A genetic test for Alzheimer's disease?

*Simon Lovestone and Peter Harper**

Recent years have seen considerable progress in understanding the genetic basis of many diseases. There has also been a welcome and informed public debate regarding the ethical and social implications of genetic research, including predictive testing of adult onset illnesses. The UK Huntington's Prediction Consortium, a forum open to scientists, clinicians and representives from patient organisations, has established protocols for testing and has facilitated development of clinical genetic services. It has been suggested that the Huntington's disease experience might prove informative for other conditions, and a meeting was held on 5 January 1994 at the Institute of Psychiatry, London, to discuss recent research findings and possible genetic testing in Alzheimer's disease (AD). Professionals from a number of disciplines took part along with representatives of the Alzheimer's Disease Society. It was decided to form a consortium that would meet regularly and produce guidelines for future clinical applications of possible genetic tests.

It has long been recognised that some early onset forms of AD are inherited in a dominant pattern. For some of these very rare families a mutation has been found in the APP gene on chromosome 21 and others have shown linkage to chromosome 14. Other families with early onset AD show no linkage to these loci. Late onset AD more often occurs as a sporadic non-familial form and yet the risk to relatives of patients with late onset AD is considerably greater than the general population risk. Recently an association with the apolipoprotein E & 4 allele on chromosome 19 has been demonstrated in both familial and apparently non-familial cases, raising the possibility of the development of predictive or diagnostic testing.

Discovering the genetic factors involved in AD is potentially one of the most important advances in the understanding of this devastating disorder. The potential for predictive testing of AD does, however, raise ethical concerns – some of which also apply to Huntington's disease. These include the possibility of psychological problems following testing and the ethical problems relating to use of the information by other agencies. The implications of testing for AD differ from Huntington's disease in several important aspects. AD is a common disorder, suggesting that the demand for testing might be greater than for any other genetic disorder. Unlike Huntington's disease, genetic testing for AD is more likely to indicate susceptibility to the disorder, rather than the certainty of developing it. Another important difference is that the prospect of treatment for AD is closer, with many agents being tested in clinical trials. However the introduction of testing should be in a controlled and carefully considered manner. Development of consensus strategies and clinical protocols will ensure that adequate safeguards are established and the needs of patients and their families are met.

The UK Alzheimer's Disease Genetics Consortium has considered the evidence to date on the genetic factors involved in Alzheimer's disease. For the very small proportion of Alzheimer's disease showing a clear familial pattern and with a recognisable genetic mutation, presymptomatic testing of those at risk is now feasible, but should only be undertaken in the framework of appropriate counselling and support, comparable to that already used for disorders such as Huntington's disease. The great majority of Alzheimer type dementia cases, particularly those of late onset, do not show a clear pattern of inheritance; despite the recent research findings, no genetic test currently exists that can diagnose the condition in patients or predict the occurrence of Alzheimer's disease in relatives.

There is time now to develop guidelines and protocols for the introduction for clinically appropriate scientifically rigorous and ethically sensitive genetic testing of this prevalent disease. The Alzheimer's Disease Genetics Consortium will be considering these issues and will welcome contributions from all interested parties.

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