Brain Foundation – Essay on the neurological disorder of migraine

Migraine is a debilitating neurological disorder, characterised by recurrent headache and associated with nausea and/or vomiting, photophobia and phonophobia. The prevalence of migraine varies between different racial groups but is highest in Caucasian populations (12-14%). The International Headache Society (IHS) has formally classified migraine into two main subtypes; migraine *with aura* (MA) and migraine *without aura* (MO). These subtypes have substantial symptomatic overlap, but MA sufferers also experience distinguishing neurological disturbances that usually precede the headache phase of an attack [Headache Classification Committee, IHS, 2004]. Pharmaceutical treatments for migraine show variable usefulness and there are no laboratory-based diagnostic tests. The underlying pathological mechanisms for migraine also remain poorly understood, however, family and twin studies suggest a significant genetic component for migraine. Although a number of genes involved in a rare severe form of migraine, termed familial hemiplegic migraine, have now been identified, the number and identity of genes that are involved in the more common types of migraine are yet to be defined. Our Genomics Research Centre has been involved in migraine molecular genetic studies for a number of years with our laboratory mapping the first migraine susceptibility locus in 1998 [Nyholt et al, 1998a]. We have subsequently mapped other migraine genomic regions [Nyholt et al 1998b, Lea et al, 2002] and implicated a number of genetic variants in the disorder [Lea et al 2009, Colson et al 2004, Colson et al 2005 and Lafraniere et al 2010]. We have also assembled a very significant migraine cohort for our DNA studies, with many migraine multigenerational families and migraine cases.

Significance of Migraine

Migraine is a painful and incapacitating neurological disorder for which there is currently no cure. Characteristic clinical features of migraine include throbbing headpain, nausea, vomiting, photophobia and often severe, neurological disturbances. In predisposed individuals migraine attacks can be triggered by specific environmental factors, such as particular foods and smells, fluctuating hormonal levels and fatigue. The disorder is very common with results of a large epidemiological survey conducted in the US showing greater prevalence of migraine in females compared to males (18.2%:6.5%) [Lipton et al, 2001]. These findings combined with other similar studies worldwide, established the overall prevalence of migraine in the general Caucasian population as around 12%. Migraine can impose a severe personal burden on sufferers and their families. During a migraine attack all areas of a patient's life (work, home and leisure) can be considerably disrupted. The disease also incurs substantial economic costs on society. A national health survey by the Australian Bureau of Statistics suggested that the total cost of migraine to the Australian community could be as high as $721 million per year. Most of this annual financial burden is thought to stem from lost productivity at work due to total absenteeism and/or reduced occupational effectiveness. The costs associated with healthcare utilization are also sizable, with millions being spent on medical consultation, hospital beds and drug treatment.

Diagnosis and Pathophysiology

Migraine is clinically diagnosed based on criteria specified by the International Headache Society (IHS), with MO and MA sufferers accounting for ~70% and 20-30% of migraineurs, respectively There are a number of other less common types or sub-types of migraine that are accompanied by distinctive neurological symptoms, including retinal migraine, in which unilateral visual disorders, which may involve temporary blindness, occur with or without headache; and familial hemiplegic migraine, in which headache is accompanied by prolonged weakness to one side of body. The pathophysiology of migraine is not completely

understood. For MA, a dramatic reduction in cerebral blood flow has been associated with a depolarisation wave that propagates across the brain cortex (cortical spreading depression. The characteristic head pain that is common to both MA and MO may arise due to dilation of cerebral blood vessels following activation of the trigeminovascular system, which may be activated by the cortical spreading depression. Therefore, biochemical factors that have the potential to disrupt vascular endothelial function and cerebral blood flow, are important targets for involvement in migraine susceptibility.

The Genetic Basis of Migraine

Migraine shows a significant genetic component with the overall risk to relatives of affected individuals estimated to be at least twice that of the general population depending on the type of migraine. The mode of inheritance of the common forms of the disorder is not clear but is most likely multifactorial involving multiple genes as well as environmental triggers. Thus, migraine can be considered a complex disease with the susceptibility probably governed by multiple genes, as well as environmental predictors. Moreover, it is likely that these factors combine together to contribute an interactive effect on the disease.

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