

NIH Funding for Research on Headache Disorders: Does It Matter?

Migraine disorders and the epilepsies have much in common. Both are highly prevalent paroxysmal neurological disorders that have peak incidence prior to adulthood and may be life-long. They are also often co-morbid. Both appear to share important pathogenic mechanisms involving the same genes and electrophysiological events, and they are often responsive to the same medications.¹ Both are associated with huge economic costs and profound disabilities. While prolonged seizures may be fatal, the far higher prevalence of migraine leads to >85% more lost years annually from death or disability than the epilepsies.²

Given the close parallels between these disorders, why then, over the past 15 years, have 10 new medications been FDA-approved for the treatment of epilepsy, whereas only 1 new medication (plus 6 “me-too” drugs) has been approved for migraine (Table)? One possibility is that research efforts have been similarly aggressive for both groups of disorders but that comparatively more migraine trials failed. It is also conceivable that fewer headache clinical trials were performed due to a lack of interest on the part of the pharmaceutical industry, though this is unlikely given the enormous size of the migraine market. Regardless, these possibilities are beyond investigation given the absence of a comprehensive national registry of clinical trials. There is, however, a much more plausible and simple explanation for the discrepancy in drug approvals: there were fewer promising compounds available to test in migraine clinical trials. Why might this be so?

Abundant evidence shows that the seminal studies that lead to innovative pharmaceuticals are most often performed in publicly funded research laboratories, not those of the pharmaceutical industry.³ Federal funding of research on epilepsy has always hugely out-

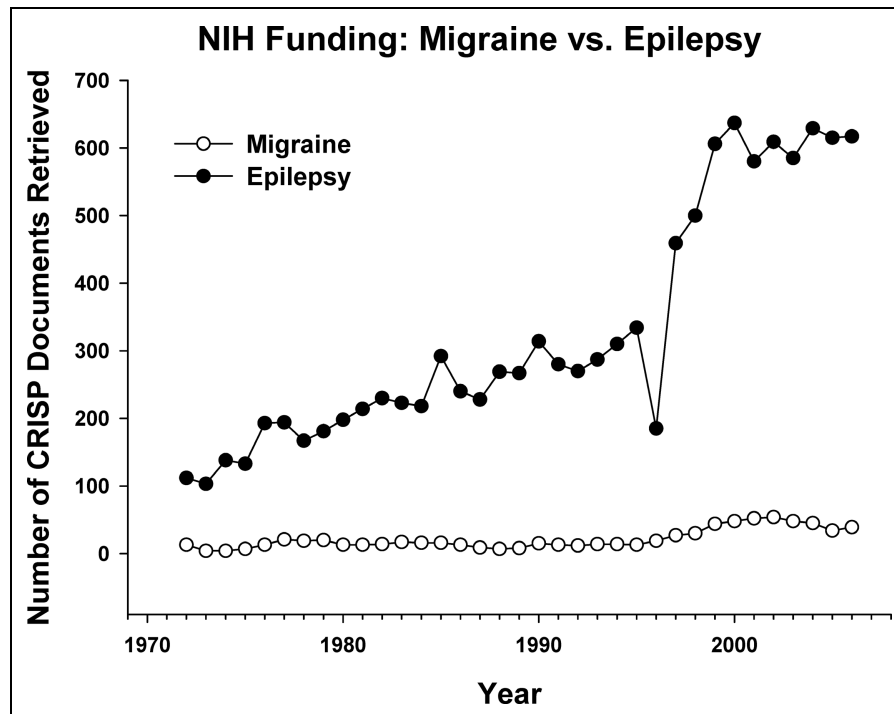
paced that for migraine. Over the past several years, mean annual NIH expenditures for epilepsy have been ~\$101M⁴ compared to ~\$13M⁵ for migraine, with a comparable disparity in funding every year since 1972 — the earliest year of available records for NIH grants (Figure).

What did the federal funding for epilepsy purchase? Fundamental research beginning in the 1970s led to the development of epilepsy animal models that enabled the screening of drugs for anticonvulsant properties. The NIH then funded and provided oversight of a program of accelerated screening of

Table—New Molecular Entities Approved by the FDA Since 1992 by Indication

	Priority Review	Standard Review
Epilepsy	Felbamate 1993 Gabapentin 1993 Lamotrigine 1994 Pregabalin 2004	Fosphenytoin 1996 Topiramate 1996 Tiagabine 1997 Levetiracetam 1999 Oxcarbazepine 2000 Zonisamide 2000
Migraine	Sumatriptan 1992	Zolmitriptan 1997 Naratriptan 1998 Rizatriptan 1998 Almotriptan 2001 Frovatriptan 2001 Eletriptan 2002

An NME is defined as a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act. A priority review by the FDA is accorded drugs that are believed to represent a significant improvement compared to marketed products, in the treatment, diagnosis, or prevention of a disease. A standard review by the FDA is accorded drugs that appear to have therapeutic qualities similar to those of 1 or more already marketed drugs.



Figure—NIH funding for migraine versus epilepsy. The relative funding for each disorder is obtained by comparing the number of documents retrieved for the keywords “migraine” and “epilepsy” from the Computer Retrieval of Information on Scientific Projects (CRISP)⁸ database of U.S. federally funded biomedical research projects. CRISP includes a document for every year of every federally funded (mostly NIH) biomedical research grant, and an analysis of the relative number of CRISP documents provides an approximation of the relative weight of U.S. federal funding for each disorder.

compounds developed by academia and industry.⁶ Thirty years later, patients with epilepsy have a considerably wider set of therapeutic options.

Headache medicine is also on the threshold of new insights into the pathogenesis of the primary headache disorders. Animal models relevant to drug screening are beginning to appear.⁷ What is needed now is a commitment to headache medicine from federal agencies similar to that which has been appropriately extended to epilepsy. Headache medicine requires and deserves a 7.5-fold increase in NIH funding to bring it to parity with the epilepsies. Such a funding boost would dramatically increase the number of laboratories in this field and ensure the training of an expanded generation of dedicated clinician-investigators. Moreover, newly funded laboratories would be welcomed into academic neurology departments where they would provide visibility for headache medicine and a nidus for headache specialty clinical training programs. Based on the example of the epilepsies, real benefits will likely be felt by headache patients over time in

the form of improved access to specialty care and the development of novel effective therapies.

No one should expect the NIH to spontaneously increase headache research funding to >\$100M annually. Any such funding increase will be the hard-won consequence of vigorous and persistent advocacy on the part of the community of headache medicine specialists and headache disorder patients. As a part of this process, we are developing a program to bring this issue to the close attention of federal lawmakers. We are working to mobilize headache patients to advocate for their interests. Furthermore, on September 25 and 26, 2007, headache medicine clinicians from across the country will participate in an event in Washington, DC, that we call “Headache on the Hill.” At that time, we will meet with our Senators and Representatives and press them to take Congressional action to increase NIH funding. We welcome, and strongly urge, all U.S. headache specialists to join us. The success of this initiative depends on large numbers of participants coming from widespread Congressional districts. For

information on participation in this event, please email me at robert.shapiro@uvm.edu.

The lack of NIH funding for headache research is an injustice that receives no media attention. Its repercussions limit the therapeutic options and hope for women who suffer in greater numbers from migraine or chronic daily headache, as well as for men who may preferentially suffer from cluster headache or posttraumatic headache. The NIH is mandated to improve the health and welfare of all Americans, however, its expenditures do not reflect the societal distribution of disease-related economic costs and disabilities. Disabled headache patients have been denied equal access to the benefits of publicly funded research. Redress of this inequity should have a transformative beneficial effect on the practice of headache medicine.

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