Mental disorders and genetics: the ethical context

Preface

By Professor Lewis Wolpert
Professor of Biology as Applied to Medicine,
University College, London
While the main aim of this new preface was to provide information on developments in the field since the report was published, there has not been a significant change in the ethical views and while I will discuss some relevant scientific advances I also want to take the opportunity to make some comments, some critical, on the original report.

Two major scientific advances have been made since the report was published in 1998. The human genome has been sequenced and there has been significant progress in the study of stem cells. Both of these are highly relevant to the genetics of mental disorders. Both might have been anticipated but the report, disappointingly, gave little attention to the science underlying mental disorders. I do not think the neurons whose behaviour is fundamental to brain and whose behaviour, in turn, is highly influenced by genes, are ever mentioned in the report. It thus fails to make clear that it is during development of the fertilised egg in the womb that our body form and brain are specified. Genes are the main determinants of all of our bodily functions and forms from the shape of our noses to our height. The brain is no exception. The way we behave is determined by our brains and the function of the brain is determined by the billions of cells, especially neurons, that are its key constituents. Genes act by controlling almost all aspects of brain development.

The report emphasises that the whole human be viewed as a person, and in doing so may have neglected to explain just how genes affect all aspects of our life, not least our behaviour. They thus have leaned somewhat towards a holistic anti-reductionist view of human psychology and made no attempt to respond to the anti-reductionist approach which even goes so far as to oppose genetic research into mental disorders. I would argue that all of science is essentially reductionist. In failing to make this clear they may have done bad service to genetics, developmental biology and neuroscience. Thus even when the report discusses the key issue of heritability that estimates how much variation is due to genetic factors and how much due to the environment, the actual figures are placed in an appendix. Admittedly these numbers may be somewhat controversial, but they do suggest that for depression, at least half of the cause is due to genes, for manic depression even more so, and for schizophrenia, around 70%.

But genes are themselves rather dull and they are within the cell essentially passive as their function is to provide the code both for making proteins and for providing a programme for where and when in the developing embryo these proteins should be made. They function in a similar manner in the adult. It is proteins that are the true wizards and workhorses in the cell. It is proteins that allow nerves to conduct their impulses and that ensure that during development the correct connections are made. A faulty gene - due to a mutation - can thus lead to abnormal brain development and thus predispose an individual to a mental disorder. Environmental factors can, however, influence development in the womb and so the brain, and thus can play a key role in whether or not the mental disorder actually occurs. People need to be explained these basic facts and there is nothing to be ashamed of in having a genetic predisposition to mental illness any more than any other illness from cancer to heart disease. Regrets, but no shame.

Yet the report quotes with apparent approval, a statement that supports the view that one cannot distinguish the effects of genes and the environment since they are so intimately connected. This view claims that the ‘effect of a gene being activated will depend on the state of the rest of the developmental system.’ This is simply false as far embryonic development is concerned. Gene activation in a cell during development - hormones apart - depends on signals from cells only a few tens of cells away. It is a key principle in the developing embryo that early on different regions are specified and then develop autonomously.
The decoding of the human genome opens up exciting new possibilities for understanding the genetics of mental disorders. There is good evidence that many genes are involved in the predisposition or development of a mental illness. Identifying these genes has been and still is complex and difficult but access to the human genome greatly facilitates the research. However even though knowing the genome tells us what genes we have it does not at this stage enable us to know their role and when and where they are turned on in our development and in the adult. This is a formidable task for the future.

There have been in the last couple of years significant advances in understanding the genetic basis of neurodegenerative diseases including Parkinson’s. Also progress is being made in designing drugs to help with Huntington’s - the protein has been identified and attempts are being made to prevent it aggregating.

It is not only the underlying genetics of the disorder that matter but the response of individuals to drugs used to treat mental illness. There are, for example, a large number of anti-depressants available, and none are significantly different in their effectiveness. They help about one-third of those treated but their side effects vary a lot. It is believed that the response is most likely to be genetically determined and thus genetic analysis of patients could identify the appropriate drug for a particular individual.

Stem cells are receiving a great deal of attention. These are cells which can differentiate into a wide variety of different cell types including neurons. There is thus hope that grafting such cells into particular regions of the brain could be a valuable therapeutic approach. Again, understanding the genetic basis of a mental disorder will greatly help designing and modifying stem cells. There are claimed to be ethical issues when stem cells are obtained from human embryos but individual life does not begin with fertilisation of the egg and thus it should not be used as an argument against creating embryonic stem cells. Human reproduction by IVF involves the fertilisation of the egg and the early development of the embryo and large numbers of such embryos are destroyed. There is thus no ethical difference between IVF and creating stem cells as both require the creation and destruction of embryos. One can be, for religious reasons against both, but not against one and not the other. IVF has been of enormous value to couples with some reproductive problems and so too, it is predicted, will stem cells in relation to providing cells for grafting into the brain to cure genetic disorders.

The problem of stigma in relation to mental illness has been receiving increasing attention and the Royal College of Psychiatry is making particular efforts in this direction and has launched its Changing Minds Stigma Campaign with a five-year strategy from 1998 to 2003. It is not clear to what extent having a genetic basis for a mental illness does affect stigmatisation. The report does not give this topic the detailed analysis it deserves as several of the so-called ethical issues reflect peoples’ attitude to mental illness and genetics. Is the diagnosis of a genetic basis for an illness so much less acceptable than for it to be due to an environmental cause? The report argues that patients who are told of the genetic basis for their illness may use this information to confirm their low opinion of themselves and decrease their motivation to get better. The evidence for this is not given and to not give such information to patients is to deny their right to have it should they want it. Doctors should tell the patients the truth if that is what they want. The report gives no attention to that most important principle - personal autonomy. They also fail to clearly illustrate why the ethical issues with mental problems are basically different from those of other illnesses like diabetes or heart disease. It would have been helpful for them to recommend research into the views of those with mental illness as to what their views about a genetic basis for the illness actually are.
Public education on the role of genetics should be a major aim. And should the public not be encouraged to donate their DNA and to take part in clinical trials as they and many others have and will benefit from such knowledge?