



Neurology at the crossroads

Advances in neurology over the past 15 years have transformed the treatment of a number of conditions but have also raised new questions and challenges.

“ key opinion leaders explore subspecialties of neurology in which a turning point has been reached ”

Since the launch of our journal as *Nature Clinical Practice Neurology* back in 2005, we have witnessed substantial progress in several areas of neurology, including disease-modifying drugs for multiple sclerosis (MS), thrombolysis and thrombectomy for acute ischaemic stroke and, most recently, genetic therapies for spinal muscular atrophy (SMA). As we highlight in this 15th anniversary issue, these advances have raised new questions and challenges that will need to be addressed in the future.

In a specially commissioned series of Comment articles on the overarching theme ‘neurology at the crossroads’, key opinion leaders explore subspecialties of neurology in which a turning point has been reached, for example, in light of the success of a new therapy or the failure of a specific approach. The authors of each article were asked to consider how these pivotal events might necessitate a change in thinking to move the field forward.

Alan Thompson and Olga Ciccarelli acknowledge the rapid expansion of treatment options for relapsing–remitting forms of MS over the past few years, and they propose that we now need to turn our attention to tackling progressive MS¹. This endeavour will require a better understanding of the mechanisms underlying MS progression and the development of biomarkers to identify patients who are entering the progressive phase of the disease.

The introduction of mechanical thrombectomy for the treatment of acute ischaemic stroke is enabling recanalization of the occluded vessel to be achieved in an increasing number of patients. However, as Guido Stoll and Mirko Pham point out in their Comment article², many individuals still experience poor outcomes owing to factors such as delays in treatment initiation, and ischaemia–reperfusion injury following recanalization. The authors suggest that these issues could be addressed through a combination of traditional neuroprotective strategies and novel therapies.

The approval of the antisense oligonucleotide nusinersen is transforming SMA from a lethal to a treatable disease. Michelle Farrar and Matthew Kiernan consider how this rapidly evolving clinical landscape is uncovering health-care disparities and provoking debate regarding drug pricing³, as well as creating new challenges for the long-term management of individuals with SMA.

As the remaining two Comment articles illustrate, not all changes of direction in the neurology field have been fuelled by success. Michael Rafii and Paul Aisen⁴ highlight the persistent failure of anti-amyloid therapies for Alzheimer disease (AD), which has led to suggestions from some quarters to abandon this approach and investigate new therapeutic targets, such as tau pathology. However, the authors argue that earlier intervention and better trial designs could still enable amyloid-targeting therapies to fulfil their potential.

The past three decades have seen the development of a plethora of antiepileptic drugs, yet the incidence of pharmacoresistant epilepsy has remained largely unchanged. In his Comment article⁵, Holger Lerche discusses the prospect of novel treatment approaches that target the underlying epileptogenic mechanisms rather than individual seizures.

The anniversary issue is accompanied by an online collection containing some of our most-cited articles from the past 15 years, including a Review by Martin Bendszus and Guido Stoll from the very first issue. Bringing the field right up to date, the issue also includes two Perspectives on the neurological consequences of COVID-19 — an important emerging area of research that we will continue to follow closely.

The rapid proliferation of scientific data during the current pandemic has underlined the importance of monitoring and filtering the literature to provide timely and accurate information, and the *Nature Reviews* journals have a vital part to play in this ongoing effort. We would like to take this opportunity to thank the editorial and production staff, authors, peer reviewers and journal advisors who have contributed to the journal over the past 15 years, and we look forward to providing a valuable service to our authors and readers for many years to come.

1. Thompson, A. & Ciccarelli, O. Towards treating progressive multiple sclerosis. *Nat. Rev. Neurol.* <https://doi.org/10.1038/s41582-020-00421-4> (2020).
2. Stoll, G. & Pham, M. Beyond recanalization — a call for action in acute stroke. *Nat. Rev. Neurol.* <https://doi.org/10.1038/s41582-020-00417-0> (2020).
3. Farrar, M. A. & Kiernan, M. C. Spinal muscular atrophy — the dawning of a new era. *Nat. Rev. Neurol.* <https://doi.org/10.1038/s41582-020-00410-7> (2020).
4. Author, A., Rafii, M. S. & Aisen, P. S. The search for Alzheimer disease therapeutics — same targets, better trials? *Nat. Rev. Neurol.* <https://doi.org/10.1038/s41582-020-00414-3> (2020).
5. Lerche, H. Drug-resistant epilepsy — time to target mechanisms. *Nat. Rev. Neurol.* <https://doi.org/10.1038/s41582-020-00419-y> (2020).