

# EAN Panel Yearbook 2025

The Scientific and Coordinating Panels listed below were invited to provide content for the EAN Panel Yearbook 2025. We would like to thank all Panels who contributed.



ALS and Frontotemporal Dementia



Autonomic Nervous System Disorders



Child Neurology



Clinical Neurophysiology



Coma & Chronic Disorders of Consciousness



Dementia & Cognitive Disorders



Diversity, Equity & Inclusion in Neurology



Epilepsy



Functional Neurological Disorders



Headache



Higher Cortical Functions



Infectious Diseases



Movement Disorders



Multiple Sclerosis



Muscle & NMJ Disorders



Neurocritical Care



Neuroepidemiology



Neurogenetics



Neuroimaging



Neuroimmunology



Neuro-oncology



Neuro-ophthalmology & -otology



Neuropathies



Neurorehabilitation



Neuroscience / Translational Neurology



Neurosonology



Neurotraumatology



Pain



Palliative Care



Rare Neurological Diseases



Sleep-wake Disorders



Stroke

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# Foreword



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Committee Chair*

Neurological disorders heavily contribute to the global disease burden, affecting more than 40% of the world's population. In this concerning context, scientific advancements in our field are more critical than ever. Recent estimates show that millions of people in the WHO European Region are living with a neurological disease, highlighting the immense impact of these conditions on individuals and society.

Improving care of people living with neurological disorders and preventing neurological diseases depends on science and can be achieved by building a deep foundation of knowledge about neurological diseases and their prevention that guide our actions. The EAN provides a unique opportunity to bring together brilliant minds working collectively to address significant societal challenges.

In this context, we are proud to present the first EAN Panel Yearbook, an initiative that aims to highlight the most outstanding advances and key scientific developments in neurology since summer 2023.

The highlights presented in this yearbook have been carefully selected from international literature by the EAN Scientific & Coordinating Panels, which are often regarded as the Academy's "scientific backbone". EAN panel members have also made short summaries, providing valuable insights into the latest progress in the field.

Beyond serving as a scientific reference, this yearbook raises awareness of the need for increased research funding and highlights the current research gaps. These critical issues have also been addressed in [A strategic neurological research agenda for Europe: Towards clinically relevant and patient-centred neurological research priorities](#) by P. Boon et al.

The initiative of the EAN Panel Yearbook supports the essential need to enhance research in Europe and beyond. Advancing neurosciences and neurology, with the collaboration of physicians, allied health professionals, and people living with neurological disorders, is fundamental to reducing the burden of neurological diseases, driving prevention strategies, and ensuring brain health for all.

On behalf of the EAN Board and the whole EAN membership, we would like to [thank the EAN Panels' working groups](#) for their hard work and commitment. Their dedication and expertise are crucial in promoting excellence in neurological science, guiding future research, and ultimately improving the lives of those affected by neurological diseases.

# Scientific Panels

# ALS and Frontotemporal Dementia



## Real-world impact of tofersen in SOD1-ALS patients

A multicenter study evaluated the use of tofersen, an antisense oligonucleotide, in patients with amyotrophic lateral sclerosis (ALS) caused by mutations in the superoxide dismutase 1 (SOD1) gene. Over 12 months, patients receiving tofersen showed a slower decline in motor function and significant reductions in neurofilament levels—biomarkers of nerve cell damage. These findings, obtained in a real-world setting, support tofersen's role as a disease-modifying therapy for SOD1-ALS with manageable safety concerns.

### Reference

Wiesenfarth, M., Dorst, J., Brenner, D., Elmas, Z., Parlak, Ö., Uzelac, Z., ... & Ludolph, A. C. (2024). Effects of tofersen treatment in patients with SOD1-ALS in a “real-world” setting – a 12-month multicenter cohort study from the German early access program. *EClinicalMedicine*, 69. doi: [10.1016/j.eclinm.2024.102495](https://doi.org/10.1016/j.eclinm.2024.102495).

### Keywords

ALS, tofersen, SOD1, neurofilaments, disease progression

## Non-invasive mechanical ventilation slows ALS progression

A retrospective study involving 448 patients with amyotrophic lateral sclerosis (ALS) demonstrated that non-invasive mechanical ventilation (NIMV) significantly slows functional decline. In particular, patients receiving nighttime respiratory support experienced improved quality of life and a slower deterioration in motor function. These findings underscore the importance of respiratory support in managing ALS and suggest that early initiation of NIMV may enhance patient outcomes.

### Reference

Grassano, M., Koumantakis, E., Manera, U., Canosa, A., Vasta, R., Palumbo, F., ... & Chiò, A. (2024). Giving Breath to Motor Neurons Noninvasive Mechanical Ventilation Slows Disease Progression in Amyotrophic Lateral Sclerosis. *Annals of Neurology*, 95(4), 817–822. doi: [10.1002/ana.26875](https://doi.org/10.1002/ana.26875).

### Keywords

ALS, non-invasive ventilation, respiratory support, disease progression

## Novel biomarker from faulty RNA splicing in TDP-43-related ALS/FTD

Researchers found that when the TAR DNA-binding protein 43 (TDP-43) does not function properly, it leads to errors during RNA splicing. These errors cause the production of *de novo* proteins that are not usually present. The study detected these new proteins in both human nerve cells and the spinal fluid of patients with amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Because they can be measured, they may serve as a diagnostic and monitoring biomarker. This discovery improves our understanding of the diseases and paves the way for improved diagnostic tools.

### Reference

Seddighi, S., Qi, Y. A., Brown, A. L., Wilkins, O. G., Bereda, C., Belair, C., ... & Ward, M. E. (2024). Mis-spliced transcripts generate de novo proteins in TDP-43-related ALS/FTD. *Science Translational Medicine*, 16(734), eadg7162. doi: [10.1126/scitranslmed.adg7162](https://doi.org/10.1126/scitranslmed.adg7162).

### Keywords

TDP-43, biomarkers, RNA splicing, ALS, frontotemporal dementia (FTD)



## Improved clinical phenotyping of the postural orthostatic tachycardia syndrome

Postural Orthostatic Tachycardia Syndrome (POTS) is an extremely common but yet poorly understood cause of orthostatic intolerance. The COVID-pandemic made POTS research even more pressing as POTS incidence rose significantly. In this publication the authors attempted to define a hyperadrenergic POTS subtype through the systematic assessment of sympathetic activity (supine multiple sympathetic nerve activity, norepinephrine levels, blood pressure responses to the Valsalva maneuver) and correlated the phenotyping results to the clinical response to guanfacine, a central sympatholytic drug. Patients with hyperadrenergic POTS, as identified by autonomic phenotyping, more often reported clinical improvement and reported less chronic fatigue in response to guanfacine. These results are consistent with the concept that POTS is caused by central sympathetic activation in a subset of patients and support the use of a thorough autonomic examination to predict treatment response.

### Reference

Okamoto, L. E., Urechie, V., Rigo, S., Abner, J. J., Giesecke, M., Muldowney, J. A. S., Furlan, R., Shibao, C. A., Shirey-Rice, J. K., Pulley, J. M., Diedrich, A., & Biaggioni, I. (2024). Hyperadrenergic postural tachycardia syndrome Clinical biomarkers and response to guanfacine. *Hypertension*, 81(11), 2237–2247. doi: [10.1161/HYPERTENSIONAHA.124.23035](https://doi.org/10.1161/HYPERTENSIONAHA.124.23035).

### Keywords

orthostatic intolerance, postural orthostatic tachycardia syndrome, POTS

## Impaired cholinergic integrity of the colon and pancreas in dementia with Lewy bodies

Dementia with Lewy bodies leads to significant dysautonomia and the Lewy pathological deposits interfere with physiological sympathetic and parasympathetic activation of peripheral organs. Denervation of the pancreas and colon of patients with newly diagnosed dementia with Lewy bodies was demonstrated by showing reduced uptake of 18F-fluoroethoxybenzovesamicol, a PET tracer that binds to the acetylcholine transporter in cholinergic presynaptic terminals. Reduced uptake of the tracer in the brainstem was also noted and this correlated with autonomic and non-motor symptoms, measured both by subjective and objective means. This could serve as a novel imaging biomarker in the diagnosis of prodromal dementia with Lewy bodies.

### Reference

Okkels, N., Horsager, J., Fedorova, T. D., ... & Borghammer, P. (2024). Impaired cholinergic integrity of the colon and pancreas in dementia with Lewy bodies. *Brain*, 147(1), 255–266. doi: [10.1093/brain/awad391](https://doi.org/10.1093/brain/awad391).

### Keywords

dementia, Lewy bodies, cholinergic, dysautonomia

## Randomized controlled trial of intravenous immunoglobulin for autoimmune postural orthostatic tachycardia syndrome

Postural Orthostatic Tachycardia Syndrome (POTS) is defined by an excessive increase in heart rate on standing with orthostatic symptoms without hypotension. It often affects young women. The cause of POTS is multifactorial. POTS may be associated with autoimmune disorders and has been reported after viral infection. Immunomodulatory therapy (in particular intravenous immunoglobulin, IVIG) has been proposed to treat immune-mediated dysautonomia. However, randomized controlled trials are lacking.

In this study, the authors compared IVIG with intravenous albumin infusions in a single-site randomized controlled trial. 30 patients with POTS, autonomic symptoms (assessed by COMPASS-31) and predetermined criteria suggesting autoimmunity received eight infusions (0.4 gm/kg each) over 12 weeks.

No statistical difference was found between the groups comparing IVIG with albumin. However, both groups showed some clinical improvement possibly related to volume expansion or possible other factors. Larger randomized controlled trials are warranted with well-defined inclusion criteria, and careful control of confounding factors.

### Reference

Vernino, S., Hopkins, S., Bryarly, M., Hernandez, R. S., & Salter, A. (2024). Randomized controlled trial of intravenous immunoglobulin for autoimmune postural orthostatic tachycardia syndrome (iSTAND). *Clinical Autonomic Research*, 34(1), 153–163. doi: [10.1007/s10286-024-01020-9](https://doi.org/10.1007/s10286-024-01020-9).

### Keywords

postural tachycardia syndrome, autoimmune, intravenous immunoglobulin, dysautonomia



## Evaluation of safety and efficacy of new treatment option in adolescent patients with generalized myasthenia gravis

Eculizumab is a medicine that can be used to treat myasthenia gravis in situations when other medicines do not work. Eculizumab affects patients' immune system, and accordingly, there is a risk for serious infections. Recently Eculizumab's safety and efficacy were studied in 11 adolescents (ages 12–17) with refractory generalized myasthenia gravis (gMG). Patients received eculizumab for 26 weeks, showing significant improvements in disease severity scores ( $p < 0.01$ ). The treatment demonstrated a rapid and sustained effect, improving muscle function and quality of life. Adverse events were mild to moderate, mainly headaches and respiratory infections; no serious infections like meningococcal infections. In conclusion, eculizumab proved to be effective and well tolerated in adolescents with refractory gMG.

### Reference

Brandsema, J. F., Ginsberg, M., Hoshino, H., et al. (2024) Eculizumab in Adolescent Patients With Refractory Generalized Myasthenia Gravis: A Phase 3, Open-Label, Multicenter Study. *Pediatric neurology*, 156, 198–207. doi: [10.1016/S1474-4422\(24\)00220-5](https://doi.org/10.1016/S1474-4422(24)00220-5).

### Keywords

generalized myasthenia gravis, eculizumab, phase 3

## Evaluation of safety and efficacy of novel treatment for children with ataxia telangiectasia

Ataxia-telangiectasia (AT) is a rare disease that affects one's nervous and immune systems. The recent high-quality multicenter treatment trial to find a cure for AT was performed in 12 countries. Participants (aged 6 years or older) were randomly assigned to low-dose (approximately 5–10 mg), or high-dose (approximately 14–22 mg) intra-erythrocyte dexamethasone sodium phosphate treatment, or placebo. Compared with the placebo group, no statistically significant differences were identified with regard to change in specific ataxia rating scale score, mICARS (modified International Cooperative Ataxia Rating Scale). No significant adverse events were reported. Subgroup analyses identified a potential benefit of treatment in patients aged 6–9 years, and therefore the studies will continue in participants in this age group.

### Reference

Zielen S, Crawford T, Benatti L, et al. Safety and efficacy of intra-erythrocyte dexamethasone sodium phosphate in children with ataxia telangiectasia (ATTeST) a multicentre, randomised, double-blind, placebo-controlled phase 3 trial. *Lancet Neurology*. 2024 Sep;23(9):871–882. doi: [10.1016/S1474-4422\(24\)00220-5](https://doi.org/10.1016/S1474-4422(24)00220-5).

### Keywords

ataxia telangiectasia, dexamethasone sodium phosphate, phase 3

## Guidelines for pediatric status dystonicus

Status dystonicus (SD) is the most dangerous complication of dystonia and is more frequent in the pediatric population. A panel of experts published consensus-based recommendations regarding management of SD. Importantly, a stepwise approach has been used including recommendations about diagnosis and treatment of pre-dystonic status, SD and refractory SD. Two principles are of utmost importance: early recognition and therapy. Clinicians are recommended to follow the Acute Dystonic Clinical Pathway: 1. First step is evaluation of dystonia severity with video assessment, the Dystonia Severity Scale and the sleep–wake dystonia diary. 2. Secondly, active evaluation of worsening triggers such as illness or distress should be implemented. Furthermore, supportive measures should be initiated and, if needed, pharmacological therapy with such agents as diphenhydramine, diazepam, clonidine, chloral hydrate, dexmedetomidine or midazolam should be considered. In case of refractory SD, genetic testing and advanced therapies such as baclofen pump or deep brain stimulation could be used.

### Reference

Vogt LM, Yang K, Tse G, et al. Recommendations for the Management of Initial and Refractory Pediatric Status Dystonicus. *Movement Disorders*. 2024 Apr 15; 39(9):1435–1445. doi: [10.1002/mds.29794](https://doi.org/10.1002/mds.29794).

### Keywords

pediatric status dystonicus, deep brain stimulation, guidelines, treatment

## Understanding the effects of perinatal stroke on brain networks and cognition in children at the connectome level by examining functional brain networks

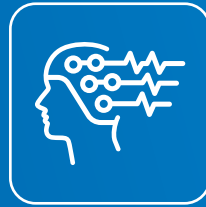
Brain network science, or connectomics, represents connections between simultaneously active brain regions. Functional network organization is associated with cognitive performance, especially intelligence. This study investigated the correlation between functional brain network characteristics and cognitive functions in children after perinatal stroke. The resting state functional connectomes in the alpha frequency band and mental abilities were analyzed from a 64-channel resting state EEG in 24 children with a history of perinatal stroke and compared with the healthy controls. The correlation between network characteristics and specific cognitive functions was investigated. Functional network modularity was positively correlated with IQ and processing speed. Higher network segregation and stronger whole-brain and interhemispheric connectivity were positively associated with impulsive decision-making. The data showed that specific cognitive functions were associated with distinct brain network properties and that functional network properties after perinatal stroke reflected poorer cognitive function.

### Reference

Kavčič A, Borko DK, Kodrič J, Georgiev D, Demšar J, Soltirovska-Šalamon A. EEG alpha band functional brain network correlates of cognitive performance in children after perinatal stroke. *NeuroImage*. 2024 Aug 15;297:120743. doi: [10.1016/j.neuroimage.2024.120743](https://doi.org/10.1016/j.neuroimage.2024.120743).

### Keywords

perinatal stroke, children, resting state functional connectomes, EEG, cognition



## The link between epilepsy and late-onset Alzheimer's disease: insights and challenges

The connection between late-onset epilepsy and Alzheimer's disease (AD) has been identified, presenting epileptiform activity as a potential early marker of cognitive decline. Novel findings suggest that epileptiform activity can precede cognitive deterioration and predict faster progression. Detecting these abnormal brain discharges in AD patients may have significant clinical value and could serve as a modifiable risk factor for dementia. Early identification of epilepsy-related brain activity could enable more targeted interventions, and potentially slow AD progression. While epileptiform activity seems to worsen neurodegeneration, the effectiveness of current anti-seizure medication on cognitive function remains uncertain. These interactions still need to be clarified to improve clinical outcomes for patients facing this dual burden of neurodegeneration and epilepsy. Enhanced clinical awareness and new therapeutic approaches are essential to addressing this challenge.

### Reference

Kamondi, A., Grigg-Damberger, M., Löscher, W., Tanila, H., & Horvath, A. A. (2024). Epilepsy and epileptiform activity in late-onset Alzheimer disease clinical and pathophysiological advances, gaps and conundrums. *Nature Reviews Neurology*, 20(3), 162–182. doi: [10.1038/s41582-024-00932-4](https://doi.org/10.1038/s41582-024-00932-4).

### Keywords

epilepsy, Alzheimer's disease, cognitive decline, seizures, neuroinflammation

## Transcranial pulsed shockwave stimulation as a novel approach for Alzheimer's disease

First non-controlled data suggests that transcranial pulsed shockwave stimulation (TPS) may influence cortical oscillations and the connectivity of electrical brain networks in Alzheimer's disease (AD). TPS is a non-invasive neuromodulation technique with the potential to enhance neural connectivity and support cognitive function. Preliminary findings indicate measurable changes in brain network activity post-stimulation, suggesting possible therapeutic benefits. However, some uncertainties persist regarding the long-term effects and optimal stimulation parameters for sustained cognitive improvements. While early results underscore improved functional connectivity, larger trials are warranted to establish clinical efficacy.

### Reference

Wojtecki, L., Cont, C., Stute, N., Galli, A., Schulte, C., & Trenado, C. (2024). Electrical brain networks before and after transcranial pulsed shockwave stimulation in Alzheimer's patients. *GeroScience*. doi: [10.1007/s11357-024-01305-x](https://doi.org/10.1007/s11357-024-01305-x).

### Keywords

transcranial pulsed shockwave stimulation, Alzheimer's disease, neuromodulation, brain networks

## Exploring connectivity networks in temporal lobe epilepsy

This summary integrates findings from two complementary studies that explore functional brain network alterations in temporal lobe epilepsy (TLE) using multimodal neuroimaging techniques. One study by Wirsich et al. examines EEG-fMRI connectivity, revealing lateralized differences in network reorganization. Right TLE exhibits increased EEG-fMRI connectivity correlation, suggesting compensatory reorganization, while left TLE shows a localized reduction, particularly in the default mode network. The study by Xie et al. employs MRI-based connectome analysis, identifying disrupted topographic gradients and hierarchical signal flow, which are independent of cortical atrophy but mediated by superficial white matter microstructural alterations. These insights provide a neurobiological basis for cognitive impairments in TLE, particularly memory dysfunction. Both studies emphasize that TLE-related brain alterations extend beyond the seizure focus, affecting large-scale functional and structural networks. Together, these studies underscore the importance of multimodal imaging for epilepsy research and clinical applications, providing a comprehensive framework for improving diagnosis and treatment planning.

### References

Xie, K., Royer, J., Larivière, S., Rodriguez-Cruces, R., Frässle, S., Cabalo, D. G., Ngo, A., DeKraaker, J., Auer, H., Tavakol, S., Weng, Y., Abdallah, C., Arafat, T., Horwood, L., Frauscher, B., Caciagli, L., Bernasconi, A., Bernasconi, N., Zhang, Z., Concha, L., ... Bernhardt, B. C. (2024). Atypical connectome topography and signal flow in temporal lobe epilepsy. *Progress in neurobiology*, 236, 102604. doi: [10.1016/j.pneurobio.2024.102604](https://doi.org/10.1016/j.pneurobio.2024.102604).

Wirsich, J., Iannotti, G. R., Ridley, B., Shamshiri, E. A., Sheybani, L., Grouiller, F., Bartolomei, F., Seeck, M., Lazeyras, F., Ranjeva, J. P., Guye, M., & Vulliemoz, S. (2024). Altered correlation of concurrently recorded EEG-fMRI connectomes in temporal lobe epilepsy. *Network Neuroscience*, 8(2), 466–485. doi: [10.1162/netn\\_a\\_00362](https://doi.org/10.1162/netn_a_00362).

### Keywords

temporal lobe epilepsy, EEG-fMRI connectivity, multimodal neuroimaging, functional connectome, multimodal brain networks

## Real-time monitoring to preserve speech during brain surgery using cortico-cortical evoked potentials

A novel approach in brain tumor surgery enables real-time monitoring of language pathways improving patient safety and surgical precision. Cortico-cortical evoked potentials (CCEPs) allow real-time tracking and protection of critical language tracts during glioma removal, reducing the risk of postoperative speech deficits. This technique provides immediate feedback on language function under anesthesia, enhancing the safety and effectiveness of minimally invasive surgeries. This method offers continuous, objective data without requiring active patient participation, unlike traditional awake mapping, which can be stressful for patients. Integrating CCEP monitoring into neurosurgical procedures may optimize tumor removal while preserving essential brain function, which may lead to better long-term outcomes.

### Reference

Seidel, K., Wermelinger, J., Alvarez-Abut, P., Deletis, V., Raabe, A., Zhang, D., & Schucht, P. (2024). Cortico-cortical evoked potentials of language tracts in minimally invasive glioma surgery guided by Penfield stimulation. *Clinical Neurophysiology*, 161, 256–267. doi: [10.1016/j.clinph.2023.12.136](https://doi.org/10.1016/j.clinph.2023.12.136).

### Keywords

neurosurgery, language preservation, intraoperative monitoring, evoked potentials

# Coma and Chronic Disorders of Consciousness



## Multimodal assessment improves neuroprognosis in acute disorders of consciousness

Outcome prediction for unresponsive patients in the intensive care setting is a complex but important challenge with scientific, ethical and medical implications. Using a multimodal approach combining behavioral, neuroimaging, and electrophysiological markers improves the accuracy of predicting one-year functional outcomes for unresponsive patients with acute brain injury. By categorizing patients using this multimodal assessment between ‘good’, ‘uncertain’ and ‘poor’ prognosis, ‘good’ prognosis is strongly associated with better long-term functional outcome. Increasing the number of assessment modalities reduces uncertainty and enhances prognostic accuracy, providing a stronger basis for clinical decision-making.

### Reference

Rohaut, B., Calligaris, C., Hermann, B., Perez, P., Faugeras, F., Raimondo, F., ... & Naccache, L. (2024). Multimodal assessment improves neuroprognosis performance in clinically unresponsive critical-care patients with brain injury. *Nature Medicine*, 30(8), 2349–2355. doi: [10.1038/s41591-024-03019-1](https://doi.org/10.1038/s41591-024-03019-1).

### Keywords

prognosis, disorders of consciousness, coma, multimodal

## Transcranial direct current stimulation is beneficial for patients in prolonged disorders of consciousness, specifically for patients in minimally conscious state and those with traumatic etiology

Transcranial direct current stimulation (tDCS) is known to be a safe neuromodulation technique for patients with disorders of consciousness (DoC). This European multicenter randomized controlled trial investigated its effects during rehabilitation, applying 2 mA tDCS over the left prefrontal cortex for 20 minutes daily over four weeks. The study found no significant effect at the group level. However, subgroup analyses at three months’ follow-up suggested a benefit for patients in the subgroup of patients in a minimally conscious state (MCS) and with traumatic brain injury. These findings highlight the importance of diagnosis and etiology in determining response to neuromodulation.

### Reference

Thibaut, A., Fregni, F., Estraneo, A., Fiorenza, S., Noe, E., Llorens, R., ... & IBIA DOC-SIG. (2023). Sham-controlled randomized multicentre trial of transcranial direct current stimulation for prolonged disorders of consciousness. *European Journal of Neurology*, 30(10), 3016–3031. doi: [10.1111/ene.15974](https://doi.org/10.1111/ene.15974).

### Keywords

neuromodulation, transcranial direct current stimulation, disorders of consciousness, minimally conscious state

## Active fMRI and EEG paradigms reveal cognitively mediated responses in 25 % of behaviorally unresponsive patients in a large scale multicenter study

Cognitive motor dissociation (CMD) is a condition in which a patient with severe brain injury appears behaviorally unresponsive but can perform cognitive tasks that are detected using functional MRI (fMRI) or electroencephalography (EEG). This large international study prospectively examined clinical, behavioral, and neuroimaging data from 353 adults with disorders of consciousness (DoC). Among the 241 participants without an observable response to commands, 25 % exhibited CMD on fMRI or EEG. In contrast, 38 % of those with an observable response to commands also showed responses on these neuroimaging tests. CMD was more frequent in younger patients, those with longer time since injury, and those with traumatic brain injury. These findings highlight the limitations of bedside behavioral assessments and reinforce the need for multimodal evaluations in DoC patients.

### Reference

Bodien, Y. G., Allanson, J., Cardone, P., Bonhomme, A., Carmona, J., Chatelle, C., ... & Schiff, N. D. (2024). Cognitive motor dissociation in disorders of consciousness. *New England Journal of Medicine*, 391(7), 598–608. doi: [10.1056/NEJMoa2400645](https://doi.org/10.1056/NEJMoa2400645).

### Keywords

cognitive motor dissociation, disorders of consciousness, active paradigm, magnetic resonance imaging, electroencephalography

## Neuroimmune activation is associated with neurological outcome in anoxic and traumatic coma

The role of neuroinflammation in the pathophysiology of coma remains largely unknown. Positron emission tomography (PET) imaging with the 18-kDa translocator protein (TSPO) radioligand 18F-DPA714 was used to quantify neuroimmune activation in 17 coma patients with post-anoxic or post-traumatic lesions, compared to matched healthy controls. Interestingly, immune activation was observed within key cortical and subcortical structures involved in consciousness recovery, including the mesocircuit and frontoparietal networks. Distinct neuroimmune activation profiles emerged between post-anoxic and post-traumatic patients, differing in intensity and spatial distribution. These findings could also serve as a prognostic tool as the extent and localization of neuroinflammation within the mesocircuit correlated with recovery potential of the patients. Therefore, TSPO PET imaging could potentially be used both as a prognostic tool but also to guide future therapeutical clinical trials in acute severe brain injury.

### Reference

Sarton, B., Tauber, C., Fridman, E., Péran, P., Riu, B., Vinour, H., ... & Silva, S. (2024). Neuroimmune activation is associated with neurological outcome in anoxic and traumatic coma. *Brain*, 147(4), 1321–1330. doi: [10.1093/brain/awae045](https://doi.org/10.1093/brain/awae045).

### Keywords

coma, neuroinflammation, positron emission tomography, anoxic brain injury, traumatic brain injury

## Care pathways for individuals with post-anoxic disorder of consciousness

Despite the availability of solid bedside predictors of poor outcome in post-anoxic patients (i. e., the absence of bilateral somatosensory-evoked potentials) and validated diagnostic tools (as recommended by EAN guidelines), the management and care of patients with disorders of consciousness (DoC), especially with post-anoxic encephalopathy, vary significantly between countries and regions. This multidisciplinary intersociety Consensus Conference provided the first operational recommendations for guiding clinicians in the management of post-anoxic coma and prolonged DoC, and prompted an international consensus on diagnostic and prognostic procedures for these patients. A multimodal assessment combining clinical, neurophysiological and neuroimaging findings easy to record at bedside in all clinical settings from the acute phase, is crucial for improving accuracy in diagnosis and in neuroprognostication. Additionally, active and collaborative participation of family members, from the acute phase after training, is recommended for gathering valuable information for diagnostic evaluation, monitoring the patient's progress, and participating in rehabilitative treatment.

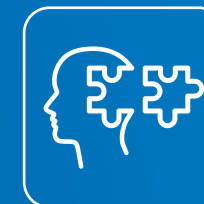
### Reference

Estraneo A, Magliacano A, De Bellis F, Amantini A, Lavezzi S, Grippo A; CaPIADoC study group. Care pathways for individuals with post-anoxic disorder of consciousness (CaPIADoC) an inter-society Consensus Conference. *Neurological Sciences*. 2024 Nov 26. doi: [10.1007/s10072-024-07875-0](https://doi.org/10.1007/s10072-024-07875-0).

### Keywords

anoxia, consciousness disorders, diagnosis, prognosis, rehabilitation, vegetative state

# Dementia and Cognitive Disorders



## Gaps in biomedical research in frontotemporal dementia: a call for diversity and disparities focused research

Ancestral and ethnocultural background influences the risk factors, clinical expression, distribution, recognition, diagnosis, and treatment of frontotemporal dementia syndromes. Authors have recommended few initial proposals for resolving these gaps like leveraging and expanding current funding, building research expertise, supporting research personnel and developing and building resources for biomarker analyses in research and clinical settings.

### Reference

Nuytemans, K., Franzen, S., Broce, I. J., Caramelli, P., Ellajosyula, R., Finger, E., ... & ISTAART Frontotemporal Dementia and Related Disorders PIA, ISTAART Diversity and Disparities PIA (2024). Gaps in biomedical research in frontotemporal dementia: A call for diversity and disparities focused research. *Alzheimer's & Dementia*, 20(12), 9014–9036. doi: [10.1002/alz.14312](https://doi.org/10.1002/alz.14312).

### Keywords

frontotemporal dementia (FTD), cross-cultural aspects, biomarkers, cultural diversity

## Progranulin AAV gene therapy for frontotemporal dementia: translational studies and phase 1/2 trial interim results

Frontotemporal dementia is a neurodegenerative disorder affecting behaviour and cognition. Mutation in granulin gene (GRN) causes progranulin haploinsufficiency and can cause frontotemporal dementia. PRO06 is an investigational gene therapy delivering the GRN using an adeno-associated virus serotype 9 (AAV9) vector to persons with GRN mutation. In the mouse model, there was improvement in the pathological process. First-in-human phase study was started to evaluate, as primary endpoint, safety and bioactivity, and as secondary endpoint, clinical improvement. This study provides preliminary insights into the safety and bioactivity of PRO06 and longer follow-up is needed to confirm the safety and potential efficacy. Clinical trials with investigational gene therapy for genetic frontotemporal dementia with GRN mutation are ongoing.

### Reference

Sevigny, J., Uspenskaya, O., Heckman, L. D., Wong, L. C., Hatch, D. A., Tewari, A., ... & Hefti, F. (2024). Progranulin AAV gene therapy for frontotemporal dementia translational studies and phase 1/2 trial interim results. *Nature Medicine*, 30(5), 1406–1415. doi: [10.1038/s41591-024-02973-0](https://doi.org/10.1038/s41591-024-02973-0).

### Keywords

frontotemporal dementia (FTD), GRN gene, progranulin, PRO06

## Analysis of cerebrospinal fluid protein revealed 5 molecular subtypes of Alzheimer's disease in regard to the pathophysiology

In this study cerebrospinal fluid proteomics were analysed to see if there are differences among patients with Alzheimer's disease. They have found 5 different molecular subtypes according to different pathological processes leading to Alzheimer's disease: subtype 1 was characterized by proteins related to neuronal hyperplasticity; subtype 2 by innate immune activation; subtype 3 by RNA dysregulation; subtype 4 by choroid plexus dysfunction; and subtype 5 by blood-brain barrier impairment. Subtypes also differed in clinical outcomes, survival times and anatomical patterns of brain atrophy. They have concluded that Alzheimer's disease does not have a unique pathological process, and that treatment should be personalized according to each subtype.

### Reference

Tijms, B. M., Vromen, E. M., Mjaavatten, O., Holstege, H., Reus, L. M., van der Lee, S., ... & Visser, P. J. (2024). Cerebrospinal fluid proteomics in patients with Alzheimer's disease reveals five molecular subtypes with distinct genetic risk profiles. *Nature Aging*, 4(1), 33–47. doi: [10.1038/s43587-023-00550-7](https://doi.org/10.1038/s43587-023-00550-7).

### Keywords

Alzheimer's disease, proteomics, cerebrospinal fluid, subtypes

## ApoE4 and connectivity-mediated spreading of tau pathology at lower amyloid levels

Alzheimer's disease is a neurodegenerative disorder with beta amyloid plaques and aggregation of abnormal tau protein. Carriership of apolipoprotein E  $\epsilon$ 4 (ApoE4) form is linked to faster disease progression. This study was performed to assess if ApoE4 carriers show accelerated amyloid-related tau spreading. The results presented in this study indicate that amyloid-related tau accumulation was accelerated in ApoE4 carriers already at lower amyloid levels. This suggests that ApoE4 is responsible for earlier amyloid-driven tau spreading across connected brain regions. The results of this study may have therapeutic implications to determine when best to prevent tau spreading depending on ApoE4 status.

### Reference

Steward, A., Biel, D., Dewenter, A., Roemer, S., Wagner, F., Dehsarvi, A., ... & Franzmeier, N. (2023). ApoE4 and Connectivity-Mediated Spreading of Tau Pathology at Lower Amyloid Levels. *JAMA Neurology*, 80(12), 1295–1306. doi: [10.1001/jamaneurol.2023.4038](https://doi.org/10.1001/jamaneurol.2023.4038).

### Keywords

Alzheimer's disease, ApoE4, tau pathology, amyloid

# Epilepsy



## Paternal use of valproic acid during spermatogenesis

Concerns exist about teratogenic and long-term neurodevelopmental outcomes of paternal use of valproate during spermatogenesis. The results of a large nationwide cohort study in Denmark suggested that exposure to valproate during spermatogenesis was not associated with offspring risk of congenital malformations or neurodevelopmental disorders, including autism spectrum disorder.

### Reference

Christensen, J., Trabjerg, B. B., & Dreier, J. W. (2024). Valproate Use During Spermatogenesis and Risk to Offspring. *JAMA network open*, 7(6), e2414709. doi: [10.1001/jamanetworkopen.2024.14709](https://doi.org/10.1001/jamanetworkopen.2024.14709).

### Keywords

valproic acid, spermatogenesis, teratogenesis, congenital malformations, neurodevelopmental disorders

## Successful epilepsy surgery in children and cessation of antiseizure medication may not halt but even reverse presurgical neuropsychological decline

This retrospective study in 500 children with drug-resistant epilepsy who underwent epilepsy surgery showed declines in all investigated neuropsychological domains during the time leading to surgery. After surgery, no statistically significant group differences were apparent in the whole group. However, in seizure free children and especially in those who could discontinue antiseizure medication improvements were even greater.

### Reference

Eriksson, M. H., et al. (2024). Long-term neuropsychological trajectories in children with epilepsy does surgery halt decline? *Brain*, 147(8)2791–2802. doi: [10.1093/brain/awae121](https://doi.org/10.1093/brain/awae121).

### Keywords

epilepsy surgery, children, neuropsychology, outcome

## Load of unspecific white and gray matter brain MRI abnormalities are associated with epilepsy in older adults

This prospective study shows that there is an association between not only clearly lesional, but also rather unspecific, i. e., especially slight atrophy and microangiopathic, brain abnormalities and the incidence of epilepsy in older adults. 1251 patients aged 45–65 years had an MRI between 2011 and 2013 and were followed for ten years. The risk for developing epilepsy was 2–3 times increased in patients with unspecific white and gray matter after controlling for demographic and vascular risk factors and dementia.

### Reference

Gugger, J. J., et al. (2024). Association between structural brain MRI abnormalities and epilepsy in older adults. *Annals Clinical Translational Neurology*, 11(2), 342–354. doi: [10.1002/acn3.51955](https://doi.org/10.1002/acn3.51955).

### Keywords

epilepsy, older adults, brain MRI abnormalities, risk

## Timely comprehensive workup after the first seizure improves outcome of epilepsy

This 7-year cohort study demonstrates the remarkable added value of a timely comprehensive workup already at the occurrence of the first seizure in the emergency department for the diagnosis of new-onset epilepsy versus non-epileptic causes of seizure mimickers. The findings show the benefit of first-seizure tracks or even units with overnight electroencephalogram, similar to stroke units, activated upon admission in the emergency room.

### Reference

De Stefano, P., et al. (2023). Added value of advanced workup after the first seizure: A 7-year cohort study. *Epilepsia*, 64(12), 3246–3256. doi: [10.1111/epi.17771](https://doi.org/10.1111/epi.17771).

### Keywords

first seizure, advanced workup, outcome, cohort study, benefit

## Automated interpretation of clinical EEGs using artificial intelligence

Electroencephalograms (EEGs) are a fundamental evaluation in neurology but require special expertise unavailable in many regions of the world. Artificial intelligence (AI) has the potential to address these unmet needs. SCORE-AI achieved human expert level performance in fully automated interpretation of routine EEGs. Application of SCORE-AI may improve diagnosis and patient care in underserved areas and improve efficiency and consistency in specialized epilepsy centers.

### Reference

Tveit, J., et al. (2023). Automated Interpretation of Clinical Electroencephalograms Using Artificial Intelligence. *JAMA neurology*, 80(8), 805–812. doi: [10.1001/jamaneurol.2023.1645](https://doi.org/10.1001/jamaneurol.2023.1645).

### Keywords

EEG, artificial intelligence (AI), diagnosis, interictal epileptiform abnormalities

# Headache



## Experience in the real-world calls for early treatment with anti-calcitonin gene-related peptide (CGRP) therapies

Two recent studies have highlighted the benefits of early treatment with anti-CGRP monoclonal antibodies for migraine prevention. The APPRAISE trial was a prospective open-label global trial that compared erenumab, an anti-CGRP monoclonal antibody, to standard oral migraine preventives in episodic migraine sufferers who did not respond to 1–2 previous treatments. At 12 months, erenumab demonstrated superior adherence (with 6 times higher retention rates), efficacy (56.2% vs. 16.8% of patients achieving  $\geq 50\%$  reduction in monthly migraine days), and clinical improvement (13 times higher Patient Global Impression of Change scores). The EUREKA study examined real-world data from 5,818 European patients and found that higher migraine frequency and greater disability reduce the likelihood of responding to anti-CGRP MAb. Taken together, the results of these studies demonstrate the importance of early anti-CGRP treatment in enhancing adherence, satisfaction, and clinical outcomes for migraine prevention.

### References

Pozo-Rosich, P., Dolezil, D., Paemeleire, K., Stepien, A., Stude, P., Snellman, J., ..., & Gil-Gouveia, R. (2024). Early use of erenumab vs nonspecific oral migraine preventives: The APPRAISE randomized clinical trial. *JAMA Neurology*, 81(5), 461–470. doi: [10.1001/jamaneurol.2024.0368](https://doi.org/10.1001/jamaneurol.2024.0368).

Caronna, E., Gallardo, V. J., Egeo, G., Vázquez, M. M., Castellanos, C. N., Membrilla, J. A., ... & Pozo-Rosich, P. (2024). Redefining migraine prevention: Early treatment with anti-CGRP monoclonal antibodies enhances response in the real world. *Journal of Neurology, Neurosurgery, and Psychiatry*, 95(10), 927–937. doi: [10.1136/jnnp-2023-333295](https://doi.org/10.1136/jnnp-2023-333295).

### Keywords

CGRP, anti-CGRP mAbs, early treatment, migraine

## Anti-pituitary adenylate cyclase-activating polypeptide (PACAP) monoclonal antibody for migraine prevention

In a recent landmark study, the HOPE trial, a promising therapeutic avenue for migraine prevention through a monoclonal antibody targeting pituitary adenylate cyclase-activating polypeptide (PACAP) was introduced. This novel approach is based on PACAP's significant role in the pathophysiology of migraines, acting as a key modulator within the inflammatory and vasodilatory pathways associated with migraine episodes. The clinical trial demonstrated that the monoclonal antibody significantly reduces the frequency of migraine days compared to placebo, offering a new hope for patients who are refractory to traditional treatments. The specificity and efficacy of this treatment underscore a shift towards more targeted therapies in neurology, providing a foundation for future innovations in the treatment of migraine and potentially other neurological disorders where PACAP is implicated.

## Reference

Ashina, M., Phul, R., Khodaie, M., Löf, E., & Florea, I. (2024). A monoclonal antibody to PACAP for migraine prevention. *The New England Journal of Medicine*, 391(9), 800–809. doi: [10.1056/NEJMoa2314577](https://doi.org/10.1056/NEJMoa2314577).

## Keywords

PACAP, anti-PACAC Mab, migraine treatment, migraine prevention

## Acute pharmacological migraine treatment

In a comprehensive systematic review and network meta-analysis, the efficacy and safety of seventeen licensed oral drugs for the acute management of migraine episodes in adults were evaluated. Analyzing 137 randomized controlled trials involving 89,445 participants, the study compared multiple drug classes including NSAIDs, triptans, ditans, gepants, and antipyretics. The results revealed that all active interventions outperformed placebo for achieving pain freedom at two hours, with triptans such as eletriptan, rizatriptan, sumatriptan, and zolmitriptan demonstrating superior efficacy. The findings support the prioritization of specific triptans in clinical guidelines, underscoring the importance of personalized treatment and global accessibility to effective migraine therapies for improved outcomes.

## Reference

Karlsson, W. K., Ostinelli, E. G., Zhuang, Z. A., Kokoti, L., Christensen, R. H., Al-Khazali, H. M., ... & Ashina, M. (2024). Comparative effects of drug interventions for the acute management of migraine episodes in adults Systematic review and network meta-analysis. *BMJ*, 386, e080107. doi: [10.1136/bmj-2024-080107](https://doi.org/10.1136/bmj-2024-080107).

## Keywords

acute treatment, migraine treatment, oral migraine medications, triptans, network meta-analysis

## Basic science – migraine pathophysiology

This study investigates how cerebrospinal fluid (CSF) solutes activate trigeminal ganglion neurons in a migraine model. The research highlights a newly identified communication pathway between the brain and peripheral sensory neurons, where cortical spreading depression (CSD), a brain event associated with migraine aura, triggers the release of specific proteins into CSF. These proteins, including calcitonin gene-related peptide (CGRP), travel to the trigeminal ganglion, directly activating sensory neurons that are implicated in migraine pain. Imaging and proteomic analysis confirmed that this CSF influx is rapid and aligns with typical aura-to-headache timing. The findings suggest that the direct transport of signaling molecules from the brain to peripheral neurons may underlie migraine pain onset, offering potential new therapeutic targets for migraine prevention by modulating this CSF-based signaling pathway.

## Reference

Kaag Rasmussen, M., Møllgård, K., Bork, P. A. R., Weikop, P., Esmail, T., Drici, L., ... & Nedergaard, M. (2024). Trigeminal ganglion neurons are directly activated by influx of CSF solutes in a migraine model. *Science*, 385(6704), 80–86. doi: [10.1126/science.adlo544](https://doi.org/10.1126/science.adlo544).

## Keywords

CSF influx, trigeminal ganglion, migraine models

# Infectious Diseases



## New European guidelines for the diagnosis and treatment of brain abscess in children and adults

In the absence of randomized clinical trials and clinical practice guidelines, there is wide variation across Europe in how brain abscesses are diagnosed and treated. The European Society of Clinical Microbiology and Infectious Diseases published new guidelines offering recommendations for clinicians providing care for children and adults with brain abscess. Based on available scientific evidence, clinical experience, and expert opinion, these guidelines aim to inform best medical practice and will hopefully contribute to a better standardization of care. Due to lack of evidence, no recommendations could be made on early transition from intravenous to oral antibiotics. This remains a high priority topic for physicians managing these patients and is the subject of an ongoing clinical trial.

## References

Bodilsen J, D'Alessandris QG, Humphreys H, et al. European society of Clinical Microbiology and Infectious Diseases guidelines on diagnosis and treatment of brain abscess in children and adults. *Clinical Microbiology and Infection*. 2024;30(1):66–89. doi: [10.1016/j.cmi.2023.08.016](https://doi.org/10.1016/j.cmi.2023.08.016).

Bodilsen J, Brouwer MC, van de Beek D, et al. Partial oral antibiotic treatment for bacterial brain abscess: an open-label randomized non-inferiority trial (ORAL). *Trials*. 2021;22(1):796. doi: [10.1186/s13063-021-05783-8](https://doi.org/10.1186/s13063-021-05783-8).

## Keywords

brain abscess, brain infection, antibiotic, antimicrobial, guidelines

## Tick-borne diseases in the North Sea Region. A comprehensive overview and recommendations for diagnostics and treatment

Specialists in the field of tick-borne diseases from seven North Sea countries co-operated with patient organisations and governmental health care institutions to provide a comprehensive overview of diagnostics and treatment recommendations in the region for Lyme borreliosis, *Borrelia miyamotoi* infection, tick-borne encephalitis, human granulocytic anaplasmosis, rickettsiosis, neohrlichiosis and babesiosis. The recommendations in these countries are essentially the same, with few and minor differences. The overview presents the current diagnostics and provides useful clinical guidance. The work has been part of the NorthTick project, co-funded by the European Union through the European Regional Development Fund and the North Sea Region Programme.

## Reference

Eikeland R, Henningsson AJ, Lebech AM et al. Tick-borne diseases in the North Sea region-A comprehensive overview and recommendations for diagnostics and treatment. *Ticks Tick Borne Diseases*. 2024;15(2):102306. doi: [10.1016/j.ttbdis.2023.102306](https://doi.org/10.1016/j.ttbdis.2023.102306).

## Keywords

clinical picture, diagnostics, recommendations, tick-borne diseases, treatment

## Persistent complement dysregulation with signs of thromboinflammation in active long COVID

Long COVID is a debilitating condition of unknown etiology. This study performed multi-modal proteomics analyses of blood serum from COVID-19 patients followed up to 12 months after confirmed severe acute respiratory syndrome coronavirus 2 infection. Analysis of more than 6500 proteins in 268 longitudinal samples revealed dysregulated activation of the complement system, an innate immune protection and homeostasis mechanism, in individuals experiencing long COVID. Active long COVID was characterized by terminal complement system dysregulation and ongoing activation of the alternative and classical complement pathways. The latter was associated with increased antibody titers against several herpesviruses possibly stimulating this pathway. Markers of hemolysis, tissue injury, platelet activation, and monocyte-platelet aggregates were increased in long COVID. Machine learning confirmed complement and thromboinflammatory proteins to be top biomarkers. Diagnostic and therapeutic strategies may be targeted to interfere with these systems.

### Reference

Cervia-Hasler C, Brüningk SC, Hoch T et al. Persistent complement dysregulation with signs of thromboinflammation in active Long Covid. *Science*. 2024;383(6680). doi: [10.1126/science.adg7942](https://doi.org/10.1126/science.adg7942).

### Keywords

long COVID, proteomics, complement dysregulation, thromboinflammation

# Multiple Sclerosis



## Novel markers to improve the diagnostic work-up of multiple sclerosis

Last year, the integration of optic nerve imaging into the diagnostic criteria for multiple sclerosis (MS) has been suggested. This addition could improve sensitivity, potentially allowing for earlier diagnosis. At the same time, novel magnetic resonance imaging (MRI) markers —such as paramagnetic rim lesions and the central vein sign— showed high specificity for MS, improving diagnostic accuracy, while other MRI findings have been shown to serve as reliable predictors of disease progression. These advancements promise to reshape the upcoming diagnostic criteria, favoring earlier intervention, and to optimize an individualized follow-up.

### References

Vidal-Jordana, A., Rovira, A., Calderon, W., Arrambide, G., Castelló, J., Moncho, D., ... & MAGNIMS. (2024). Adding the Optic Nerve in Multiple Sclerosis Diagnostic Criteria: A Longitudinal, Prospective, Multicenter Study. *Neurology*, 102(1), e200805. doi: [10.1212/WNL.000000000000209214](https://doi.org/10.1212/WNL.000000000000209214).

Rocca, M. A., Preziosa, P., Barkhof, F., Brownlee, W., Calabrese, M., De Stefano, N., ... & Filippi, M. (2024). Current and future role of MRI in the diagnosis and prognosis of multiple sclerosis. *The Lancet Regional Health-Europe*, 44. doi: [10.1016/j.lanepe.2024.100978](https://doi.org/10.1016/j.lanepe.2024.100978).

### Keywords

central vein sign (CVS), paramagnetic rim lesions (PRLs), optic nerve

## Updates on the role of body fluid biomarkers

Intrathecal immunoglobulin G (IgG) synthesis in cerebrospinal fluid (CSF) is a key marker for multiple sclerosis (MS), traditionally detected by CSF-restricted oligoclonal bands (OCBs). Kappa-free light chains (k-FLCs), produced by B cells, have emerged as a promising biomarker. Their diagnostic accuracy is comparable to OCBs, but k-FLC detection is faster, more cost-effective, reliable, and rater-independent. A panel of international experts in MS and CSF diagnostics developed consensus recommendations for k-FLC testing, emphasizing that k-FLC results should be interpreted alongside clinical and imaging findings. Cut-off values for the k-FLC index require further validation through multicenter studies. Borderline k-FLC results should prompt OCB testing, and a combination of both tests is recommended until clear thresholds are established. Detection of intrathecal k-FLC synthesis is included in the 2024 revision of MS diagnostic criteria, as recommended by experts.

### References

Hegen H, Arrambide G, Gnanapavan S, Kaplan B, Khalil M, Saadeh R, et al. Cerebrospinal fluid kappa free light chains for the diagnosis of multiple sclerosis: A consensus statement. *Multiple Sclerosis Journal*. 2023 Feb;29(2):182–195. doi: [10.1177/13524585221134217](https://doi.org/10.1177/13524585221134217).

Di Filippo M, Gaetani L, Centonze D, Hegen H, Kuhle J, Teunissen CE, et al. Fluid biomarkers in multiple sclerosis: from current to future applications. *Lancet Regional Health-Europe*. 2024 Aug 22;44:101009. doi: [10.1016/j.lanepe.2024.101009](https://doi.org/10.1016/j.lanepe.2024.101009).

## Keywords

serum neurofilament light chain (sNfL), intrathecal kappa-free light chains (k-FLCs)

## Radiologically isolated syndrome and multiple sclerosis prodrome

Radiologically isolated syndrome (RIS) represents the presymptomatic phase of the multiple sclerosis (MS) disease continuum, wherein brain and/or spinal cord lesions highly suggestive of MS are discovered incidentally, in the absence of MS-related clinical symptoms. Approximately 50% of RIS patients will develop MS after 10 years. The 2023 revised RIS diagnostic criteria allow the diagnosis in people with lesions in one or two dissemination in space locations, who associate two of the three risk factors for developing MS: at least one spinal cord lesion, oligoclonal bands, dissemination in time on follow-up magnetic resonance imaging (MRI). Although recent clinical trials have shown that dimethyl fumarate and teriflunomide can delay or prevent the first clinical event, the decision to treat RIS patients remains challenging, and the prescription of disease-modifying therapies remains off-label. The revised 2024 McDonald criteria will characterize RIS patients with additional biological and MRI biomarkers as having preclinical MS.

## References

Lebrun-Fréney C, Kantarci O, Siva A, Azevedo CJ, Makhani N, Pelletier D, et al. Radiologically isolated syndrome. *Lancet Neurology*. 2023 Nov;22(11):1075–1086. doi: [10.1016/S1474-4422\(23\)00281-8](https://doi.org/10.1016/S1474-4422(23)00281-8).

Lebrun-Fréney C. The confavreux lecture: The radiologically isolated syndrome diagnosis, prognosis and perspectives. *Multiple Sclerosis Journal*. 2025 Jan 17. doi: [10.1177/13524585241311217](https://doi.org/10.1177/13524585241311217).

## Keywords

magnetic resonance imaging, preclinical MS, radiologically isolated syndrome

## Recommendation for vaccination in multiple sclerosis

The broad use of disease-modifying treatments (DMTs), especially high-efficacy agents, has made vaccination an essential component of risk management strategy for patients with MS. The 2023 European consensus by EAN andECTRIMS provides 53 recommendations on optimal vaccination strategies. These include confirmation that vaccination does not increase relapse or disability risk, as supported by COVID-19 vaccine safety studies. Vaccine efficacy varies by DMTs, with sphingosine-1-phosphate modulators and anti-CD20 drugs significantly reducing antibody production. Vaccination should ideally be performed at diagnosis, though inactivated vaccines can be administered at any time. Live-attenuated vaccines require a 4–6 week window before treatment and should generally be avoided under DMTs, except for interferons, glatiramer acetate, and, in some cases, dimethyl fumarate or natalizumab. Special considerations apply to pediatric, pregnant, elderly, and traveling patients, who should follow tailored vaccination strategies to maintain health and mobility. The benefits of immunization far outweigh potential risks.

## References

Otero-Romero S, Lebrun-Fréney C, Reyes S, Amato MP, Campins M, Farez M, et al.ECTRIMS/EAN consensus on vaccination in people with multiple sclerosis: Improving immunization strategies in the era of highly active immunotherapeutic drugs. *Multiple Sclerosis Journal*. 2023 Jun 9;29(8):904–925. doi: [10.1177/13524585231168043](https://doi.org/10.1177/13524585231168043).

Moisset X, Leray E, Chenaf C, Taithe F, Vukusic S, Mulliez A, et al. Risk of Relapse After COVID-19 Vaccination Among Patients With Multiple Sclerosis in France: A Self-Controlled Case Series. *Neurology*. 2024 Sep 10;103(5). doi: [10.1212/WNL.000000000209662](https://doi.org/10.1212/WNL.000000000209662).

## Keywords

vaccination, infections, disease-modifying therapy (DMT), risk management

# Muscle and Neuromuscular Junction Disorders



## Erythromycin for myotonic dystrophy type 1: a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial

Myotonic dystrophy type 1 (DM1) is the most common form of muscular dystrophy in adults, currently without treatment. DM1 is caused by the expansion of a Cytosine-Guanine-Thymine (CGT) repeat of the Dystrophia Myotonica Protein Kinase (DMPK) gene, which leads to toxic Ribonucleic Acid (RNA) and abnormal splicing. This phase 2 trial investigated the safety of erythromycin, which can suppress RNA toxicity and improve splicing abnormalities in a cell model. 30 genetically confirmed DM1 patients were randomly assigned to placebo, 500 mg erythromycin, or 800 mg erythromycin during 24 weeks. There were no serious safety concerns. Dose-dependent splicing improvement of two splicing biomarkers was seen. Secondary endpoints (6-meter walking test, myotonia score, Individualized Neuromuscular Quality of Life (INQoL) overall score) did not show any significant changes. The authors conclude there is promising evidence of the safety and potential efficacy of erythromycin. They deem it necessary to proceed with a phase 2b trial to define the choice of splicing biomarkers and clinical endpoints.

## Reference

Nakamori M, Nakatani D, Sato T, Hasuike Y, Kon S, Saito T, Nakamura H, Takahashi MP, Hida E, Komaki H, Matsumura T, Takada H, Mochizuki H. Erythromycin for myotonic dystrophy type 1: a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. *EClinicalMedicine*. 2023 Dec 26;67:102390. doi: [10.1016/j.eclinm.2023.102390](https://doi.org/10.1016/j.eclinm.2023.102390).

## Keywords

myotonic dystrophy, DM1, erythromycin, clinical trial

## Safety and efficacy of losmapimod in facioscapulohumeral muscular dystrophy (ReDUX4): a randomised, double-blind, placebo-controlled phase 2b trial

Facioscapulohumeral muscular dystrophy (FSHD) is a progressive genetic muscle disorder linked to aberrant Double Homeobox 4 (DUX4) expression in skeletal muscle, with no approved treatments available. This phase 2b randomized, double-blind, placebo-controlled trial assessed the safety and efficacy of losmapimod, a p38 $\alpha$ / $\beta$  Mitogen-Activated Protein Kinase (MAPK) inhibitor targeting DUX4 expression, in 80 adults with FSHD across 17 international centers. Participants received either losmapimod (15 mg twice daily) or placebo for 48 weeks, with changes in DUX4-driven gene expression as the primary endpoint. Results showed no significant differences in DUX4 expression between groups, but losmapimod demonstrated good tolerability with no treatment-related deaths or discontinuations.

Encouraging trends were observed in muscle structure (fat infiltration), function (reachable workspace), and patient-reported outcomes. These findings have informed the design of a phase 3 trial to further explore losmapimod's potential as a treatment for FSHD. This study underscores the challenges and opportunities in targeting FSHD's underlying mechanisms.

### Reference

Tawil R, Wagner KR, Hamel JI, Leung DG, Statland JM, Wang LH, et al. Safety and efficacy of losmapimod in facioscapulohumeral muscular dystrophy (ReDUX4): a randomised, double-blind, placebo-controlled phase 2b trial. *The Lancet Neurology*. 2024 Apr 15;23(5):477–486. doi: [10.1016/S1474-4422\(24\)00073-1764](https://doi.org/10.1016/S1474-4422(24)00073-1764).

### Keywords

facioscapulohumeral muscular dystrophy (FSHD), losmapimod, clinical trial, randomised, p38 $\alpha$ / $\beta$  MAPK inhibitor

## AI in the diagnostics of neuro-muscular disorders—successful applications, challenges and gaps

Machine learning (ML) and deep learning (DL) models have been most broadly applied in electromyography (EMG) and in neuromuscular ultrasound. These models achieve accuracy rates ranging from 67% to 99.5% for EMG. In neuromuscular ultrasound, DL models using segmentation techniques have reached over 90% accuracy for nerve entrapment disorders and 87% for inflammatory myopathies. Other artificial intelligence (AI) applications include predicting treatment outcomes and application in the diagnosis of patients with myasthenia gravis (among others, analysis of the eyelid distances). While many studies report high accuracy, they often suffer from bias, overtraining, and limited applicability. Additionally, these models often compare patients to healthy individuals, ignoring other neuromuscular conditions commonly seen in clinical practice, which further limits their effectiveness. Current AI models for EMG signals are

not yet ready for clinical practice use due to small study sizes, poor generalization, and limited performance. These challenges should be addressed in the next years.

### References

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De Jonge S, Potters WV, Verhamme C. Artificial intelligence for automatic classification of needle EMG signals: A scoping review. *Clinical Neurophysiology*. 2024 Jan 4;159:41–55. doi: [10.1016/j.clinph.2023.12.134](https://doi.org/10.1016/j.clinph.2023.12.134).

### Keywords

artificial intelligence (AI), neuromuscular disorders, segmentation, machine learning (ML), deep learning (DL)

## Functional improvement of the neurons in MELAS by mitochondrial transfer from highly purified mesenchymal stem cells

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome, caused by a mitochondrial mutation, is one of the most common maternally inherited mitochondrial diseases accompanied by neuronal damage due to defects in the oxidative phosphorylation system. Nowadays, there is no established treatment for MELAS. In the actual study utilizing induced pluripotent stem cells, the authors cultured MELAS neurons and mesenchymal stem cells (MSCs), as well as highly purified rapid expanding clones (RECs) of mesenchymal stem cells. Both RECs and MSCs can donate mitochondria to MELAS neurons, but RECs are more excellent than MSCs for mitochondrial transfer. In addition, REC-mediated mitochondrial transfer significantly restored mitochondrial function, including mitochondrial membrane potential, adenosine triphosphate and reactive oxygen species production, intracellular calcium

storage, and oxygen consumption rate. Moreover, mitochondrial function was maintained for at least three weeks. Thus, REC-donated exogenous mitochondria might offer a potential therapeutic strategy for treating neurological dysfunction in MELAS.

### Reference

Liu L, Yang J, Otani Y, Shiga T, Yamaguchi A, Oda Y, Hattori M, Goto T, Ishibashi S, Kawashima-Sonoyama Y, Ishihara T, Matsuzaki Y, Akamatsu W, Fujitani M, Taketani T. MELAS-Derived Neurons Functionally Improve by Mitochondrial Transfer from Highly Purified Mesenchymal Stem Cells (REC). *International Journal of Molecular Sciences*. 2023 Dec 6;24(24):17186. doi: [10.3390/ijms242417186](https://doi.org/10.3390/ijms242417186).

### Keywords

MELAS, mitochondria, mesenchymal cells, mitochondrial transfer



## Positive results of a phase III trial of the IDH inhibitor vorasidenib in patients with radio- and chemo-naive IDH1/2 mutant grade 2 gliomas

Vorasidenib is an oral isocitrate dehydrogenase (IDH)1/2 inhibitor. In the phase III INDIGO trial, vorasidenib significantly increased both progression-free survival and time to next intervention compared to placebo in grade 2 IDH mutant gliomas that had undergone no previous treatment other than surgery. This is the first positive phase III trial of a targeted therapy in adult gliomas. Based on these results, in August 2024, FDA approved vorasidenib for radio- and chemo-naive IDH1/2 mutant grade 2 gliomas.

### Reference

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### Keywords

low-grade gliomas, IDH, IDH inhibitor, vorasidenib, neuro-oncology

## BRAF inhibitors are effective in both newly diagnosed and relapsing/refractory BRAF-altered pediatric low-grade gliomas

Pediatric-type low-grade gliomas (pLGGs) are a heterogeneous group of tumors with frequent BRAF (B-Raf proto-oncogene, serine/threonine kinase) alterations, such as BRAF V600E mutations and KIAA1549::BRAF fusions. In a phase II trial in patients with newly diagnosed BRAFV600 mutant pLGGs, the combination of BRAF inhibitor dabrafenib plus MEK inhibitor trametinib showed increased response rate (47% vs 11%), increased progression-free survival (median 20.1 vs 7.4 months), and reduced grade 3 adverse events rate (47% vs 94%) compared to standard chemotherapy. In the phase II FIREFLY-1 trial, the pan-RAF inhibitor tovorafenib showed a 67% response rate in relapsing/refractory (r/r) BRAF-altered pLGGs. These results led to FDA approvals of dabrafenib-trametinib in newly diagnosed BRAFV600E mutant pLGGs and of tovorafenib in r/r BRAF-altered pLGGs, respectively.

### References

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### Keywords

BRAF, pediatric gliomas, dabrafenib, trametinib, tovorafenib

## Dordaviprone (ONC201) shows efficacy in histone H3 K27M-mutant diffuse midline gliomas by epigenetically reprogramming tumor cells

Histone H3 K27M-mutant diffuse midline gliomas (H3K27M-DMG) are aggressive tumors with a dismal prognosis affecting mostly pediatric and young adult patients. Their current management relies on radiotherapy, as no chemotherapy proved effective. Dordaviprone (previously ONC201), a first-in-class imipridone drug, showed to induce sustained tumor responses in a subset of H3K27M-DMG cases. The anticancer mechanism of dordaviprone in H3K27M-DMG has been recently described. The drug acts by disrupting the metabolism of H3K27-altered glioma cells. Dordaviprone treatment leads to the accumulation of L-2-hydroxyglutarate, a potent inhibitor of  $\alpha$ -ketoglutarate-dependent histone demethylases. The consequent increase in repressive histone methylation promotes epigenetic reprogramming that suppresses tumor growth. Current trials of dordaviprone in both newly diagnosed and recurrent H3K27M-DMG are ongoing.

### References

Arrillaga-Romany I, Gardner SL, Oda Y, Aguilera D, Allen JE, Batchelor T, et al. ONC201 (Dordaviprone) in Recurrent H3 K27M-Mutant Diffuse Midline Glioma. *Journal of Clinical Oncology*. 2024 Feb 9;42(13):1542–1552. doi: [10.1200/jco.23.01134](https://doi.org/10.1200/jco.23.01134).

Venneti S, Kawakibi AR, Ji S, Waszak SM, Sweha SR, Mota M, et al. Clinical Efficacy of ONC201 in H3K27M-Mutant Diffuse Midline Gliomas Is Driven by Disruption of Integrated Metabolic and Epigenetic Pathways. *Cancer Discovery*. 2023 Nov 1;13(11):2370–2393. doi: [10.1158/2159-8290.CD-23-0131](https://doi.org/10.1158/2159-8290.CD-23-0131).

### Keywords

diffuse midline gliomas, H3 K27M mutations, ONC201, dordaviprone, neuro-oncology



## Characterization of FGF14-related ataxia, eye movement and vestibular pattern and response to treatment with 4-aminopyridine

A trinucleotid-expansion in the FGF14 gene has been recently identified as a frequent cause of idiopathic downbeat nystagmus and late-onset cerebellar ataxia, referred to as SCA27B. The phenotype of FGF14-related ataxia includes slowly progressive gait and balance impairment, downbeat nystagmus and may also present with (mild-to-moderate) bilateral vestibulopathy. Frequently an episodic component is identified as well. Several studies have reported high response rates to treatment with 4-aminopyridine, being significantly higher than in patients with idiopathic downbeat nystagmus. These studies support targeted drug treatment for oscillopsia due to downbeat nystagmus in those patients with confirmed FGF14 GAA $\geq$ 250 expansion and further add to the value of targeted drug treatment in hereditary ataxias.

### References

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### Keywords

cerebellar ataxia, treatment, downbeat nystagmus, eye movements

## Improved bedside diagnostic accuracy for identifying dangerous central causes in acutely dizzy patients

A tenth of acute vestibular syndrome patients in ED have stroke and 5% have recurrent vertigo. A recent systematic review and meta-analysis of high-quality original studies confirmed that in acute vestibular syndrome the HINTS (Head Impulse, Nystagmus, Test of Skew) examination by appropriately trained clinicians can differentiate peripheral from central causes and has higher diagnostic accuracy for stroke than MRI-DWI in the first 24–48 hours. Half of strokes with vestibular features did not have nystagmus in another key study, emphasizing the importance of combining eye examination with other tests such as graded gait and truncal instability ratings. These publications therefore promote that such bedside techniques should be disseminated to all clinicians evaluating dizziness/vertigo and in particular confirm that more rigorous training in vestibular neurology is required for neurologists and this should be reflected in the neurology training curriculum.

### References

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### Keywords

diagnostic accuracy, acute vestibular syndrome, acute imbalance syndrome, eye movements, MRI

## New insights into the role of anti-ganglioside antibodies in autoimmune-related vestibular disorders

Major advances have recently been made in the understanding of autoimmune-mediated vestibular syndromes. Anti-GQ1b antibody syndrome may present with diverse neurological manifestations, including ophthalmoplegia, ataxia, areflexia, central or peripheral vestibulopathy, and optic neuropathy as recently summarized in a topical review. Advances made include the recent characterization of an association between anti-ganglioside antibodies and acute unilateral vestibulopathy. Thus, an immune-mediated mechanism in acute vestibular failure is suggested, extending further the clinical spectrum of antiganglioside antibody syndrome. This work provides a detailed characterization of an underlying cause of acute unilateral vestibulopathy that has caught little attention in the past, opening the door also to targeted, immunomodulatory treatment in this condition.

### References

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### Keywords

neuro-immunology, vestibular hypofunction, autoimmune disorders

## New findings regarding vestibular perceptual brain networks may provide new insight into developing targets for treating balance disorders in brain disease

MRI-guided focused ultrasound (MRgFUS) applied to the nucleus ventralis intermedialis of the thalamus (for treating essential tremor) commonly provokes vestibular sensations of whole-body motion during the c. 8s period of sonication. Ciocca and colleagues map the locations and ultrasound power involved and link these to illusory whole-body motion. The authors conclude that a transient unilateral modulation of vestibular pathways (via MRgFUS) exposes the brain's adaptation to the magnetic field-induced peripheral vestibular bias (i.e. the phenomenon of magnetic vestibular stimulation described by David Zee and colleagues to explain the illusions of self-motion). Systematic mapping of vestibular perceptual pathways using MRgFUS may reveal new intracerebral targets of use for improving vestibular function such as postural control, in brain disease.

## References

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Ciocca M, Jameel A, Yousif N, Patel N, Smith J, Akgun S, et al. Illusions of Self-Motion during Magnetic Resonance-Guided Focused Ultrasound Thalamotomy for Tremor. *Annals of Neurology*. 2024 Jul;96(1):121–132. doi: [10.1002/ana.26945](https://doi.org/10.1002/ana.26945).

## Keywords

vestibular perception, balance, MRI guided focused ultrasound

## Closed-loop cerebellar transcranial electric stimulation improved gait in patients with Parkinson's Disease (PD), offering new non-invasive treatment options for patients

Open-loop non-invasive cranial electrical stimulation has received huge interest for treating neurological disorders including gait and balance in PD, which respond poorly to standard therapy (e.g. L-Dop and deep brain stimulation). So far, such approaches have obtained limited benefit. Nojima and colleagues used a closed-loop cerebellar stimulation to improve gait in PD, time locking the phase of transcranial electrical stimulation to that of the gait cycle. Notably they already deployed their approach in post-stroke. They found that gait function (speed and stride length) improved with cerebellar stimulation but not sham. While larger studies are needed to reproduce this important finding, closed-loop non-invasive brain stimulation is the future of neuromodulation approaches requiring personalization of the stimulation protocol.

## References

Nojima I, Horiba M, Sahashi K, Koganemaru S, Murakami S, Aoyama K, et al. Gait-combined closed-loop brain stimulation can improve walking dynamics in Parkinsonian gait disturbances a randomised-control trial. *Journal of Neurology Neurosurgery & Psychiatry*. 2023 Nov;94(11):938–944. doi: [10.1136/jnnp-2022-329966](https://doi.org/10.1136/jnnp-2022-329966).

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## Keywords

Parkinson's disease, non-invasive brain stimulation, closed-loop stimulation, gait

# Neurocritical Care



## Early minimally invasive removal of intracerebral hemorrhage

In patients presenting within 24 hours after an acute supratentorial lobar intracerebral hemorrhage (ICH) of 30 to 80 ml, minimally invasive surgical evacuation of the hematoma plus guideline-based medical management improved functional outcomes as compared with medical management alone.

## Reference

Pradilla G. et al. Trial of early minimally invasive removal of intracerebral hemorrhage. *New England Journal of Medicine*. 2024 Apr 11;390(14):1277–1289. doi: [10.1056/NEJMoa2308440](https://doi.org/10.1056/NEJMoa2308440).

## Keywords

spontaneous intracerebral hemorrhage, minimally invasive surgery

## Effectiveness of lumbar cerebrospinal fluid drain among patients with aneurysmal subarachnoid hemorrhage

Prophylactic lumbar drainage after aneurysmal subarachnoid hemorrhage lessened the burden of secondary infarction and decreased the rate of unfavorable outcome at 6 months. These findings support the use of lumbar drains after aneurysmal subarachnoid hemorrhage.

## Reference

Wolf S. et al. Effectiveness of lumbar cerebrospinal fluid drain among patients with aneurysmal subarachnoid hemorrhage. *JAMA Neurology* 2023 June 18;80(8):833–842. doi: [10.1001/jamaneurol.2023.1792](https://doi.org/10.1001/jamaneurol.2023.1792). Erratum in *JAMA Neurology*. 2023 Aug 1;80(8):873. doi: [10.1001/jamaneurol.2023.3002](https://doi.org/10.1001/jamaneurol.2023.3002).

## Keywords

prophylactic lumbar cerebrospinal fluid drainage, aneurysmal subarachnoid hemorrhage

## Role of hypothermia on cognitive outcomes in survivors of cardiac arrest

Targeted hypothermia has no significant effect on societal participation or cognitive function compared with targeted normothermia at 6 months in survivors of out-of-hospital cardiac arrest.

## Reference

Lilja G et al. Effects of Hypothermia vs Normothermia on Societal Participation and Cognitive Function at 6 Months in Survivors After Out-of-Hospital Cardiac Arrest. *JAMA Neurology* 2023 Oct 1;80(10):1070–1079. doi: [10.1001/jamaneurol.2023.2536](https://doi.org/10.1001/jamaneurol.2023.2536).

## Keywords

body temperature management after cardiac arrest, clinical outcomes



## Brain ageing patterns in a large and diverse cohort

The ageing brain is shaped by lifestyle, environmental, genetic factors, and age-related conditions. Using advanced brain imaging and artificial intelligence, researchers have uncovered how these factors contribute to changes in brain structure over time. A groundbreaking method called Surreal-GAN analyzed data from 49,482 individuals across 11 studies to identify five key patterns of brain shrinkage (atrophy). These patterns, measured using R-indices, reveal differences in how the brain ages and are linked to lifestyle, biomedical, and genetic factors. Importantly, these R-indices can predict disease progression and mortality, offering early warning signs for age-related brain disorders. They also pave the way for more precise diagnoses and personalized treatments by identifying specific brain ageing patterns. This approach could improve clinical trial recruitment and enable tailored patient care before significant symptoms appear, revolutionizing how we manage brain health during ageing.

### Reference

Yang, Z., Wen, J., Erus, G., Govindarajan, S. T., Melhem, R., Mamourian, E., ... & Davatzikos, C. (2024). Brain aging patterns in a large and diverse cohort of 49,482 individuals. *Nature Medicine*, 30(10), 3015–3026. doi: [10.1038/s41591-024-03144-x](https://doi.org/10.1038/s41591-024-03144-x).

### Keywords

environmental risk factors, lifestyle factors, artificial intelligence (AI), prognostic/diagnostic algorithm

## Global, regional, and national burden of stroke and its risk factors

The global stroke burden has increased significantly across regions and populations from 1990 to 2021, with notable disparities by region, country, and socio-demographic index. The effect of several modifiable risk factors, including hypertension, diet, and physical inactivity, has also grown, contributing to rising stroke rates. Low- and middle-income countries face higher mortality and disability burdens compared to high-income regions. The findings highlight the urgent need for targeted prevention strategies, tailored interventions, and policies to address regional disparities and reduce the growing impact of stroke worldwide.

### Reference

Feigin, V. L., Abate, M. D., Abate, Y. H., Abd ElHafeez, S., Abd-Allah, F., Abdelalim, A., ... & Arifin, H. (2024). Global, regional, and national burden of stroke and its risk factors, 1990–2021. A systematic analysis for the Global Burden of Disease Study 2021. *The Lancet Neurology*, 23, 973–1003. doi: [10.1016/S1474-4422\(24\)00369-7](https://doi.org/10.1016/S1474-4422(24)00369-7).

### Keywords

descriptive epidemiology, global burden of disease, stroke

## Enhanced genetic discovery using multi-omics in the UK Biobank

Researchers utilized multi-omics and biomarkers from the UK Biobank to improve disease prediction with machine learning (ML). By identifying and correcting undiagnosed cases at recruitment, they created an augmented cohort with fewer misclassification errors. This enhanced dataset enabled genome-wide association studies (PheWAS) that uncovered novel genetic variants linked to various diseases, including neurological conditions. This approach demonstrates the power of integrating multi-modal data with AI-driven methods to address traditional epidemiological challenges. By refining phenotype classification, the study enhances the accuracy and scope of case-control analyses, revealing previously hidden genetic associations. These findings highlight the transformative potential of multi-omics and machine learning in genetic research, paving the way for more precise insights into the mechanisms driving complex diseases.

### Reference

Garg, M., Karpinski, M., Matelska, D., Middleton, L., Burren, O. S., Hu, F., ... & Vitsios, D. (2024). Disease prediction with multi-omics and biomarkers empowers case-control genetic discoveries in the UK Biobank. *Nature Genetics*, 56(9), 1821–1831. doi: [10.1038/s41588-024-01898-1](https://doi.org/10.1038/s41588-024-01898-1).

### Keywords

observational studies, registry, neuroepidemiology, artificial intelligence (AI), machine learning (ML)

## Long-term disability trajectories in multiple sclerosis

This study identified three distinct disability trajectories in multiple sclerosis (MS): no/minimal, moderate, and severe. Patients in the no/minimal trajectory exhibited little to no disability progression (median Expanded Disability Status Scale) EDSS score ~1 after 10 years, while those in moderate and severe trajectories experienced significant disability worsening, reaching EDSS 4 in a median of 9 and 7 years, respectively. Older age, a higher number of relapses within the first five years post-diagnosis, and baseline comorbidities were associated with worse trajectories. Interestingly, baseline MRI findings and the initial symptom's anatomical site did not significantly impact long-term outcomes.

These findings suggest that early clinical features can help identify individuals at higher risk of rapid disability progression.

### Reference

Zarghami A, Hussain MA, Van Der Mei I, Simpson-Yap S, Ponsonby AL, Lechner-Scott J, et al. Long-term disability trajectories in multiple sclerosis a group-based trajectory analysis of the AusLong cohort. *Journal of Neurology Neurosurgery Psychiatry*. 2024 Sep 4; [jnnp-2024-333632](https://doi.org/10.1136/jnnp-2024-333632). doi: [10.1136/jnnp-2024-333632](https://doi.org/10.1136/jnnp-2024-333632).

### Keywords

prognostic algorithm, multiple sclerosis, disease trajectory

## Trajectory of cognitive decline before and after stroke

Poststroke cognitive impairment is a common condition, but how cognition changes over time after a first stroke is not well understood. This study analyzed data from 14 community-based studies conducted between 1993 and 2019 to compare cognitive changes in stroke survivors with individuals who did not experience a stroke. The findings revealed that stroke survivors experienced faster declines in all four cognitive domains – language, memory, processing speed, and executive function – compared to those who did not have a stroke. These results highlight the need for early interventions to address cognitive challenges following a stroke and improve long-term outcomes.

### Reference

Lo, J. W., Crawford, J. D., Lipnicki, D. M., Lipton, R. B., Katz, M. J., Preux, P. M., ... & Sachdev, P. S. (2024). Trajectory of cognitive decline before and after stroke in 14 population cohorts. *JAMA Network Open*, 7(10), e2437133. doi: [10.1001/jamanetworkopen.2024.37133](https://doi.org/10.1001/jamanetworkopen.2024.37133).

### Keywords

stroke, cognition, prognostic algorithm

# Neurogenetics



## Optical genome mapping (OGM)

The advancements in optical genome mapping (OGM) technology in 2023 reflect significant progress in enhancing genomic analysis capabilities. Its advantages stem from its ability to detect a broader range of structural variants (SVs) with high resolution, addressing limitations of methods like short-read next-generation sequencing (NGS), chromosomal microarray (CMA), karyotyping, and even emerging long-read sequencing. These developments underscore the technology's potential to transform our understanding of genetics and improve patient outcomes through more accurate diagnoses and targeted therapies. It is especially important in the diagnostic of “Undiagnosed Rare Neurological Diseases” since many rare neurological conditions remain unsolved due to cryptic structural variants. OGM's genome-wide view captures these anomalies with high sensitivity.

### Reference

Kernohan, K. D., & Boycott, K. M. (2024). The expanding diagnostic toolbox for rare genetic diseases. *Nature Reviews Genetics*, 25(6), 401–415. doi: [10.1038/s41576-023-00683-w](https://doi.org/10.1038/s41576-023-00683-w).

### Keywords

molecular techniques, sequencing

## Long read sequencing

Many neurogenetic disorders involve structural variations or repeat expansions that are challenging to detect with short reads due to their fragmented nature. Long read sequencing (LRS) provides a continuous view of the genome, allowing scientists to identify pathogenic mutations that were previously invisible or ambiguous. This has led to the discovery of new monogenic disorders and clarified the genetic basis of known conditions, especially in the brain, with high-level genomic complexity. Long-read sequencing technologies, as developed by PacBio and Oxford Nanopore, have dramatically improved screening accuracy and throughput, Nanopore Sequencing Innovations allows very long read lengths exceeding 2.3 megabases (Mb). PacBio's High-Fidelity sequencing in the range of 10–20 kilobases (kb) has improved accuracy approaching 99.99%, allowing better structural variants detection and genome assemblies. These improvements allow comprehensive analyses of complex genomic regions, which have been very challenging in the past whilst using back then the only available short-read sequencing methods.

### Reference

Iyer, S. V., Goodwin, S., & McCombie, W. R. (2024). Leveraging the power of long reads for targeted sequencing. *Genome Research*, 34(11), 1701–1718. doi: [10.1101/gr.279168.124](https://doi.org/10.1101/gr.279168.124).

### Keywords

molecular techniques, sequencing

## Gene therapy for Duchenne muscular dystrophy

Elevidys (delandistrogene moxeparvovec-rokl) is a groundbreaking, single-dose, iv-injection gene therapy developed for the treatment of Duchenne muscular dystrophy (DMD) that uses an adeno-associated virus (AAV) vector, specifically AAVrh74, to deliver a shortened, functional version of the dystrophin gene called micro-dystrophin. Approval by the Food and Drug Administration (FDA) in 2023 was for ambulatory DMD patients aged 4 and older, confirming functional benefits (improved outcomes). Accelerated Approval occurred in 2024 for non-ambulatory patients aged 4 and older, still requiring confirmatory trials to verify clinical benefit. Contraindications: Not suitable for patients with elevated anti-AAVrh74 antibody titers ( $\geq 1:400$ ) or specific DMD mutations (exon 8/9 deletions), as these increase risks of adverse reactions. Further research is in progress: the EMBARK trial (results expected late 2025) aims to confirm clinical benefits, potentially securing full approval for non-ambulatory patients. Ongoing further studies explore efficacy in older patients, combination therapies (e.g., with exon-skipping drugs), and next-generation vectors to enhance delivery.

### Reference

Hoy, S. M. (2023). Delandistrogene Moxeparvovec First Approval. *Drugs*, 83(14), 1323–1329. doi: [10.1007/s40265-023-01929-x](https://doi.org/10.1007/s40265-023-01929-x).

### Keywords

gene therapy, Duchenne muscular dystrophy

# Neuroimaging



## Novel imaging measures for the differential diagnosis of inflammatory, immunomediated diseases

The use of magnetic resonance imaging (MRI) for the diagnostic work-up of multiple sclerosis (MS) and allied white matter diseases is continuously evolving. The 2017 McDonald criteria show high sensitivity and accuracy in predicting MS and allow an earlier diagnosis. To limit the risk of misdiagnosis, they should be applied by expert clinicians only after the careful exclusion of alternative diagnoses. Application of MRI techniques to evaluate the presence and features of lesions in the cortex, spinal cord and optic nerve provides fundamental pieces of information for differentiating the main immunomediated conditions of the central nervous system. New MRI markers may improve diagnostic specificity for MS and reduce the risk of misdiagnosis. These include assessment of the central vein sign and chronic active lesions.

### References

Vidal-Jordana A, Rovira A, Calderon W, Arrambide G, Castelló J, Moncho D, et al. Adding the Optic Nerve in Multiple Sclerosis Diagnostic Criteria A Longitudinal, Prospective, Multicenter Study. *Neurology*. 2024 Jan 9;102(1):e200805. doi: [10.1212/WNL.0000000000207805](https://doi.org/10.1212/WNL.0000000000207805).

Cagol A, Cortese R, Barakovic M, Schaedelin S, Ruberte E, Absinta M, et al. Diagnostic Performance of Cortical Lesions and the Central Vein Sign in Multiple Sclerosis. *JAMA Neurology*. 2024 Feb 1;81(2):143–153. doi: [10.1001/jamaneurol.2023.4737](https://doi.org/10.1001/jamaneurol.2023.4737).

### Keywords

central vein sign (CVS), paramagnetic rim lesions (PRLs), cortical lesions, optic nerve lesions, spinal cord lesions

## In vivo evaluation of glymphatic system dysfunction in several neurological diseases and its clinical correlates

Recent studies have highlighted the significant role of glymphatic system dysfunction in various systemic and neurological diseases. Different methods of analysis are currently being employed to quantify in vivo non-invasively dysfunction of this system. In Alzheimer's disease, impaired glymphatic clearance has been linked to increased amyloid-beta accumulation, contributing to disease progression. Similarly, research indicates that glymphatic dysfunction may exacerbate neuroinflammation, further influencing Alzheimer's pathology. Additionally, studies have found that glymphatic dysfunction correlates with cognitive impairments in conditions like multiple sclerosis and cerebral small vessel disease, underscoring its broader impact on neurological health. Emerging research also suggests that sleep disturbances and certain sleep positions may influence glymphatic function, potentially affecting the brain's waste clearance and overall health. These findings collectively emphasize the critical role of the glymphatic system in maintaining neurological health and its potential as a therapeutic target across various neurodegenerative and neuroinflammatory conditions.

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Gueye M, Preziosa P, Ramirez GA, Bozzolo EP, Canti V, Margoni M, et al. Choroid plexus and perivascular space enlargement in neuropsychiatric systemic lupus erythematosus. *Molecular Psychiatry*. 2024 Feb;29(2):359–368. doi: [10.1038/s41380-023-02332-4](https://doi.org/10.1038/s41380-023-02332-4).

## Keywords

glymphatic system, diffusion along the perivascular space (DTI-ALPS) index, multiple sclerosis, NLES, Alzheimer's disease

## Alzheimer disease anti-amyloid immunotherapies: imaging recommendations and practice considerations for monitoring of amyloid-related imaging abnormalities

With Food and Drug Administration (FDA) approval and Medicare coverage for lecanemab and donanemab, more clinics now offer anti-amyloid immunotherapy to eligible Alzheimer's patients. This article provides expert clinicians with updated guidance on magnetic resonance imaging (MRI) protocols, workflows, and reporting for monitoring amyloid-related imaging abnormalities (ARIA). Based on discussions within the American Society of Neuroradiology (ASNR) Alzheimer, ARIA, and Dementia Study Group, the article aims to: (1) summarize FDA guidelines for ARIA evaluation, (2) review key MRI sequences and standardized imaging protocols, (3) offer imaging recommendations for specific patient scenarios, (4) emphasize the role of the neuroimaging specialist in patient care, (5) address MRI protocol implementation across diverse practices, and (6) present findings from the 2023 ASNR survey on dementia and ARIA imaging. These insights help optimize radiologic

assessment, ensuring safer and more effective monitoring of patients receiving anti-amyloid therapies.

## Reference

Cogswell PM, Andrews TJ, Barakos JA, Barkhof F, Bash S, Benayoun MD, et al. Alzheimer's Disease Anti-Amyloid Immunotherapies Imaging Recommendations and Practice Considerations for Monitoring of Amyloid-Related Imaging Abnormalities. *AJNR American Journal of Neuroradiology*. 2025 Jan 8;46(1):24–32. doi: [10.3174/ajnr.A8469](https://doi.org/10.3174/ajnr.A8469).

## Keywords

Alzheimer's disease, anti-amyloid immunotherapies, imaging, recommendations

## Localization of cerebrospinal fluid-venous fistulas

Recent advancements in the localization of cerebrospinal fluid-venous fistulas (CVF) have significantly improved diagnostic accuracy, particularly through advanced myelographic techniques. A 2024 study by Madhavan et al. reviewed various imaging modalities for CVF detection, highlighting their advantages and limitations while recommending provocative maneuvers to enhance visualization. Similarly, Schwartz et al. compared energy-integrating detector Computed Tomography (CT) myelography with photon-counting detector CT for diagnosing CVF in patients with spontaneous intracranial hypotension. Their findings demonstrated that photon-counting technology improves spatial resolution and detection capabilities. These studies emphasize the growing role of advanced myelographic techniques and emerging CT technologies in accurately diagnosing CVF. Improved detection facilitates more targeted and timely therapeutic interventions, ultimately benefiting patient outcomes.

## References

Madhavan AA, Brinjikji W, Cutsforth-Gregory JK, Amrhein TJ, Kranz PG, Benson JC, et al. Myelographic Techniques for the Localization of CSF-Venous Fistulas Updates in 2024. *AJNR American Journal of Neuroradiology*. 2024 Oct 3;45(10):1403–1412. doi: [10.3174/ajnr.A8299](https://doi.org/10.3174/ajnr.A8299).

Schwartz FR, Kranz PG, Malinzak MD, Cox DN, Ria F, McCabe C, et al. Myelography Using Energy-Integrating Detector CT Versus Photon-Counting Detector CT for Detection of CSF-Venous Fistulas in Patients With Spontaneous Intracranial Hypotension. *AJR American Journal of Roentgenology*. 2024 Apr;222(4):e2330673. doi: [10.2214/AJR.23.30673](https://doi.org/10.2214/AJR.23.30673).

## Keywords

myelography, CSF hypotension



## Diagnosing MOG antibody-associated disease: international consensus criteria and diagnostic implications of MOG IgG in cerebrospinal fluid

MOGAD or MOG antibody associated-disease can only be diagnosed in the presence of MOG IgG and can have a monophasic or relapsing disease course. The most common clinical presentations are acute disseminated encephalomyelitis (ADEM), optic neuritis (ON), or transverse myelitis (TM). Less frequently, cerebral cortical encephalitis (CE), brainstem or cerebellar presentations may occur. Interestingly, one study demonstrated that serum MOG-IgG was associated with ON and ADEM, whereas MOG-IgG in cerebrospinal fluid (CSF) was associated with ADEM and CE. Both the consensus diagnostic criteria and the significance of MOG-IgG require validation and further studies. These advancements will aid significantly in the design of future clinical trials and studies and will enhance our understanding of this rare disease.

### References

Banwell B, Bennett JL, Marignier R, Kim HJ, Brilot F, Flanagan EP, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease International MOGAD Panel proposed criteria. *Lancet Neurology*. 2023 Mar;22(3):268–282. doi: [10.1016/S1474-4422\(22\)00431-8](https://doi.org/10.1016/S1474-4422(22)00431-8).

Matsumoto Y, Kaneko K, Takahashi T, Takai Y, Namatame C, Kuroda H, et al. Diagnostic implications of MOG-IgG detection in sera and cerebrospinal fluids. *Brain*. 2023 Sep 1;146(9):3938–3948. doi: [10.1093/brain/awad122](https://doi.org/10.1093/brain/awad122).

### Keywords

MOGAD, diagnostic criteria, MOG IgG, cerebrospinal fluid

## The race towards a cure? CAR T and CAAR T cell-based treatments for autoimmune neurological conditions

Chimeric antigen receptor (CAR) T cell treatments have revolutionized the treatment of B cell-derived hematological malignancies and also hold the potential to transform the treatment paradigm in patients with treatment-refractory neurological autoimmune diseases, such as myasthenia gravis, stiff person syndrome, multiple sclerosis. CAR T cells offer the advantage of significant tissue penetration in comparison to B cell-depleting monoclonal antibodies and potentially lead to increased duration of remission. However, logistics are complex, and vigilance is required for treatment related side effects. A more targeted approach is the development of chimeric autoantibody receptor T cells, which selectively deplete only the autoantibody producing B cells, leaving other B cells intact. This approach has been demonstrated in an animal model for NMDAR encephalitis, paving the road for CAAR T cell phase I/II trials. Early phase clinical trials in various neurological autoimmune conditions are ongoing and we eagerly await the results.

### References

Haghikia A, Schett G, Mougiakakos D. B cell-targeting chimeric antigen receptor T cells as an emerging therapy in neuroimmunological diseases. *Lancet Neurology*. 2024 Jun;23(6):615–624. doi: [10.1016/S1474-4422\(24\)00140-6](https://doi.org/10.1016/S1474-4422(24)00140-6).

Reinke SM, von Wardenburg N, Homeyer MA, Kornau HC, Spagni G, Li LY, et al. Chimeric autoantibody receptor T cells deplete NMDA receptor-specific B cells. *Cell*. 2023 Nov 9;186(23):5084–5097.e18. doi: [10.1016/j.cell.2023.10.001](https://doi.org/10.1016/j.cell.2023.10.001).

### Keywords

CAR T, CAAR T, cell-based treatment, autoimmune neurological conditions, NMDAR encephalitis

## Identification of three distinct endoimmunophenotypes in patients with multiple sclerosis

This translational study identified three distinct types of endoimmunophenotype in multiple sclerosis, using a combination of high-dimensional flow cytometry and serum proteomics on blood samples. These seminal findings will pave the way for personalized treatment decisions and more individualized predictions of disease course.

### Reference

Gross CC, Schulte-Mecklenbeck A, Steinberg OV, Wirth T, Lauks S, Bittner S, et al. Multiple sclerosis endophenotypes identified by high-dimensional blood signatures are associated with distinct disease trajectories. *Science Translational Medicine*. 2024 Mar 27;16(740):eade8560. doi: [10.1126/scitranslmed.ade8560](https://doi.org/10.1126/scitranslmed.ade8560).

### Keywords

multiple sclerosis, precision neuroimmunology, endophenotype, blood immune signature

## Autoreactive T cells in Guillain-Barré syndrome

Guillain-Barré syndrome (GBS) is a rare post-infectious immune-mediated acute polyneuropathy, which can be life-threatening due to the rapid development of progressive muscle weakness. The immunopathogenesis is incompletely understood. In this study, the authors identified autoreactive memory CD4+ cells, with a cytotoxic T helper 1 (TH1)-like phenotype, as well as a rare population of CD8+ T cells targeting peripheral nerve myelin antigens. More than 1000 autoreactive single T cell clones were characterized that recognized immunodominant epitopes. Interestingly, autoreactive T cell clones were similar in the blood and the cerebrospinal fluid of different patients with GBS, but not in control individuals. Further evidence for the direct contribution of peripheral nerve myelin-reactive T cells was found in peripheral nerve tissue, obtained by nerve biopsy in one patient: myelin-reactive T cells were identified in the biopsy. These findings provide novel insights into the immunopathophysiology of GBS, potentially leading to the development of targeted treatments.

### Reference

Súkeníková L, Mallone A, Schreiner B, Ripellino P, Nilsson J, Stoffel M, et al. Autoreactive T cells target peripheral nerves in Guillain-Barré syndrome. *Nature*. 2024 Feb;626(7997):160–168. doi: [10.1038/s41586-023-06916-6](https://doi.org/10.1038/s41586-023-06916-6).

### Keywords

peripheral nervous system, Guillain-Barré syndrome, inflammatory peripheral neuropathy, autoreactive T cells



## Improvements in vulnerable plaque imaging

Saba et al. present a novel classification system (Carotid Plaque-RADS) of arterio-arterial embolic risk of atherosclerotic carotid artery disease. Beyond degree of stenosis, the classification uses plaque morphology and composition to indicate stroke risk. While Plaque-RADS 1 indicates a regular vessel wall, Plaque-RADS 2 describes eccentric vessel wall thickening (MWT) of <3 mm. Plaque-RADS 3 is defined by the presence of an ulcerated plaque or MWT ≥3 mm, whereas Plaque-RADS 4 indicates intraplaque hemorrhage (IPH), a ruptured fibrous cap, or an intraluminal thrombus. A strength of the classification is the comprehensive approach including ultrasound, computed tomography, and magnetic resonance imaging.

### Reference

Saba L, Cau R, Murgia A, Nicolaidis AN, Wintermark M, Castillo M, et al. Carotid Plaque-RADS A Novel Stroke Risk Classification System. *JACC Cardiovasc Imaging*. 2024 Jan;17(1):62–75. doi: [10.1016/j.jcmg.2023.09.005](https://doi.org/10.1016/j.jcmg.2023.09.005).

### Keywords

ischemic stroke, carotid artery plaque, MRI, ultrasound

## Advances in neuromuscular ultrasound (sensory neuronopathy, lower limb nerve ultrasound, axonopathy)

Neuromuscular ultrasound as a marker for inherited sensory neuronopathy: A review of eight studies on 49 patients with inherited sensory neuronopathy found that reduced nerve cross-sectional area (CSA) is highly specific to this diagnosis. This aligns with the prediction that losing 90 % of afferent axons results in a 45 % CSA decrease. Lower limb nerve ultrasound: A four-way comparison of acquired and inherited axonopathy, inherited neuronopathy and healthy controls: This study compared sural and tibial nerve ultrasounds in 17 CANVAS, 18 CMT2, and 18 acquired neuropathy patients, revealing that inherited neuropathies reduce nerve size, while acquired neuropathies increase it due to inflammatory repair. The findings confirm that axon loss decreases nerve CSA by 30–50 %, depending on connective tissue content, and highlight the fundamental difference between inherited and acquired neuropathies: genetic disorders cause pure axon loss, whereas acquired conditions involve repair responses like edema and scarring.

### References

Pelosi L, van Alfen N. Neuromuscular ultrasound as a marker for inherited sensory neuronopathy. *Muscle Nerve*. 2023 Nov;68(5):718–721. doi: [10.1002/mus.27934](https://doi.org/10.1002/mus.27934).

Pelosi L, Coraci D, Mulroy E, Leadbetter R, Padua L, Roxburgh R. Lower limb nerve ultrasound: A four-way comparison of acquired and inherited axonopathy, inherited neuronopathy and healthy controls. *Muscle Nerve*. 2024 Dec;70(6):1263–1267. doi: [10.1002/mus.28260](https://doi.org/10.1002/mus.28260).

### Keywords

sensory neuronopathy, lower limb nerve ultrasound, axonopathy

## Ultrasound for treating movement disorders (focused ultrasound thalamotomy, essential tremor)

Kaplitt et al. reported about safety and efficacy of staged, bilateral focused ultrasound thalamotomy in essential tremor: In this open-label trial, 51 patients with essential tremor treated successfully unilaterally underwent focused ultrasound thalamotomy on the opposite side. Tremor/motor, positional tremor, and functional disability improved significantly, and adverse events were almost always mild and frequently resolved.

### Reference

Kaplitt MG, Krishna V, Eisenberg HM, Elias WJ, Ghanouni P, Baltuch GH, et al. Safety and Efficacy of Staged, Bilateral Focused Ultrasound Thalamotomy in Essential Tremor An Open-Label Clinical Trial. *JAMA Neurology*. 2024 Sep 1;81(9):939–946. doi: [10.1001/jamaneurol.2024.2295](https://doi.org/10.1001/jamaneurol.2024.2295).

### Keywords

movement disorders, focused ultrasound, essential tremor, thalamotomy

## Developments in TCD with microbubbles (right-to-left shunt detection)

A recently published review by Palazzo et al. supports the value of TCD for shunt detection: Right-to-left shunt represents the likely cause of approximately 10 % of ischemic strokes in young and middle-aged adults. TCD with bubble test has a mean specificity of 86 % and a sensitivity of 93 % for shunt detection and serves as optimal screening tool after an ischemic stroke in young and middle-aged adults.

### Reference

Palazzo P, Heldner MR, Nasr N, Alexandrov AV. Transcranial Doppler With Microbubbles Screening Test to Detect and Grade Right-to-Left Shunt After an Ischemic Stroke A Literature Review. *Stroke*. 2024 Dec;55(12):2932–2941. doi: [10.1161/STROKEAHA.124.046907](https://doi.org/10.1161/STROKEAHA.124.046907).

### Keywords

TCD, microbubbles, right-to-left shunt



## Alterations in aquaporin-4 impair glymphatic function following mild traumatic brain injury

Recent research has identified that mild traumatic brain injury (mTBI) can lead to significant changes in the expression and distribution of aquaporin-4 (AQP4), a crucial water channel protein in the brain. These alterations disrupt the glymphatic system, responsible for clearing metabolic waste from the brain, potentially increasing the risk of neurodegenerative diseases such as Alzheimer's. Notably, studies have demonstrated that such impairments are not exclusive to blast-induced injuries but also occur in mTBI resulting from mechanical impacts. This underscores the importance of targeting AQP4 functionality in therapeutic strategies aimed at restoring glymphatic flow and preventing long-term neurological deficits.

### References

Braun, M., Sevaio, M., Keil, S.A., Gino, E., Wang, M. X., Lee, J., ... & Iliff, J.J. (2024). Macroscopic changes in aquaporin-4 underlie blast traumatic brain injury-related impairment in glymphatic function. *Brain*, 147(6), 2214–2229. doi: [10.1093/brain/awae065](https://doi.org/10.1093/brain/awae065).

Michalaki, E., Pulliam, A.N., Datta Roy, P.M., Dixon, J.B., & LaPlaca, M.C. (2024). Near-Infrared Imaging of Glymphatic Clearance in a Pre-Clinical Model of Repetitive Closed Head Traumatic Brain Injury. *Neurotrauma Reports*, 6(1), 115–128. doi: [10.1089/neur.2024.0128](https://doi.org/10.1089/neur.2024.0128).

### Keywords

mild traumatic brain injury, aquaporin-4, glymphatic system, neurodegeneration

## Thalamic deep brain stimulation enhances cognitive function post-traumatic brain injury

Cognitive impairments are common sequelae of moderate to severe traumatic brain injury (TBI), often resulting from disrupted thalamocortical networks. A pioneering phase 1 randomized feasibility study investigated the effects of deep brain stimulation (DBS) targeting the central lateral nucleus of the thalamus in individuals with chronic TBI. The findings revealed that thalamic DBS led to significant improvements in executive functions and overall quality of life. These results suggest that neuromodulation of specific thalamic nuclei may offer a promising therapeutic avenue for cognitive rehabilitation in TBI patients.

### References

Schiff, N.D., Giacino, J.T., Butson, C.R., Choi, E.Y., Baker, J.L., O'Sullivan, K.P., ... & Henderson, J.M. (2023). Thalamic deep brain stimulation in traumatic brain injury: a phase 1, randomized feasibility study. *Nature Medicine*, 29(12), 3162–3174. doi: [10.1038/s41591-023-02638-4](https://doi.org/10.1038/s41591-023-02638-4).

Arnts, H., Tewarie, P., van Erp, W., Schuurman, R., Boon, L.I., Pennartz, C.M., ... & van den Munckhof, P. (2024). Deep brain stimulation of the central thalamus restores arousal and motivation in a zolpidem-responsive patient with akinetic mutism after severe brain injury. *Scientific Reports*, 14(1), 2950. doi: [10.1038/s41598-024-52267-1](https://doi.org/10.1038/s41598-024-52267-1).

### Keywords

traumatic brain injury, deep brain stimulation, thalamus, cognitive rehabilitation, neuromodulation

## The role of multimodal brain monitoring in severe traumatic brain injury: still an open debate

Intracranial pressure (ICP) monitoring is the cornerstone of severe traumatic brain injury (TBI) management. The OXY-TC trial (2023) found that adding brain tissue oxygenation (PbtO<sub>2</sub>) monitoring to ICP did not significantly improve neurological outcomes at six months compared to ICP monitoring alone. However, more recent systematic evidence suggests that specific subgroups of patients with severe TBI — particularly those with high intracranial pressure or poor baseline oxygenation — may benefit from a multimodal monitoring approach. These contrasting results highlight the ongoing need for individualized strategies and further research to better define when and for whom PbtO<sub>2</sub> monitoring is truly effective.

### References

Payen, J.-F., Launey, Y., Chabanne, R., Gay, S., Francony, G., Gergele, L., ... & Mallaret, M. (2023). Intracranial pressure monitoring with and without brain tissue oxygen pressure monitoring for severe traumatic brain injury in France (OXY-TC): an open-label, randomised controlled superiority trial. *Lancet Neurology*, 22(11), 1005–1014. doi: [10.1016/S1474-4422\(23\)00290-9](https://doi.org/10.1016/S1474-4422(23)00290-9).

Zhang, C., Zhou, L., Zhang, K., Huang, J., Cao, L., Lou, Y., ... & Zhang, G. (2024). Brain tissue oxygen pressure combined with intracranial pressure monitoring may improve clinical outcomes for patients with severe traumatic brain injury: a systematic review and meta-analysis. *PeerJ*, 12, e18086. doi: [10.7717/peerj.18086](https://doi.org/10.7717/peerj.18086).

### Keywords

severe traumatic brain injury, intracranial pressure, brain oxygen monitoring, multimodal monitoring, individualized treatment



## Management of chronic pain associated with temporomandibular disorders: a clinical practice guideline

This clinical practice guideline provides evidence-based recommendations for managing chronic pain associated with temporomandibular disorders (TMD).

Strong recommendations in favor of cognitive behavioral therapy (CBT) with or without bio-feedback or relaxation therapy, therapist-assisted mobilization, trigger point manual therapy, supervised postural exercises, supervised jaw exercises and stretches with or without trigger point manual therapy, and usual care (such as home exercises, stretches, reassurance, and education).

Conditional recommendations in favor of manipulation, supervised jaw exercises with mobilization, CBT with nonsteroidal anti-inflammatory drugs (NSAIDs), manipulation with postural exercises, and acupuncture.

Conditional recommendations against reversible occlusal orthotics, arthrocentesis, cartilage supplements with or without hyaluronic acid injections, low-level laser therapy, transcutaneous electrical nerve stimulation, gabapentin, botulinum toxin injections, hyaluronic acid injections, relaxation therapy, trigger point injections, acetaminophen, topical capsaicin, biofeedback, corticosteroid injections (with or without NSAIDs), benzodiazepines, and beta-blockers.

Strong recommendations against irreversible oral orthotics, discectomy, and NSAIDs combined with opioids.

## References

Busse JW, Casassus R, Carrasco-Labra A, Durham J, Mock D, Zakrzewska JM, et al. Management of chronic pain associated with temporomandibular disorders a clinical practice guideline. *BMJ*. 2023 Dec 15;383:e076227. doi: [10.1136/bmj-2023-076227](https://doi.org/10.1136/bmj-2023-076227).

Yao L, Sadeghirad B, Li M, Li J, Wang Q, Crandon HN, et al. Management of chronic pain secondary to temporomandibular disorders: a systematic review and network meta-analysis of randomised trials. *BMJ*. 2023 Dec 15;383:e076226. doi: [10.1136/bmj-2023-076226](https://doi.org/10.1136/bmj-2023-076226).

## Keywords

temporomandibular disorders, chronic pain, clinical practice guideline, cognitive behavioral therapy, manual therapy

## Chronic visceral pain: new peripheral mechanistic insights and resulting treatments

This review article delves into the complexities of chronic visceral pain, a prevalent issue among patients with gastrointestinal disorders such as inflammatory bowel disease and disorders of brain-gut interaction. The authors highlight recent advancements in understanding peripheral pain signaling and the specific physiological and pathophysiological mechanisms that lead to the sensitization of peripheral pain pathways. By focusing on preclinical mechanisms that have been translated into treatment approaches, the review summarizes current evidence from clinical trials that target these mechanisms. The article emphasizes the substantial burden chronic visceral pain places on patients, including its association with anxiety, depression, reduced quality

of life, and impaired social functioning. It underscores the necessity for a deeper understanding of peripheral pain mechanisms to develop novel therapeutic interventions aimed at improving patient outcomes.

## Reference

Ford AC, Vanner S, Kashyap PC, Nasser Y. Chronic Visceral Pain New Peripheral Mechanistic Insights and Resulting Treatments. *Gastroenterology*. 2024 Feb 5;166(6):976–994. doi: [10.1053/j.gastro.2024.01.045](https://doi.org/10.1053/j.gastro.2024.01.045).

## Keywords

chronic visceral pain, gastrointestinal disorders, peripheral sensitization, pain mechanisms, therapeutic interventions

## Chronic pain in pediatric patients: epidemiology, pathophysiology, and mitigation strategies

This review provides an updated summary on the epidemiology, pathophysiology, and treatment strategies of chronic pain in pediatric patients, highlighting differences from adult chronic pain. Chronic pain in children is common, can be debilitating, and may progress into adulthood, necessitating interdisciplinary evaluation and management. Interdisciplinary care, including psychology, physical, and/or occupational therapy, has been shown to improve pain and function. The recent decline in mental health post-pandemic has correlated with an increase in pediatric chronic pain, emphasizing the need to identify at-risk patients and offer early interdisciplinary treatment. The authors advocate for addressing chronic pediatric pain under the biopsychosocial model, evaluating biological, psychological, and social factors influencing pain perception, experience, functional ability, and treatment focus. Educating patients and their families is deemed a crucial initial step toward functional rehabilitation of pain.

## Reference

Rodriguez-Restrepo A, AuBuchon JD. Chronic pain in pediatric patients epidemiology, pathophysiology, and mitigation strategies. *Current Opinion in Anaesthesiology*. 2024 Mar 8;37(3):245–250. doi: [10.1097/ACO.0000000000001372](https://doi.org/10.1097/ACO.0000000000001372).

## Keywords

pediatric chronic pain, epidemiology, pathophysiology, interdisciplinary care, biopsychosocial model

## Chronic postsurgical pain: a European survey

This observational study investigates the incidence, characteristics, and risk factors of chronic postsurgical pain (CPSP) across Europe. Conducted in 18 hospitals, the study included 3,297 patients undergoing breast cancer surgery, sternotomy, endometriosis surgery, or total knee arthroplasty. Patients completed standardized questionnaires at multiple intervals up to six months post-surgery. The overall incidence of CPSP at six months was 10.5%, varying by surgery type: sternotomy (6.9%), breast surgery (7.4%), total knee arthroplasty (12.9%), and endometriosis surgery (16.2%). Neuropathic pain characteristics were common, especially after breast surgery (67.6%). Severe CPSP and its neuropathic components negatively impacted psychological well-being, functionality, and quality of life. The study did not identify universal risk factors for CPSP but provides valuable data on its prevalence and effects, highlighting the need for further research.

## Reference

Martinez V, Lehman T, Lavand'homme P, Harkouk H, Kalso E, Pogatzki-Zahn EM, et al. Chronic postsurgical pain A European survey. *European Journal of Anaesthesiology*. 2024 Feb 27;41(5):351–362. doi: [10.1097/EJA.0000000000001974](https://doi.org/10.1097/EJA.0000000000001974).

## Keywords

chronic postsurgical pain, CPSP, neuropathic pain, incidence, risk factors

## Virtual reality-based training in chronic low back pain: systematic review and meta-analysis of randomized controlled trials

This meta-analysis evaluated the immediate and short-term effects of virtual reality (VR) training on pain, fear of pain, and disability in people with chronic low back pain. Twenty randomized controlled trials involving 1,059 patients were included. Results showed significant improvements immediately after intervention in pain reduction (mean difference [MD]  $-1.43$ ; 95% CI  $-1.86$  to  $-1.00$ ), reduction in fear of pain (MD  $-5.46$ ; 95% CI  $-9.40$  to  $-1.52$ ), and reduction in disability (MD  $-11.50$ ; 95% CI  $-20.00$  to  $-3.01$ ). However, no significant differences were observed in the short term (3–6 months after intervention) for these measures. The study suggests that VR-based training may be effective in the short term in managing chronic low back pain, but further high-quality studies are needed to confirm long-term benefits.

### Reference

Li R, Li Y, Kong Y, Li H, Hu D, Fu C, et al. Virtual Reality-Based Training in Chronic Low Back Pain Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Journal of Medical Internet Research*. 2024 Feb 26;26:e45406. doi: [10.2196/45406](https://doi.org/10.2196/45406).

### Keywords

virtual reality, chronic low back pain, meta-analysis, VR-based training, rehabilitation

# Palliative Care



## New initiatives on the role of advance care plan in multiple sclerosis

Implementation of advance care planning (ACP) in people with progressive multiple sclerosis (PwPMS) is limited. The paper aimed to involve users (PwPMS, significant others, and healthcare professionals involved in PwPMS care) in the evaluation and refinement of a booklet to be used during the ACP conversations. Appraisal of the booklet was instrumental in improving its acceptability and understandability before using it in the ConCure-SM feasibility trial.

### Reference

Giordano, A., De Panfilis, L., Veronese, S., Bruzzone, M., Cascioli, M., Farinotti, M., ... & Solari, A. (2024) User appraisal of a booklet for advance care planning in multiple sclerosis: a multicenter, qualitative Italian study. *Neurological Sciences*,45(3),1145–1154. doi: [10.1007/s10072-023-07087-y](https://doi.org/10.1007/s10072-023-07087-y).

### Keywords

multiple sclerosis, advance care planning, goals of care, palliative care, qualitative research

## Novel data on the role of palliative care in multiple system atrophy

People with Multiple System Atrophy (MSA) and their carers continue to face many complex physical and emotional issues that would benefit from palliative care. This survey of people with MSA and their carers aimed to increase understanding of end-of-life care and palliative care for this group. Discussions about care at the end of life were generally perceived as helpful, but although the deterioration was often discussed, many families seemed unprepared for the death. Palliative care services were involved but this appeared limited.

### Reference

Oliver D, Barrick A, Kobylecki C, Panicker J, Quinn N, Rushton E, et al. End-of-life care in multiple system atrophy: UK survey of patients and families. *BMJ Supportive & Palliative Care*. 2024 Aug 13; 14(e3):e3019-e3023. doi: [10.1136/spcare-2024-005045](https://doi.org/10.1136/spcare-2024-005045).

### Keywords

advance directives, chronic conditions, palliative care, quality of life, terminal care

## What education needs in palliative care do residents in neurology have in Italy?

Of 854 residents, 188 (22 %) participated. Few (6 %) reported that a teaching course in Palliative care (PC) was part of the graduate programme, and 3 % of the postgraduate programme. During their residency, 9 % of participants received PC training, and 18 % Advance Care Plan (ACP) training. Only 13 % reported having participated in the ACP process, half within their neurology residency programme. Residents considered PC support very/extremely important in all the pre-specified clinical situations, with values ranging between 78 % and 96 %. Over 70 % of residents revealed education needs, particularly concerning ACP.

This paper confirms the need for improving PC training in the graduate and postgraduate curriculum. This, together with collaboration and joint training of neurology and PC, is essential to improve the quality and continuity of care and respond to the complex needs of people with neurological disorders causing severe disability.

### Reference

Bombaci A, Di Lorenzo F, Pucci E, Solari A, Veronese S. Education needs in palliative care and advance care planning of Italian residents in neurology: an online survey. *European Journal of Neurology*. 2024 Jun 3;31(9):e16376. doi: [10.1111/ene.16376](https://doi.org/10.1111/ene.16376).

### Keywords

advance directives, chronic conditions, palliative care, quality of life, terminal care

# Sleep-wake Disorders



## Upcoming treatments for central disorders of hypersomnolence – orexin receptor 2 agonists

It has been more than two decades since the discovery that narcolepsy type 1 is caused by a lack of the neuropeptide hypocretin. Several hypocretin receptor 2 agonists are now under development. The first reports in humans were very promising, yet the first trial was stopped because of hepatotoxicity. Several new trials are ongoing. If effective, this new class of drugs will create a paradigm shift in how we would causally treat narcolepsy type 1 and possibly other central disorders of hypersomnolence.

### References

Dauvilliers, Y., Mignot, E., del Río Villegas, R., Du, Y., Hanson, E., Inoue, Y., ... & von Hehn, C. (2023). Oral Orexin Receptor 2 Agonist in Narcolepsy Type 1. *New England Journal of Medicine*, 389(4), 309–321. doi: [10.1056/NEJMoa2301940](https://doi.org/10.1056/NEJMoa2301940).

Evans, R., Kimura, H., Alexander, R., Davies, C. H., Faessel, H., Hartman, D. S., ... & Mignot, E. (2022). Orexin 2 receptor-selective agonist danavorexton improves narcolepsy phenotype in a mouse model and in human patients. *Proceedings of the National Academy of Sciences*, 119(35), e2207531119. doi: [10.1073/pnas.2207531119](https://doi.org/10.1073/pnas.2207531119).

### Keywords

narcolepsy, hypocretin, orexin, hypersomnolence

## Is brain clearance enhanced during sleep or not?

In recent years, several literature studies suggested that the brain clearance might be enhanced during sleep, especially during non-rapid eye movement sleep (NREM). It has been hypothesized that metabolites and toxins might be cleared from the sleeping brain through the glymphatic system. However, a recent animal model study found that brain clearance was reduced during sleep and anesthesia. This finding contradicts previous studies, raising the question of whether the brain clearance is dependent on sleep.

### Reference

Miao, A., Luo, T., Hsieh, B., Edge, C. J., Gridley, M., Wong, R. T. C., ... & Franks, N. P. (2024). Brain clearance is reduced during sleep and anesthesia. *Nature neuroscience*, 27(6), 1046–1050. doi: [10.1038/s41593-024-01638-y](https://doi.org/10.1038/s41593-024-01638-y).

### Keywords

glymphatic system, brain clearance, neurodegenerative disorders, sleep

## New treatment for insomnia

Insomnia is a very common disorder (up to 10 % of the adult population in Europe), causing a huge burden for physical, emotional health and socioeconomic well-being. Currently, there are two ways to treat insomnia: cognitive behavioural therapy for insomnia (CBT-i) and pharmacological treatment. The latter treatment has been challenging because of the wearing off efficacy and dependence risk for the majority of the recommended sleep aid medications. The introduction of dual orexin receptor antagonists (DORAs) has been the most significant recent development in the pharmacological treatment of insomnia. Daridorexant is the only one DORA approved by the European Medicines Agency so far to treat adult insomnia for a duration of at least 3 months.

### Reference

Riemann D, Espie CA, Altena E, Arnardottir ES, Baglioni C, Bassetti CL, et al. The European Insomnia Guideline An update on the diagnosis and treatment of insomnia 2023. *Journal of Sleep Research*. 2023 Dec;32(6):e14035. doi: [10.1111/jsr.14035](https://doi.org/10.1111/jsr.14035).

### Keywords

insomnia, orexin, hypocretin

## Biological definition/classification of $\alpha$ -synuclein disease: relevance for rapid eye movement behaviour disorder (RBD)

Recent biomarkers advances led to two proposals of biological definition/classification of neuronal  $\alpha$ -synuclein diseases. The SynNeurGe classification uses I.) pathological  $\alpha$ -synuclein in tissues or CSF; II.) neurodegeneration, i. e. dopaminergic deficit demonstrated by neuroimaging; and III.) pathogenetic gene variants. Here, Rapid eye movement behaviour disorder (RBD) is considered probably related to Parkinson's Disease Polysomnography-confirmed. The neuronal  $\alpha$ -synuclein disease integrated staging system (NSD-ISS) proposes a new definition of  $\alpha$ -synuclein disease, based on the in vivo detection of pathological neuronal  $\alpha$ -synuclein. Subtle clinical manifestations without functional impairment (including iRBD) are defined as stage 2, with sub-classification based on dopaminergic neuronal dysfunction. Biomarker advancements in this field are indeed promising, however at the moment these definition/classification systems should be used for research only, pending future studies.

### References

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Höglinger, G. U., Adler, C. H., Berg, D., Klein, C., Outeiro, T. F., Poewe, W., ... & Lang, A. E. (2024). A biological classification of Parkinson's disease: the SynNeurGe research diagnostic criteria. *Lancet Neurology*, 23(2), 191–204. doi: [10.1016/S1474-4422\(23\)00404-0](https://doi.org/10.1016/S1474-4422(23)00404-0).

### Keywords

rem sleep behavior disorder, Parkinson's disease, sleep

# Stroke



## Endovascular thrombectomy

The following studies address the challenges and advancements in managing distal medium vessel occlusions (DMVO). The DUSK study compared endovascular treatment (EVT) and medical management (MM) for DMVO strokes, analysing data from 321 patients. It found no significant differences in outcomes or safety between the two approaches, emphasizing the need for randomized trials to clarify EVT's role in DMVO treatment. Meanwhile, the review highlights the growing recognition of DMVOs, which account for 25–40 % of ischemic strokes and can cause significant disability. It discusses current diagnostic and therapeutic strategies, including the challenges of EVT due to smaller vessel size, and underscores the importance of refining technology and standardizing treatment approaches. Both works advocate further research to optimize outcomes and better address DMVO-related stroke disability.

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Nogueira, R. G., Doheim, M. F., Al-Bayati, A. R., Lee, J. S., Haussen, D. C., Mohammad, M., ... & Bhatt, N. R. (2024). Distal Medium Vessel Occlusion Strokes Understanding the Present and Paving the Way for a Better Future. *Journal of stroke*, 26(2), 190–202. doi: [10.5853/jos.2023.02649](https://doi.org/10.5853/jos.2023.02649).

Mohammad, M. H., Souza Viana, L., Abdelhamid, H., Olive-Gadea, M., Rodrigo-Gisbert, M., Requena, M., ... & Nogueira, R. G. (2024). Endovascular Versus Medical Management in Distal Medium Vessel Occlusion Stroke: The DUSK Study. *Stroke*, 55(6), 1489–1497. doi: [10.1161/STROKEAHA.123.045228](https://doi.org/10.1161/STROKEAHA.123.045228).

### Keywords

distal medium vessel occlusion, DMVO, endovascular thrombectomy (EVT)

## Intravenous thrombolysis update

In the past year, a significant breakthrough in thrombolytic therapy was the exploration of tenecteplase (TNK) for ischemic stroke (IS) caused by large-vessel occlusion (LVO), administered 4.5 to 24 hours after onset. This approach showed less disability and similar survival rates compared to standard treatment, though it was associated with a higher incidence of symptomatic intracranial hemorrhage (ICH). In contrast, another trial indicated that patients with minor stroke and intracranial occlusion should not receive TNK within the 4.5-hour window due to lack of benefit and potential harm. Additionally, patients with minor IS treated with alteplase showed no significant improvement and had a higher risk of sICH compared to best medical treatment or antiplatelet use. Reteplase, when used within the 4.5-hour window, resulted in better functional outcomes after 90 days but was linked to a slightly higher risk of ICH and adverse events.

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Xiong, Y., Campbell, B. C. V., Schwamm, L. H., Meng, X., Jin, A., Parsons, M. W., ... & Wang, Y. (2024). Tenecteplase for Ischemic Stroke at 4.5 to 24 Hours without Thrombectomy. *The New England Journal of Medicine*, 391(3), 203–212. doi: [10.1056/NEJMoa2402980](https://doi.org/10.1056/NEJMoa2402980).

Li, S., Gu, H. Q., Li, H., Wang, X., Jin, A., Guo, S., ... & Wang, Y. (2024). Reteplase versus Alteplase for Acute Ischemic Stroke. *The New England Journal of Medicine*, 390(24), 2264–2273. doi: [10.1056/NEJMoa2400314](https://doi.org/10.1056/NEJMoa2400314).

### Keywords

intravenous thrombolysis, tenecteplase, reteplase, minor stroke, extended time-window

## Etiology and secondary prevention advancements

Recent advancements in stroke secondary management underscore the critical importance of timely intervention and individualized treatment strategies. Current evidence supporting the management of patent foramen ovale for secondary stroke prevention, suggests a tailored approach based on patient-specific risk factors. Complementing these insights, the identification of complex left atrial appendage morphology as a predictor of embolic stroke of undetermined source, highlights the necessity for precise imaging techniques to enhance diagnostic accuracy. Concurrently, ELAN and OPTIMAS trials contribute significant findings regarding the optimal timing of anticoagulation in stroke patients with atrial fibrillation, advocating for earlier intervention to minimize the risk of recurrent events. Collectively, these studies shed light on our understanding of stroke pathophysiology and secondary management, emphasizing a more personalized medicine approach in neurology.

### References

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### Keywords

patent foramen ovale, ESUS, embolic stroke of undetermined significance, anticoagulation, atrial fibrillation

## New treatment options in intracerebral hemorrhage (ICH)

Over the past year, three pivotal studies have made significant strides in treating intracerebral hemorrhage (ICH). The ENRICH trial revealed that early minimally invasive surgery significantly enhances outcomes for patients with acute ICH compared to conventional medical management. This surgical approach was especially beneficial for those with lobar ICH, reducing 30-day mortality rates to 9.3% from 18% and improving functional outcomes at 180 days. The ANNEXA-I trial assessed the effectiveness of andexanet alfa in ICH patients on factor Xa inhibitors. It proved more effective than usual care in controlling hematoma expansion, with 67.0% of patients achieving hemostatic efficacy versus 53.1%. However, andexanet was linked to a higher incidence of thrombotic events, including ischemic strokes, at 6.5% compared to 1.5%. Additionally, a randomized controlled trial provided tentative evidence supporting decompressive craniectomy in managing severe spontaneous supratentorial ICH, with fewer patients in the surgical group experiencing severe disability. However, more research is needed to confirm these findings.

### References

Pradilla, G., Ratcliff, J. J., Hall, A. J., Saville, B. R., Allen, J. W., Paulon, G., ... & Barrow, D. L. (2024). Trial of Early Minimally Invasive Removal of Intracerebral Hemorrhage. *The New England Journal of Medicine*, 390(14), 1277–1289. doi: [10.1056/NEJMoa2308440](https://doi.org/10.1056/NEJMoa2308440).

Connolly, S. J., Sharma, M., Cohen, A. T., Demchuk, A. M., Członkowska, A., Lindgren, A. G., ... & Shoamanesh, A. (2024). Andexanet for Factor Xa Inhibitor-Associated Acute Intracerebral Hemorrhage. *The New England Journal of Medicine*, 390(19), 1745–1755. doi: [10.1056/NEJMoa2313040](https://doi.org/10.1056/NEJMoa2313040).

### Keywords

minimally invasive surgery, andexanet alfa, intracerebral haemorrhage, factor Xa inhibitors

## Balloon angioplasty for stroke prevention in intracranial artery stenosis

The BASIS randomized clinical trial investigated whether balloon angioplasty combined with aggressive medical management is superior to medical management alone in treating symptomatic intracranial atherosclerotic stenosis (sICAS). Conducted at 31 centers in China, the study included 501 patients who had recently experienced a transient ischemic attack or ischemic stroke due to severe arterial stenosis. The trial found that patients who underwent balloon angioplasty had a significantly lower risk of stroke or death within one year compared to those who received only medical management (4.4% vs. 13.5%). However, procedural complications, such as arterial dissection, were observed in the angioplasty group. The findings suggest that balloon angioplasty may be a viable option for high-risk sICAS patients, though further studies are needed to assess long-term benefits and refine patient selection criteria.

### Reference

Sun, X., Deng, Y., Zhang, Y., Yang, M., Sun, D., Nguyen, T. N., ... & BASIS Investigators (2024). Balloon Angioplasty vs Medical Management for Intracranial Artery Stenosis The BASIS Randomized Clinical Trial. *JAMA*, 332(13), 1059–1069. doi: [10.1001/jama.2024.12829](https://doi.org/10.1001/jama.2024.12829).

### Keywords

balloon angioplasty, symptomatic intracranial atherosclerotic stenosis, sICAS

# Coordinating Panels



## Sexual and gender minority persons had higher odds of adverse brain health outcomes

Among the most underrepresented groups in research are sexual and gender minority (SGM) individuals. It is unclear whether brain health in these individuals is deteriorating quicker in comparison to cisgender straight (non-SGM) individuals. In a cross-sectional study by Huo et al., this problem was investigated in the US-based All of Us cohort. The primary outcome included a composite outcome of stroke, dementia, and late-life depression, while in a secondary analysis each disease was assessed independently. In a cohort of 393,041 participants, 10 % reported to belong to the SGM group. In comparison to the non-SGM group, the SGM group had 15 % higher odds of the brain health composite outcome. In the secondary analysis, all SGM groups had higher odds of dementia and late-life depression, while transgender women had higher odds of stroke. It can therefore be concluded that SGM individuals have an overall higher risk of brain health events.

### Reference

Huo S, Rivier CA, Clocchiatti-Tuozzo S, et al. Brain Health Outcomes in Sexual and Gender Minority Groups: Results From the All of Us Research Program. *Neurology* 2024 Sep 25;103(8). doi: [10.1212/WNL.000000000209863](https://doi.org/10.1212/WNL.000000000209863).

### Keywords

sexual and gender minority, brain health, dementia, stroke

## Dementia and late-life depression seem to be the most complained conditions by SGM persons

The crucial role of equity in providing health care is well recognized, but it remains concerning how little is known about the health disparities faced by sexual and gender minority (SGM) groups. In a large US population study including more than 400,000 people, SGM persons had higher odds of adverse brain health outcomes, and when assessing individual disease, all SGM groups had higher odds of dementia and late-life depression. Both these conditions are known as surrogates for brain health in the elderly, but the causes of the increased risk remain to be explored. It is important to recognize the distinct challenges and risk profiles each group encounters in order to provide equal care and avoid disparities in medical research.

### Reference

Huo S, Rivier CA, Clocchiatti-Tuozzo S, Renedo D, Sunmonu NA, de Havenon A, Sarpong DF, Rosendale N, Sheth KN, Falcone GJ. Brain Health Outcomes in Sexual and Gender Minority Groups: Results From the All of Us Research Program. *Neurology*. 2024 Oct 22;103(8). doi: [10.1212/WNL.000000000209863](https://doi.org/10.1212/WNL.000000000209863).

### Keywords

sexual and gender minority, inclusion, dementia, depression

## Female sex is associated with unfavourable pre- and in-hospital time in case of acute ischemic stroke

A retrospective study on acute ischemic stroke patients found that women experience significant delays in both pre-hospital and in-hospital care. Women had longer onset-to-door times, often arriving later to medical facilities, possibly due to differences in symptom recognition, atypical presentations, or social factors such as living alone. Once in the hospital, they also faced prolonged door-to-treatment times for interventions like endovascular therapy. These delays can negatively impact functional recovery, leading to worse long-term outcomes. Despite similar eligibility for acute stroke treatments, systemic factors contribute to prolonged response times in female patients. Addressing these disparities requires increased awareness of stroke symptoms in women, enhanced triage protocols, and targeted public health interventions. Further research is necessary to explore the underlying causes of these delays and develop strategies for timely stroke management in female patients.

### Reference

Medlin F, Strambo D, Lambrou D, Caso V, Michel P. Service delivery in acute ischemic stroke patients: Does sex matter? *European Journal of Neurology*. 2024 Mar30;31(7). doi: [10.1111/ene.16287](https://doi.org/10.1111/ene.16287).

### Keywords

stroke, gender disparities, door-to-treatment time

## Less effective stroke care delivery in female patients

Sex-based disparities exist in the care delivery of acute ischemic stroke, with female patients receiving less effective stroke management. Studies show that women experience longer hospital stays and fewer diagnostic evaluations, including carotid imaging and subacute revascularization procedures. They are also less likely to receive intensive rehabilitation, which may contribute to poorer long-term recovery. Although rates of acute revascularization treatments are comparable between sexes, inefficiencies in hospital workflow and decision-making may disadvantage female patients. Contributing factors include biases in symptom assessment, underestimation of stroke severity, and lower likelihood of aggressive intervention. While no significant differences were found in treatment goal modifications, these findings highlight the need for more equitable stroke care. Addressing these gaps requires standardized protocols that ensure timely diagnostics and interventions for female patients. Raising awareness among healthcare providers and improving hospital resource allocation may enhance stroke outcomes for women.

### Reference

Medlin F, Strambo D, Lambrou D, Caso V, Michel P. Service delivery in acute ischemic stroke patients: Does sex matter? *European Journal of Neurology*. 2024 Mar30;31(7). doi: [10.1111/ene.16287](https://doi.org/10.1111/ene.16287).

### Keywords

stroke management disparity, hospital care inequality, rehabilitation access

## Awareness of atypical presentation of hereditary neuropathy in women may be helpful to establish the right diagnosis

Neuropathies present with increasing symmetric weakness and wasting of the lower legs and hands. They are often genetic in nature. There are many different hereditary neuropathies which in themselves are rare. A particular form, caused by a gene on the X-chromosome (one of the two sex chromosomes) is one of the most frequent inherited neuropathies (X-linked Charcot-Marie-Tooth disease (X-CMT)), which can be found in men and women. However, women often have an atypical manifestation: asymmetric weakness and abnormalities on studies measuring electrical activity of the nerves resembling an inflammation of the nerves rather than a hereditary neuropathy. Hence, in these women, an inaccurate diagnosis is often established, and they are exposed to medication which may be harmful.

The take-home message is the following: if a woman has an atypical presentation of a chronic (long-lasting) neuropathy consider the possibility of X-linked CMT. This will avoid a misdiagnosis and harmful treatment.

### Reference

Du Closel LB, Bonello-Palot N, Delmont E, et al. Phenotype-genotype correlation in X-linked Charcot-Marie-Tooth disease: A French cohort study. *European Journal of Neurology*. 2024 Nov 21;32(1). doi: [10.1111/ene.16523](https://doi.org/10.1111/ene.16523).

### Keywords

hereditary neuropathy, Charcot-Marie-Tooth (CMT), female presentation, X-linked

# Functional Neurological Disorders



## Specialist physiotherapy for functional motor disorder in England and Scotland (Physio4FMD): a pragmatic, multicentre, phase 3 randomised controlled trial

In this randomized controlled trial a total of 241 patients with functional motor disorders were either assigned to specialist physiotherapy for a duration of 9 sessions or to treatment as usual. Although more participants who were assigned specialist physiotherapy self-rated their motor symptoms as improved and had better scores on subjective measures of mental health, the intervention did not result in better self-reported physical functioning at 12 months. Both the specialist and community neurological physiotherapy appeared to be a safe and a valued treatment for selected patients with functional motor disorder.

### Reference

Nielsen G, Stone J, Lee TC, Goldstein LH, Marston L, Hunter RM, et al. Specialist physiotherapy for functional motor disorder in England and Scotland (Physio4FMD): a pragmatic, multicentre, phase 3 randomised controlled trial. *The Lancet Neurology*. 2024 May 17;23(7):675–686. doi: [10.1016/S1474-4422\(24\)00135-2](https://doi.org/10.1016/S1474-4422(24)00135-2).

### Keywords

specialized physiotherapy, functional motor disorders, RCT

## Increased risk of functional neurological disorders following SARS-CoV-2 vaccination

In this prospective cohort study including 411 unvaccinated and 432 vaccinated persons, SARS-CoV-2 vaccination was associated with a significant short-term increased risk of functional neurological disorders (FND) and headache requiring hospitalization in an acute neurological setting. This study is indicative that SARS-CoV-2 vaccination may be a short-time risk factor for the development of FND.

### Reference

Pilotto A, Catania M, Mattioli I, Zoppi N, Ceccardi G, Rao R, et al. Increased risk of functional neurological disorders following SARS-CoV-2 vaccination. *European Journal of Neurology*. 2024 Jan 2;31(4). doi: [10.1111/ene.16191](https://doi.org/10.1111/ene.16191).

### Keywords

functional neurological disorder, headache, SARS-CoV-2 vaccination

## Combined physiotherapy and cognitive behavioral therapy for functional movement disorders improve patients' symptoms

In this randomized clinical trial a multidisciplinary treatment including physiotherapy plus cognitive behavioral therapy effectively improved functional movement disorders (FMD) symptoms and physical aspects of patients' quality of life. A total of 38 patients either completed 4 successive, weekly, 1-hour group sessions of cognitive behavioral therapy and 12 ambulatory 1-hour individualized physiotherapy sessions or if assigned to the control group 4 weekly 1-hour group sessions of nondirective supportive psychotherapy only. These results suggest that multidisciplinary treatment is superior to psychological treatment only in regard to physical aspects of quality of life in FMD patients.

### Reference

Macías-García D, Barrio MMD, Canal-Rivero M, Muñoz-Delgado L, Adarmes-Gómez A, Jesús S, et al. Combined Physiotherapy and Cognitive Behavioral Therapy for Functional Movement Disorders: A Randomized Clinical Trial. *JAMA Neurology*. 2024 Sep 1;81(9):966–976. doi: [10.1001/jamaneurol.2024.2393](https://doi.org/10.1001/jamaneurol.2024.2393).

### Keywords

combined treatment, multidisciplinary treatment, functional motor disorders

## Improvement of functional seizure frequency after breathing control training

In this multi-site open-label study seven out of ten patients with functional seizures had improved seizure frequency after they received an hour of breathing training from a respiratory physiotherapist and a 30-minute booster session a month later. These preliminary results support that breathing control training should prove cost-effective and acceptable, though requires confirmation by a randomised controlled trial.

### Reference

Duncan R, Berlowitz DJ, Mullen S, Bondarenko J, Winton-Brown TT, O'Brien TJ, et al. Breathing control training for functional seizures: A multi-site, open-label pilot study. *Epilepsy & Behavior*. 2024 May;154:109745. doi: [10.1016/j.yebeh.2024.109745](https://doi.org/10.1016/j.yebeh.2024.109745).

### Keywords

functional seizures, breathing control training, hyperventilation

# Neuroscience/Translational Neurology



## Immunological endophenotypes in multiple sclerosis

The German Competence Network Multiple Sclerosis (KKNMS) group has reported the identification of immunological endophenotypes in patients with early multiple sclerosis (MS) ( $\leq 2$  years from clinical onset) with an influence on treatment response to certain disease-modifying therapies (DMTs). They analysed peripheral blood mononuclear cells and serum of 309 MS patients by combining multiparameter flow cytometry and targeted proteomics and validated their findings on a second cohort of 232 MS patients using a machine learning model. They found three endophenotypes by unsupervised cluster analysis of cellular signatures. This effect of IFN- $\beta$  was not observed in other endophenotypes. In conclusion, blood immune signature could provide invaluable insight into the clinical disease trajectory and allow individually tailored therapeutic decisions.

### Reference

Gross C. C., Schulte-Mecklenbeck, A., Steinberg, O. V., Wirth, T., Lauks, S., Bittner, S., ... & German Competence Network Multiple Sclerosis (KKNMS). (2024) Multiple sclerosis endophenotypes identified by high-dimensional blood signatures are associated with distinct disease trajectories. *Science Translational Medicine*, 16(740). doi: [10.1126/scitranslmed.ade8560](https://doi.org/10.1126/scitranslmed.ade8560).

### Keywords

immunological endophenotype, immune signature

## Human-based brain organoids for the study of neurological diseases

Brain organoids, which are derived from human stem cells, represent a powerful in vitro tool for studying neurological diseases. These cells are cultured and differentiated under specific conditions to generate three-dimensional structures that mimic the nervous system. In addition, brain organoids can be generated from induced pluripotent stem cells from patients, maintaining their genetic fingerprint. Such models allow to advance the understanding of disease mechanisms and serve as platforms for testing treatments in vitro. Over the past year, significant progress has been made in modeling neurological diseases using this technology.

A notable application of this technology is in the study of Parkinson's disease, where ventral midbrain-striatum-cortex assembloids have shown the generation and development of the dopaminergic neuron circuitry affected in the disease. Similarly, another neuromuscular assembloid has allowed modelling of amyotrophic lateral sclerosis from cells of patients affected by the C9orf72 mutation.

### References

Reumann, D., Krauditsch, C., Novatchkova, M., Sozzi, E., Wong, S. N., Zabolocki, M., ... & Knoblich, J. A. (2023). In vitro modeling of the human dopaminergic system using spatially arranged ventral midbrain-striatum-cortex assembloids. *Nature Methods*, 20(12), 2034–2047. doi: [10.1038/s41592-023-02080-x](https://doi.org/10.1038/s41592-023-02080-x).

Gao, C., Shi, Q., Pan, X., Chen, J., Zhang, Y., Lang, J., ... & Lei, K. (2024). Neuromuscular organoids model spinal neuromuscular pathologies in C9orf72 amyotrophic lateral sclerosis. *Cell Reports*, 43(3). doi: [10.1016/j.celrep.2024.113892](https://doi.org/10.1016/j.celrep.2024.113892).

### Keywords

human-based models, brain organoids, stem cells, Alzheimer's disease, multiple sclerosis

## Approval of Tenecteplase as thrombolytic agent for acute ischemic stroke

In Europe, Tenecteplase has been approved for the treatment of acute ischemic stroke by the European Medicines Agency (EMA) in January 2024. This drug has the advantage of being administered as a single bolus injection rather than requiring a continuous infusion over an hour as for Alteplase: this is fundamental for the time-dependent stroke acute treatment. Two main trials have been published in 2024 investigating the use of Tenecteplase in stroke due to large-vessel occlusion and in minor stroke, respectively: TRACE-III Study (LVO-stroke), TEMPO2 Trial (Minor Stroke). Therefore, Tenecteplase is promising for moderate-to-severe LVO stroke in certain settings but shows no benefit and potential harm in minor stroke. Both studies emphasize the importance of tailoring stroke treatments to individual stroke severity and pathophysiology.

### References

Xiong Y, Campbell BCV, Schwamm LH, Meng X, Jin A, Parsons MW, et al. Tenecteplase for Ischemic Stroke at 4.5 to 24 Hours without Thrombectomy. *New England Journal of Medicine*. 2024 Jun 15;391(3):203–212. doi: [10.1056/NEJMoa2402980](https://doi.org/10.1056/NEJMoa2402980).

Coutts SB, Ankolekar S, Appireddy R, Arenillas JF, Assis Z, Bailey P, et al. Tenecteplase versus standard of care for minor ischaemic stroke with proven occlusion (TEMPO-2): a randomised, open label, phase 3 superiority trial. *Lancet*. 2024 Jun 15;403(10444):2597–2605. doi: [10.1016/S0140-6736\(24\)00921-8](https://doi.org/10.1016/S0140-6736(24)00921-8). Erratum in: *Lancet*. 2024 Jun 15;403(10444):2596. doi: [10.1016/S0140-6736\(24\)01209-1](https://doi.org/10.1016/S0140-6736(24)01209-1).

### Keywords

tenecteplase, acute ischemic stroke

## Digital biomarkers

Digital biomarkers are measurable and objective indicators of changes in behavior, obtained through portable, wearable or implantable digital devices. In recent years, with the developments in wearables, big data analysis methods and predictive models, the use of digital biomarkers to monitor neurological disease has become of interest. In 2024 FDA approved Apple AFib History Feature as the first biomarker in the clinical trials. In 2024 digital biomarkers for several neurological diseases have been developed. A combination of plasma biomarkers and 10 minutes of cognitive assessment on a tablet was optimal for predicting PET abnormalities in dementia. First efforts to standardize digital biomarkers in terms of acquisition technology, protocols and measures to be calculated have been done for ataxias. Although before applying to the clinical trial further standardization is needed, it is highly probable that digital biomarkers will soon be an integral part of clinical trials for neurological disease.

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Tsoy E, La Joie R, VandeVrede L, Rojas JC, Yballa C, Chan B, et al. Scalable plasma and digital cognitive markers for diagnosis and prognosis of Alzheimer's disease and related dementias. *Alzheimer's & Dementia*. 2024 Jan 15;20(3):2089–2101. doi: [10.1002/alz.13686](https://doi.org/10.1002/alz.13686).

Ilg W, Milne S, Schmitz-Hübsch T, Alcock L, Beichert L, Bertini E, et al. Quantitative Gait and Balance Outcomes for Ataxia Trials: Consensus Recommendations by the Ataxia Global Initiative Working Group on Digital-Motor Biomarkers. *Cerebellum*. 2023 Nov 13; 23(4):1566–1592. doi: [10.1007/s12311-023-01625-2](https://doi.org/10.1007/s12311-023-01625-2).

### Keywords

digital biomarkers, standardization, digitalization, wearables



## Gene therapy breakthroughs

Gene therapy has revolutionised the treatment of rare neurological diseases, offering hope for previously untreatable genetic disorders. By delivering functional genes or modifying defective ones, these therapies target the root cause rather than merely the symptoms. An exemplary case is Spinal Muscular Atrophy (SMA), where gene replacement therapy has significantly improved motor function and survival. A similar advance has been achieved in the treatment of adrenoleukodystrophy (ALD), a neurodegenerative condition where gene therapy slows the progression of the disease and improves outcomes. These breakthroughs represent a paradigm shift in the field, with the potential to transform patient care by providing long-term benefits with a single treatment.

### Reference

Porcari, G. S., Collyer, J. W., Adang, L. A., & Rajan, D. S. (2025). Current Advances and Challenges in Gene Therapies for Neurological Disorders. *Neurology: Genetics*, 11(1), e200229. doi: [10.1212/NXG.000000000200229](https://doi.org/10.1212/NXG.000000000200229).

### Keywords

gene therapy, SMA, rare neurological diseases

## CRISPR and gene editing technologies

Advances in CRISPR-Cas9 and other gene-editing tools are paving the way for precision medicine in rare neurological diseases, such as Huntington's disease and amyotrophic lateral sclerosis. In recent years, these technologies have progressed from laboratory experiments to early-stage human trials, offering hope of correcting genetic mutations that cause rare neurodegenerative diseases.

### Reference

Yang, X., Bui, T. A., Mei, H., Aksoy, Y. A., Deng, F., Hutvagner, G., & Deng, W. (2024). Exploring the Potential and Challenges of CRISPR Delivery and Therapeutics for Genetic Disease Treatment. *Advanced Functional Materials*, 34(38), 2402630. doi: [10.1002/adfm.202402630](https://doi.org/10.1002/adfm.202402630).

### Keywords

CRISPR-Cas9, gene editing, rare neurological diseases

## Targeted molecular therapies

Novel drugs now target specific molecular pathways in previously untreatable diseases. Examples include: (i) Risdiplam (for SMA), a small molecule that boosts SMN protein production for motor neuron survival; (ii) Tafamidis (for transthyretin amyloidosis), stabilizing misfolded proteins to slow disease progression; (iii) Miglustat, an oral therapy for type 1 Gaucher's disease, also used in Niemann-Pick type C; (iv) N-acetylcysteine, showing benefits in Niemann-Pick type C; (v) Omaveloxolone, the first FDA-approved treatment for Friedreich's Ataxia (FA), restoring mitochondrial function via Nrf2 activation. In the MOXIE Part 2 trial (NCT02255435), omaveloxolone significantly improved Friedreich Ataxia Rating Scale scores over 48 weeks.

### References

Lynch, D. R., Chin, M. P., Boesch, S., Delatycki, M. B., Giunti, P., Goldsberry, A., ... & Meyer, C. J. (2023). Efficacy of Omaveloxolone in Friedreich's Ataxia: Delayed-Start Analysis of the MOXIE Extension. *Movement disorders*, 38(2), 313–320. doi: [10.1002/mds.29286](https://doi.org/10.1002/mds.29286).

Bremova-Erti, T., Ramaswami, U., Brands, M., Foltan, T., Gautschi, M., Gissen, P., ... & Martakis, K. (2024). Trial of N-Acetyl-L-Leucine in Niemann-Pick Disease Type C. *New England Journal of Medicine*, 390(5), 421–431. doi: [10.1056/NEJMoa2310151](https://doi.org/10.1056/NEJMoa2310151).

### Keywords

Friedreich's Ataxia, Niemann-Pick type C, transthyretin amyloidosis

## Antisense oligonucleotides (ASOs)

ASOs are a novel class of therapeutics that selectively modulate gene expression by binding to RNA. They have shown promise for treating rare neurological disorders with clear genetic origins such as nusinersen, the first FDA-approved ASO, used to treat SMA by increasing the production of the functional SMN protein or tominersen, investigated for Huntington's disease, this ASO therapy aims to reduce the production of the toxic mutant huntingtin protein in the brain. In addition, recent data support the potential of ASO-mediated upregulation of Nav1.1 as a successful strategy to treat Dravet syndrome.

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### Keywords

antisense oligonucleotides, rare neurological diseases, SMA, Huntington's disease, Dravet syndrome

## Novel therapies for patients with myasthenia gravis

Generalised myasthenia gravis (MG) is a chronic autoimmune disease disturbing the communication between nerve and muscle. MG is characterized by fluctuating, fatigue, weakness, manifesting with double vision, hanging eyelids, difficulty walking and using arm muscles, and speech and swallowing difficulties. In one out of five patients a (myasthenic) crisis can occur which may be life-threatening because respiratory muscles may also be involved. ‘Conservative’ medication is effective in the majority of MG patients. However, about 15 % are so-called refractory and do not respond sufficiently, stressing the need for new treatments. A category of new treatments is the neonatal Fc receptor blockers which reduce the autoantibodies that block the transmission of the signals from nerve to muscle. These drugs are generally well tolerated and show improvements in the activities of daily life. Two drugs (efgartigimod, rozanolixizumab) which have to be administered subcutaneously have been approved for use by the European Medicines Agency.

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### Keywords

myasthenia gravis, autoimmune disease, neuromuscular junction, treatment, neonatal Fc receptor blockers

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