

## EDITORIAL

# The long drought: the dearth of public funding for headache research

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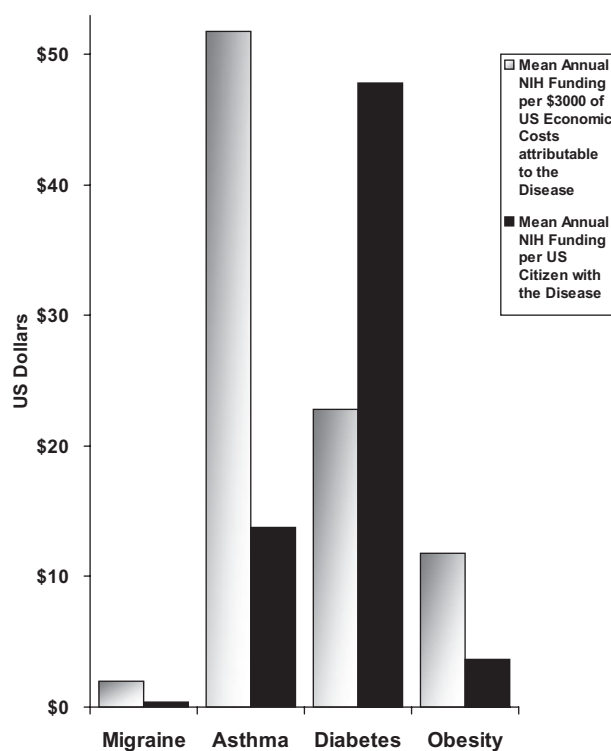
Headache disorders are the most prevalent of neurological conditions, and migraine is the most prevalent disabling neurological condition (1). Migraine affects 12% and chronic daily headache 4% of Europeans and Americans (2, 3); these disorders also predominantly afflict women during their peak years of productivity. Headache disorders account for ~9% of total lost labour productivity (>\$20 billion) (4, 5) and ~1% of total disability (6) in the United States annually. Severe migraine attacks are classified by the World Health Organization as among the most disabling illnesses, comparable to dementia, quadriplegia and active psychosis (7). Given the high global prevalence, enormous societal costs and substantial disability and suffering, one might assume that the alleviation of migraine and other headache disorders would be a major priority for the public research agencies of developed nations. Unfortunately, nothing could be further from the truth.

In this issue of *Cephalalgia*, Olesen and coworkers (8) quantify for the first time the neglect of migraine among European public research funding agencies. Their data are stark: migraine is the least publicly funded of all neurological illnesses relative to its economic impact. Moreover, these authors found that anxiety and affective disorders, two of the most prevalent categories of disorders comorbid with migraine, rank nearly as low as migraine in European public research funding priorities relative to economic impact. The cumulative effect of these funding decisions is to deny migraineurs the promise of research developments to change the courses of their illnesses.

The lack of public research support for migraine is not limited to European grant-giving agencies. The problem is equally profound in the USA. Although the precise dollar amounts of migraine-related National Institutes of Health (NIH) research grants have not been reported, the Computer Retrieval of Information on Scientific Projects (CRISP) database of US federally funded biomedical research projects can be used to infer abysmal

funding levels. CRISP includes a document for every year of every federally funded (mostly NIH) biomedical research grant. Analysis of the relative number of CRISP documents for prevalent chronic disorders provides an approximation of the relative weight of US federal funding for each disorder. The results are striking (Figure 1 and Table 1).

A comparison of the number of CRISP documents (9) with actual NIH funding levels (10) for several disorders leads to an estimate of the mean annual federal funding for migraine research at ~\$13M. This sum comprises <0.05% of the total current NIH budget of ~\$28B. By comparison, ~21 times more NIH research funding is devoted to



**Figure 1** NIH funding by disease (migraine, asthma, diabetes mellitus, obesity) relative to disease-attributable economic costs and population prevalence during FY2003 through FY2006.

**Table 1**

CRISP database keyword	CRISP (9) documents retrieved per keyword over FY2003–FY2006 (search date 13 June 2007) (no. of documents)	Mean annual NIH research funding over FY2003–FY2006 (US\$ millions)	US annual economic costs due to disorder (US\$ billions)	Mean annual NIH research funding per \$3000 of US annual economic costs due to disorder (US\$)	US annual population prevalence per disorder (millions of patients)	Mean annual NIH research funding per patient with disorder (US\$)
Migraine	166	\$13M*	\$20B (4)	\$1.95	36M (1)	\$0.36
Asthma	3 835	\$276M (10)	\$16B (18)	\$51.75	20M (19)	\$13.80
Diabetes	11 866	\$1004M (10)	\$132B (20)	\$22.82	21M (21)	\$47.81
Obesity	6 338	\$460M (10)	\$117B (22)	\$11.80	127M (23)	\$3.62

\*Mean annual NIH research funding for migraine (\$13M) is estimated by multiplying the number of Computer Retrieval of Information on Scientific Projects (CRISP) documents for migraine for FY2003–2006 (166 documents) by the estimated mean funding per document (\$0.318M) over that same time period, then dividing that product by four (for the years of reporting). The estimated mean funding per document was calculated by dividing the total NIH research funding for asthma, diabetes and obesity combined for FY2003–2006 (\$7005M (10)) by the total number of CRISP documents for the same disorders over the same period (22 039 documents).

asthma than to migraine. Normalizing these data for economic impact, the annual costs attributable to each disease relative to research expenditures are ~27 times greater for migraine compared with asthma. Normalizing these data for population prevalence, the research funding per affected patient is ~37 times less for migraine compared with asthma.

A similar analysis (11) has been reported for relative NIH funding when accounting for disease-related disability. The number of investigator-initiated ('RO1') NIH research grants retrieved from CRISP was compared with the global death and disability burden of diseases, as measured in 'disability adjusted life-years' (DALYs). This disability-sensitive analysis demonstrated a comparably meagre level of research support for migraine relative to other disorders. For example, asthma research receives ~11 times more NIH funding than migraine, after these data are normalized for rates of global disease-associated death and disability.

What has caused this world-wide institutional neglect of migraine? Many factors probably contribute, but foremost must be that migraine is commonly trivialized in western societies as 'just a headache'. The near-universal prevalence of occasional mild headaches (>95% life-time population prevalence for any kind of headache (1)) probably leads to the discounting of complaints of severe disabling headaches by many individuals who have not experienced them. Migraineurs who report pain or other disabling symptoms may be regarded as malingering, unreliable, or simply weak. Such stigmatization may threaten their employability or the stability of their interpersonal relationships. It is understandable therefore that migraineurs typically avoid public acknowledgement of attacks, and are loath to engage in public advocacy on behalf of themselves and fellow sufferers.

Unfortunately, the healthcare community has been a fundamental enabler of the problem. The misconception of migraine as 'misbehaviour' probably arose and was hardened during the first half of the last century. At that time, physicians were rarely women and physician residency training programmes, particularly in the USA, were, and often remain, arduous rites-of-passage incorporating recurrent sleep deprivation. It is unsurprising therefore that male physicians, inured to deny their own pain, grew to dismiss the seriousness of pain complaints of female migraineurs, who notably had no abnormal findings on physical examination.

For whatever reason, neurologists continue to take little interest in headache disorders. Although headache is currently the primary clinical focus area for more than half of American neurologists (12), most academic neurology departments in the USA do not have a dedicated headache specialist on faculty (13). The American Academy of Neurology currently includes ~20 000 members, but only ~1000 neurologists are currently members of the American Headache Society, where they comprise only ~60% of its membership (14).

The consequence of this historical lack of interest has been a medical culture that discourages research in headache disorders. The NIH currently has no institute, centre, or even research study section, wholly devoted to pain research, let alone headache disorders. The NIH rarely sets headache research as a priority in the form of Program Announcements and Request for Applications (15), and has consistently omitted migraine from its annual reports of disease-specific expenditures (10). The net result of this disregard has been that few high-quality grants are submitted to NIH on headache disorders and those that are submitted may be reviewed by individuals with little expertise or interest in the questions to be investigated. In this climate, why would a seasoned investigator expend vast time and energy writing an RO1 proposal on migraine when the chances of initial funding are so marginal?

Predictably, fundamental research developments on headache disorders are infrequently reported or published in major medical forums. Of 14 229 presentations at the 2006 annual meeting of the Society for Neuroscience (16), only 22 were related to headache disorders. High-impact general medical journals (e.g. *Journal of the American Medical Association*, *New England Journal of Medicine*) publish almost nine times as many articles on asthma as on migraine (11). Without exposure to quality studies, how would an investigator come to appreciate headache disorders as neurobiological problems worthy of research in the first place? Inadequate public funding for headache research leads to a vicious cycle of near invisibility in the medical literature and then to scarce quality grant proposals submitted to NIH.

A significant increase in NIH funding for headache research is urgently needed. Based on the CRISP analyses above, we estimate that a phased 7.5-fold increase in NIH research funding on headache disorders to ~\$100M annually would be appropriate to their economic impact. This increased funding is necessary to begin to redress the >\$20B

annual lost US labour as a result of headache. An increase in research expenditure for headache should not be borne at the expense of worthy research funding for other diseases. Furthermore, these funds must be sustained at this level for at least a decade to have any chance of encouraging new investigators to train in this field or persuading established neuroscientists and clinician-scientists to enter and remain in this field. Once again, unless there are reasonable assurances that grant renewal would be feasible, what established investigator would take a chance and direct their laboratory towards the study of headache disorders?

What benefits might be expected from a substantial infusion of public research funding? Simply put, it could be transformative for the field of headache medicine. An increase in NIH funding to \$100M annually might fund 200 or more new research laboratories, a dozen clinician-scientist development awards (e.g. 'K' awards), as well as translational and collaborative clinical trials. New techniques and approaches currently developing in other areas of fundamental neuroscience could be brought to bear on the pathophysiologies of the primary headache disorders. With new public funding, the research domain of headache would become less dominated by, and beholden to, the influence of the pharmaceutical and device industries, as documented for Europe by Olesen et al. (8). Moreover, abundant evidence points to publicly funded research studies, rather than the efforts of the pharmaceutical industry, as the primary source of innovative medical therapies (17). An infusion of new publicly funded investigators would be welcomed into neurology department faculties, where they would broadly increase the profile of headache medicine, become the foci of new headache fellowship programmes and result in the training of an expanded new generation of headache specialists. In short, increased NIH and other public funding should lead to marked improvements in patient access to headache specialty care and an acceleration of the development of new therapies for headache disorders.

The US Congress has declared 2001 to 2010 as the Decade of Pain Control and Research, yet, more than halfway through this decade, nothing substantive has been accomplished regarding the wide gap in research, teaching and education for all pain disorders, including headache. A consortium of US pain care professional organizations, the Pain Care Coalition, has strongly supported the passage of Congressional legislation to expand research into

pain disorders. Unfortunately, this considerable effort has been met by even greater resistance and has achieved limited success to date.

It is imperative that headache patients and headache medicine specialists join in pressing legislators for full public funding for research into headache disorders. Public grant-giving agencies on both sides of the Atlantic inadequately consider disease-related disability and economic burden in defining their research funding priorities. Equal access to the benefits of publicly funded medical research is a civil right that has long been denied headache patients.

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