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Neuromuscular disorders: from diagnosis to translational research, drug development and clinical trials

Robert C. Tasker and Basil T. Darras

Abstract

Pediatric neuromuscular disorders are a heterogeneous group of conditions that form four distinct groupings: (1) motor neuron diseases, (2) neuropathies, (3) disorders of the neuromuscular junction, and (4) myopathies.

In this issue of *Current Opinion in Pediatrics*, we focus on these disorders and provide an up-to-date overview of current therapies from basic science to evidence-based management. We start with an article by Pitt [1] that addresses new developments in electromyography and its utility in detailed physiologic characterizations of clinical phenotypes. An exciting area is the recent attempt to try and find a neurophysiologic technique that can assist clinicians in clinical trials which is a central theme taken-up by the other articles. In the second article, Singh et al. [2] focus on the motor neuron, and the rare and incurable disorder spinal muscular atrophy (SMA). The authors review and highlight past and current translational research that has now opened new possibilities for therapeutic intervention. They take us on a journey starting with the genetics of the survival motor neuron (SMN) gene, to the molecular function of SMN protein, then drug targets in this process (e.g., SMN2 gene expression, SMN protein stability), and lastly a review of recent and ongoing clinical trials of motor neuron neuroprotection. In the third article, Ryan [3] summarizes the recent literature on Guillain-Barre syndrome (GBS), an acute inflammatory polyneuropathy that is rapidly progressive with symmetric weakness and areflexia. Importantly, the author reviews recent clinical studies on treatment with corticosteroids and intravenous immunoglobulin or plasma exchange. Next, Liew and Kang [4] review the pathophysiology, clinical presentation and treatment options for juvenile myasthenia gravis. Rather like the data for GBS in children [3], Liew and Kang [4] emphasize that managing children with this rare condition relies heavily on data and information learned from adults with myasthenia gravis. They therefore summarize the recent adult data for acetylcholinesterase inhibitors, medical immunomodulation and thymectomy, and counterpoise their summary with evidence of how treatment in children differs or is similar. In the fifth article, by Mercuri and Muntoni [5], we return to the topic of translational research with a review of new

Correspondence to Robert C Tasker, MD, FRCP, Professor of Neurology and Anaesthesia (Pediatrics), Harvard Medical School; Chair in Neurocritical Care, Boston Children's Hospital, 300 Longwood Avenue, Bader 627, Boston, MA 02115, USA. Tel: +1 617 355 3508; fax: +1 617 730 0453; Robert.tasker@childrens.harvard.edu.

Conflicts of interest

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standards of care and developments in treatment for the muscular dystrophies (MD). What has been a key factor to the progress in this particular field has been the identification of the genetic basis for the most common forms of MD. These discoveries have resulted in an unexpected expansion of the clinical spectrum of several variants, an improved understanding of disease progression, and a molecular mechanistic approach to genetic therapies.

Our hope is that this issue of *Current Opinion in Pediatrics* covers the necessary background to understand the current drive towards novel therapies in pediatric neuromuscular disorders. It is an exciting time. After decades of advances in the characterization of genetic and molecular mechanisms we now have intervention clinical trials underway in children with SMA and the MDs. However, although randomized-controlled trials in these rare disorders should be the ultimate goal of clinical researchers in the wider field of pediatric neuromuscular disease, progress still relies on natural history studies. For example, the international GBS outcome study is currently examining the clinical, neurophysiologic, therapeutic, pharmacokinetic, immunologic and genetic features in at least 1000 children and adults with GBS [3, 6]. The aims are to better define the natural history of GBS and its variants and to establish outcome measures by which to assess the efficacy of new and future treatments.

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