contrast, polymethylmethacrylate (PMMA) membranes provide moderate adsorption for PBUTs and have shown favorable biocompatibility, particularly in chronic dialysis applications. These membranes are characterized by a uniform pore structure and symmetric design, enabling both diffusion and direct adsorption. Their ability to bind middle molecules, such as β2M

Table 2

Characteristics and biocompatibility of adsorbent materials used in hemoadsorption

Characteristic	Lixelle (S-15, S-25, S-35)	Jafron (HA130, HA380)	Biosky MG	Cytosorb
Type of beads	Porous cellulose beads with immobilized hexadecyl group	Neutral macroporous resin, polystyrene-divinylbenzene	Neutral macroporous resin, polystyrene-divinylbenzene	Neutral macroporous polyvinylpyrrolidone-coated polystyrene-divinylbenzene beads
Target molecules	β2-Microglobulin	Protein-bound uremic toxins (IS, p-CS, AGEs). Inflammatory cytokines, middle molecules	Protein-bound uremic toxins (IS, p-CS, AGEs). Inflammatory cytokines, middle molecules	Protein-bound uremic toxins. Inflammatory cytokines, middle molecules
Resin volume	S-15: 150 mL S-25: 250 mL S-35: 350 mL	HA130: 130 mL HA380: 380 mL	350 mL	300 mL
Blood volume	S-15: 65 mL, S-25: 105 mL S-35: 177 mL	HA130: 100 mL HA380: 180 mL	Not specified	150 mL
Pore size	4-20 kDa, designed to selectively adsorb β2-MG (11.8 kDa)	HA130: 5-30 kDa HA380: 10-60 kDa	5-50 nm	5 nm 60 kDa
Anticoagulation	Standard heparin or regional citrate anticoagulation	Standard heparin; citrate in some cases	Standard heparin; no mention of citrate usage	Standard heparin; citrate in some cases
Blood flow rate	150-250 mL/min in evaluated studies	100-700 mL/min	150-200 mL/min	150-700 mL/min

IS, indoxyl sulfate; p-CS, p-cresyl sulfate; β2-MG, beta2-Microglobulin; AGEs, advanced glycation end products.

and free light chains, as well as inflammatory mediators, has positioned them as an immunomodulatory option in selected individuals. Additionally, their bisphenol-free composition enhances their hemocompatibility. More recently, neutro-macroporous resin-based cartridges—such as HA130 and HA330/HA380—have demonstrated enhanced removal of middle molecules and protein-bound toxins, with low cytotoxicity and minimal complement activation. *In vitro* studies have confirmed that these resins do not induce apoptosis or inflammatory gene expression, suggesting a safer profile for long-term use in extracorporeal therapies.[58-60]

Information from studies that directly addressed neurological conditions—such as PD, AD, and hemoadsorption—is scarce. However, data from animal models and other patient profiles offer promising directions. Yamamoto *et al.* demonstrated *in vitro* that activated carbon-based direct hemoadsorption effectively removes IS, p-cresol sulfate, indole acetic acid, phenyl sulfate, and hippuric acid, with reduction ratios ranging from 77.7% to 99.4%.[55] Additionally, the use of a highly adsorptive PMMA membrane in hemodiafiltration significantly reduced IS concentrations over six months.[61] Zhang *et al.* showed that extending combined hemoadsorption and hemodialysis sessions to 4 hour significantly enhanced the removal of IS, p-cresol sulfate, and β2M compared to the conventional 2-hour treatments in individuals undergoing maintenance haemodialysis.[62] Regarding AGEs, neutral mesoporous resin devices achieved 45%-50% reduction ratios for these PBUTs and pro-inflammatory cytokines in individuals on maintenance hemodialysis, although the specific AGE species were not identified.[63] Our group observed a 64.7% *in vivo* reduction in N-carboxymethyl-lysine levels.[64]

Efforts targeting direct neurological pathologies have included the use of cellulose beads immobilized hexadecyl as a ligand (Lixelle®) sorbents in individuals with AD, based on the hypothesis that active removal of Aβ from the circulating blood promotes its clearance from the brain. Lixelle ahas demonstrated high removal efficiency—51.1% and 43.8% for $A\beta_{1-40}$ and $A\beta_{1-42}$, respectively—reflecting reduced Aβ accumulation in the brain and improved cognitive function in individuals undergoing maintenance hemodialysis, as well as in those without CKD.[65-68] Aβ reduction has also been reported with the use of PMMA membranes.[69]

Regarding GBS, an interesting study examined the clinical effects of hemoadsorption as a treatment. Forty-one individuals with GBS received intravenous immunoglobulin, while another 41 were treated with hemoadsorption. IL-17 and IL-22 levels were significantly elevated in the GBS group, and serum cytokines were significantly reduced in the hemoadsorption group. Moreover, the hemoadsorption group had better scores on the activities of daily living scale, indicating their improved self-care ability.[70] Other GBS cohorts have demonstrated reductions in both inflammatory markers—such as TNF-α and IL-18—and mechanical ventilation requirements.[71,72]

Additionally, studies have reported hemoadsorption benefits for neurological conditions other than those mentioned, such as inflammatory myopathies and neuromyelitis optica syndrome. However, further research is warranted in these areas [Table 3].[73,74]

Challenges and future directions for clinical translation

Despite encouraging experimental data on the potential benefits of hemoadsorption for neurological disorders—including AD, PD, GBS, and certain forms of vascular or inflammatory dementia—physiological and technical challenges limit its clinical application. Specifically, validated biomarkers to guide treatment initiation and duration in neurological contexts are lacking, and parameters such as flow rate, treatment duration, and device-membrane matching require standardization.

Future studies on hemoadsorption for neurological disorders must prioritize the identification of reliable peripheral biomarkers, such as circulating tau, neurofilament light chain, and cytokines implicated in neuroinflammation. These biomarkers may help establish biological plausibility for extracorporeal therapies. Initial studies should aim to confirm the effective removal of these mediators *via* hemoadsorption, thereby providing proof of the viability of this method.

Table 3

Clinical studies of hemoadsorption in neurological disorders

Diseases	Author	Sorbent	Patients	Treatment	Outcomes
Neuromyelitis optica	Liu[74]	HA280	Case report (1)	Once every other day - 5 treatments	No decrease in anti-AQP4 antibodies Visual acuity improvement
Idiopathic inflammatory myopathies	Li[73]	HA280	72 patients	HA for 3 times	Improvement in symptoms, autoimmune antibodies, CK, ESR, RP and ferritin levels
Guillain Barre syndrome	Yu[70]	No Data	82 patients	2 to 3 hours per session. Once every 2 days. 3 to 6 session	Higher activities of daily living scale in HA group. Reduction of IL-17 and IL-22
	Qi[71]	HA130	76 patients	2 to 3 hours per session. Once every 2 days. 3 to 6 session	Reduction of TNF-α and IL-18. Improvement in Hughes Functional Grading Scale. Improvement in mechanical ventilation requirement days
	Li[72]	HA130	64 patients	2 to 3 hours per session. Once every 2 days. 3 to 6 session	Reduction in TNF-α and IL-18. Improvement in mechanical ventilation requirement days

TNF-α, tumor necrosis factor alpha; ESR, erythrocyte sedimentation rate; IL-17, interleukin-17.

Possible early signals of efficacy include surrogate clinical outcomes, such as cognitive performance scores, delirium indices, and neurobehavioral assessments. Only after these phases are established should randomized trials be designed to assess hard clinical outcomes, including functional neurological recovery, quality of life, and long-term disability measures. This stepwise approach may enable the rational integration of hemoadsorption into therapeutic strategies for complex neuroimmune disorders.

In parallel, further refinement of adsorbent materials is needed to improve molecular targeting and biocompatibility, and to minimize off-target effects. Moreover, combining hemoadsorption with pharmacologic therapies could potentiate therapeutic effects in specific patient populations. Ultimately, personalized strategies based on neuroimmune phenotyping may allow for better patient selection and optimization of extracorporeal interventions.

However, any potential integration of hemoadsorption into chronic neuroinflammatory disease management must be preceded by long-term safety assessments. Repeated or sustained use may carry risks such as nutrient depletion or unintended drug removal. Although some preliminary data from chronic dialysis populations suggest a favorable safety profile for specific cartridges, robust prospective studies are needed to evaluate the tolerability and cumulative effects of hemoadsorption in neurologically vulnerable individuals.

Additionally, several unresolved issues must be addressed before clinical implementation can advance—including the lack of standardized thresholds for toxin removal that correlate with neurological benefits, the absence of clear selection criteria for adsorbent materials based on disease phenotype, and the limited comparative data across adsorbent technologies. Conflicting results across studies—particularly regarding neurocognitive outcomes and inflammatory mediator dynamics—underscore the urgent need for harmonized protocols and better designed clinical trials.

CONCLUSION

The rationale for using adsorption in neurological conditions is clear, and incremental advances are shedding light on what could be extended even to individuals with normal renal function. For now, however, these therapies should be promoted to benefit individuals with neurological conditions who are undergoing maintenance hemodialysis by studying surrogate outcomes such as removal of α-synuclein and Aβ protein, alongside improvements in cognitive and/or motor performance.

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Author contributions

Ramírez-Guerrero G, Ronco C: Designed the work. Ramírez-Guerrero G, Ferri-Cortés A, Cabrera-Aguilar JS, Ronco C: Collected and analyzed the data, Writing—Original draft, Writing—Review and Editing. All authors read and approved the final manuscript.

Ethics approval

Not applicable.

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Conflict of interest

Claudio Ronco is the Editor-in-Chief of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of the editor and the affiliated research groups.

Data availability statement

All data generated or analyzed during this study are included in this published article.

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