EDITORIAL

Advanced Therapies for Movement Disorders in Neurotherapeutics

The field of movement disorders has undergone remarkable progress in recent years, with considerable advancement in the understanding of the basic neurobiology of these disorders, as well as in the development of therapeutic approaches. This issue of the Journal covers a wide spectrum of therapeutic approaches, from symptomatic, neuroprotective and restorative therapies to deep brain stimulation (DBS) surgery. The major disorders, Parkinson's and Huntington's disease, dystonia and tremor, as well as Tourette's syndrome, are discussed by notable experts in the field. The reviews provide not only an update on the current topics, but also a critical look at shortcomings and future directions.

Although progress in the development of new symptomatic agents for Parkinson's disease has been measurable and continues to move forward (Factor, pp. 164–180), that has not been the case for the other major disorders. In Huntington's disease, despite significant investment, advances have been disappointing (Adam and Jankovic, pp. 181–197), and in dystonia, no new drugs have been introduced since the botulinum toxins were first developed in the 1980s. This is due, in part, to the lack of funding and to the recent burst of genetic and molecular breakthroughs. Nonetheless, novel symptomatic approaches for dystonia appear to be on the near horizon, as reviewed by Jinnah and Hess (pp. 198–209). Although neuroprotective trials have largely met with failure in Parkinson's and Huntington's disease, the reviews of LeWitt and Taylor (pp. 210–225) and Hersch and Rosas (pp. 226–236), respectively, provide a view of the issues related to trial design and the previously tested drugs and the promise of future agents. Although progress in the fields of cellular therapy, trophic factors, and gene therapy has met with major setbacks in recent clinical trials (Peterson and Nutt, pp. 270–280; Mochizuki, Yasuda, and Mouradian, pp. 260–269), work on stem cells and Spherramine show promise, as reviewed by Newman and Bakay (pp. 237–251) and Stover and Watts (pp. 252–259), respectively.

By contrast, advances in the development and application of surgical approaches, such as deep brain stimulation, have been rapid and impressive. The field of DBS has witnessed rapid growth since its initial use for tremor (Lyons and Pahwa, pp. 331–338) and Parkinson's disease (Limousin and Martinez-Torres, pp. 309–319). This is particularly true in successful application of DBS to increasing numbers of movement disorders, such as dystonia (Ostrem

and Starr, pp. 320–330) and Tourette's syndrome (Ackermans, Temel, and Visser-Vandewalle, pp. 339–344). In addition, the identification of novel targets and progress in the understanding of the mechanism of action of electrical stimulation and the effects of different stimulation parameters has been far reaching.

Although controversy and uncertainty remain as to the mechanism of action of DBS, Johnson, Miocinovic, McIntyre, and Vitek (pp. 294–308) provide an up-to-date review of the topic. DBS, thought at first to act simply like a lesion, because the clinical effects of high-frequency stimulation and ablation are so similar, is now viewed as the product of a mixture of local and remote effects, depending on the target location, of which the most relevant appears to be the regular activation of local output axons at high frequency. This effectively replaces and overrides the abnormal activity locally and downstream throughout the basal ganglia–thalamocortical circuits. The review by Gross (pp. 281–293) on the field of ablation for movement disorders asks the important question, “What happened to posteroventral pallidotomy for Parkinson's disease and dystonia?” Pallidotomy and other ablative procedures have been almost completely replaced by DBS in the developed world, not because DBS is necessarily more effective, but for other reasons. Nonetheless, ablative procedures remain the only viable approach for much of the world, because of economic and personnel shortcomings. It is fair to say that research on ablative procedures has been neglected and largely abandoned—perhaps prematurely. Finally a review of noninvasive brain stimulation for movement disorders (Wu, Fregni, Simon, Deblieck, and Pascual-Leone, pp. 345–361), largely transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (TDCS), offers insight into this promising, if still largely experimental, field.

Clearly, this issue covers many of the important and most dynamic topics in movement disorders. We believe you will find these reviews not only timely but informative and stimulating. We thank the reviewers for their generous efforts and the editorial staff for their help and patience.

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