brain sciences

Editorial

Neuromuscular Disorders: Recent Advances and Open Challenges

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Neuromuscular disorders (NMDs) encompass a heterogeneous group of acquired and inherited conditions affecting motor neurons, peripheral nerves, neuromuscular junctions, and skeletal muscle [1]. Although progressive muscle weakness remains the most prominent clinical feature, these diseases frequently involve broader multisystemic manifestations, including sensory symptoms, respiratory impairment, fatigue, pain, dysautonomia, cognitive dysfunction, and psychological burden [2]. This complexity makes diagnosis, prognostic stratification, and long-term management particularly challenging, especially in rare diseases requiring dedicated multidisciplinary expertise. In recent years, the field of NMDs has undergone substantial progress [3]. Advances in molecular, immunological, neurophysiological, and imaging techniques have improved diagnostic precision and expanded the identification of disease-specific biomarkers. At the same time, therapeutic innovation has transformed the management of several NMDs [4,5]. This is particularly evident in autoimmune NMDs, such as myasthenia gravis (MG) and immune-mediated neuropathies, where treatment strategies increasingly depend on disease subtype, pathogenic mechanisms, and real-world evidence [6,7]. In inherited muscle diseases, molecular and metabolic advances are also expanding therapeutic perspectives [8]. However, this progress also introduces new challenges. New diagnostic and therapeutic strategies need to be appropriately incorporated into personalized clinical practice. Biomarkers should support diagnosis, prognosis, disease monitoring, and treatment choices [9,10]. Similarly, new therapies should be evaluated for long-term safety, accessibility, costs, treatment sequencing, and real-world effectiveness [11]. This Special Issue aimed to provide an updated overview of recent developments in the diagnostic, prognostic, and therapeutic management of NMDs.

Overview of Published Papers

The contributions included in this Special Issue reflect the broad and multidisciplinary nature of NMDs. Ginanneschi et al. investigated the clinical value of lumbar puncture in amyotrophic lateral sclerosis, showing that routine cerebrospinal fluid abnormalities have limited clinical relevance, whereas neurodegeneration markers, particularly Aβ42, may provide prognostic information on disease progression and survival (Contribution 1). In parallel, Furia et al. reviewed the role of skin biopsy as a minimally invasive approach for assessing cutaneous innervation and pathological protein deposition, highlighting its established value in small-fiber neuropathy and its expanding applications in other neurological disorders (Contribution 2).

Autoimmune neuromuscular disorders represent another central area of this Special Issue. Vinciguerra et al. reported real-world data on mycophenolate mofetil in generalized

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MG, supporting its potential role as an effective and well-tolerated long-term immunosuppressive option (Contribution 3). Rossini et al. provided a broader immunopathological perspective on generalized MG, emphasizing disease heterogeneity and the increasing relevance of antibody status, thymic pathology, age at onset, and immune mechanisms in guiding treatment strategies (Contribution 4).

The Special Issue also addressed inherited muscle diseases from both experimental and clinical perspectives. Dias et al. explored early taurine administration in the mdx mouse model of Duchenne muscular dystrophy, showing reduced RIP1 levels and suggesting a possible role of necroptosis modulation in dystrophic muscle (Contribution 5). Tizzoni et al. reviewed cognitive, psychological, and psychosocial aspects of Duchenne muscular dystrophy, emphasizing that disease burden extends beyond motor impairment and includes quality of life, adaptation, and family resources (Contribution 6). Finally, Annunziata et al. investigated adherence to non-invasive ventilation in myotonic dystrophy type 1, showing that psychological factors may influence treatment adherence and reinforcing the importance of multidisciplinary care (Contribution 7).

Conclusions and Future Perspectives

The papers collected in this Special Issue reflect the current direction of NMDs. Diagnosis is becoming more accurate, and several biomarkers are now available or under investigation. However, their use in clinical practice should depend on their real ability to improve diagnosis, clarify prognosis, monitor disease activity, or support treatment decisions. Treatment is also changing. In autoimmune NMDs, the choice of therapy is increasingly influenced by the underlying immune mechanism, disease subtype, comorbidities, and previous response to treatment. In inherited and degenerative disorders, advances in molecular medicine are opening new perspectives, but clinical management still depends on disease stage, respiratory involvement, functional status, and long-term follow-up. Future studies should help clarify which biomarkers and treatments are clinically meaningful in daily practice. For this reason, multicenter collaborations, longitudinal cohorts, and real-world data will be particularly important, especially in rare and heterogeneous diseases. At the same time, neuromuscular care cannot be reduced to pharmacological treatment alone. Respiratory support, rehabilitation, psychological aspects, cognitive function, treatment adherence, and quality of life remain essential parts of patient management. In this scenario, the contributions included in this Special Issue highlight the need for a balanced approach, in which diagnostic and therapeutic innovation is combined with comprehensive clinical management.

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List of Contributions

1. Ginanneschi, F.; Casali, S.; Cioni, C.; Righi, D.; Emmanuello, E.; Toccaceli, C.; Plantone, D.; De Stefano, N. Does Lumbar Puncture Still Have Clinical Value for Patients with Amyotrophic Lateral Sclerosis? *Brain Sci.* **2025**, *15*, 258. https://doi.org/10.3390/brainsci15030258.

2. Furia, A.; Ragucci, C.; Liguori, R.; Rizzo, G.; Vacchiano, V.; Giannoccaro, M.P.; Donadio, V.A. The Role of Skin Innervation for Assessment of Neurological Involvement in Disorders: A Review. *Brain Sci.* **2025**, *15*, 1254. https://doi.org/10.3390/brainsci15121254.
3. Vinciguerra, C.; D'Amico, A.; Bevilacqua, L.; Rini, N.; D'Apolito, M.; Liberatoscioli, E.; Monastero, R.; Barone, P.; Brighina, F.; Di Muzio, A.; et al. Effectiveness and Safety of Mycophenolate Mophetil in Myasthenia Gravis: A Real-Life Multicenter Experience. *Brain Sci.* **2024**, *14*, 774. https://doi.org/10.3390/brainsci14080774.
4. Rossini, E.; Leonardi, L.; Morino, S.; Antonini, G.; Fionda, L. Immunological Targets in Generalized Myasthenia Gravis Treatment: Where Are We Going Now? *Brain Sci.* **2025**, *15*, 978. https://doi.org/10.3390/brainsci15090978.
5. Dias, M.; Dhuyvetter, H.; Byttebier, E.; Merckx, C.; De Bleecker, J.L.; De Paepe, B. Early Taurine Administration Decreases the Levels of Receptor-Interacting Serine/Threonine Protein Kinase 1 in the Duchenne Mouse Model *mdx*. *Brain Sci.* **2025**, *15*, 1175. https://doi.org/10.3390/brainsci15111175.
6. Tizzoni, F.; Canella, G.; Delle Fave, A.; Di Lernia, D.; Lorusso, M.L.; Nobile, M.; D'Angelo, M.G. Living with Duchenne Muscular Dystrophy Beyond the Physical Implications: Cognitive Features, Psychopathology Aspects, and Psychosocial Resources—A Narrative Review. *Brain Sci.* **2025**, *15*, 695. https://doi.org/10.3390/brainsci15070695.
7. Annunziata, A.; Simioli, F.; Polistina, G.E.; Gaeta, A.M.; Cardone, M.; Di Somma, C.; Manzo, R.; Marotta, A.; Calabrese, C.; Fiorentino, G. Adherence to Non-Invasive Ventilation in Steinert Disease: Clinical and Psychological Insights. *Brain Sci.* **2025**, *15*, 968. https://doi.org/10.3390/brainsci15090968.

References

1. Zhang, G.; Hu, F.; Zhang, Y.; Li, D.; Deng, Y.; Yang, M.; Huang, T.; Deng, X.; Li, Y.; Fu, C.; et al. Progress in precision drug delivery systems for neurodegenerative diseases with muscle atrophy. *Neuropharmacology* **2026**, *297*, 111027. [CrossRef] [PubMed]
2. Akpa, B.; Pusalavidyasagar, S.; Iber, C. Respiratory issues and current management in neuromuscular diseases: A narrative review. *J. Thorac. Dis.* **2024**, *16*, 6292–6307. [CrossRef] [PubMed]
3. Ropars, J.; Salort-Campana, E. Multidisciplinary management of Duchenne muscular dystrophy from childhood to adulthood. *Arch. Pediatr.* **2025**, *32*, 7S15–7S19. [CrossRef] [PubMed]
4. Sel, E.K.; Gkrinia, E.M.M.; Roncato, R.; Vitezić, D.; Janković, S.; Belančić, A. Pharmacokinetics of therapies approved for spinal muscular atrophy: A narrative review of current evidence. *J. Int. Med. Res.* **2025**, *53*, 03000605251397777. [CrossRef] [PubMed]
5. Farzi, F.; Soltanmohammadi, F.; Mohammadi, S.A.; Zarghami, N.; Alizadeh, E. Transforming Duchenne muscular dystrophy therapy: The multifaceted role of extracellular vesicles and exosomes. *Biochem. Biophys. Rep.* **2026**, *46*, 102578. [CrossRef] [PubMed]
6. Cavalcante, P.; Mantegazza, R.; Antozzi, C. Targeting autoimmune mechanisms by precision medicine in Myasthenia Gravis. *Front. Immunol.* **2024**, *15*, 1404191. [CrossRef] [PubMed]
7. Mair, D.; Madi, H.; Eftimov, F.; Lunn, M.P.; Keddie, S. Novel therapies in CIDP. *J. Neurol. Neurosurg. Psychiatry* **2024**, *96*, 38–46. [CrossRef] [PubMed]
8. Mariot, V.; Bloch, R.J.; Badiani, R.; Bugiardini, E.; Dumonceaux, J. Spatiotemporal DUX4 toxicity in FSHD: From epigenetic derepression to biomarker-driven targeted therapies. *Neuromuscul. Disord.* **2026**, *63*, 106420. [CrossRef] [PubMed]
9. Moriyama, H.; Shaikh, F.A.; Yokota, T. Application of Omics Analysis in the Clinical Practice and Research of Transthyretin Amyloidosis. *Genes* **2026**, *17*, 333. [CrossRef] [PubMed]
10. Dowling, P.; Bouragba, D.; Negroni, E.; Trollet, C.; Zweyer, M.; Swandulla, D.; Ohlendieck, K. Potential proteomic biomarkers for monitoring clinical studies in Duchenne/Becker muscular dystrophy. *Expert Rev. Proteom.* **2026**, *23*, 109–120. [CrossRef] [PubMed]
11. Di Stefano, V.; Rini, N.; Antozzi, C.; Alboini, P.E.; Alonge, P.; Bevilacqua, L.; Biasini, F.; Bisecco, A.; Bonanno, S.; Brighina, F.; et al. Early real-life experience on Zilucoplan for generalized myasthenia gravis: ZILU25 multicenter observational study. *J. Neurol. Sci.* **2025**, *479*, 125671. [CrossRef] [PubMed]