Mental disorders and genetics: the ethical context

Summary
**Introduction**

Mental disorders place a heavy burden on individual sufferers, on those who care for them and on society at large. Research into the genetics of mental disorders may lead to a range of potential benefits. It may add to our understanding of their underlying causes; improve diagnosis; enable the development of new drug-based or other treatments; and allow treatment to be tailored more accurately to individuals.

However, genetics and mental health are both areas which raise significant and sometimes distinctive ethical, social and legal concerns. This report examines the issues that arise when these fields come together, not only in the course of genetic research, but in the application of that research in clinical and non-clinical setting. As with other diseases, the development and course of most mental disorders are affected by a complex mixture of biological, psychological and social factors. The focus of the report on the genetics of mental disorders is not intended to imply that genetic research is the only, or even the most important, approach for understanding and treating mental disorders, or that it is the only one to raise ethical issues. The extent of current research into the genetics of mental disorders, however, suggests that it is timely to try and anticipate its consequences.

The report focuses on schizophrenia, a range of affective disorders, dementias, neurotic disorders and personality disorders. Many of these have complex causes, and any genetic influences are not well understood. So the report also draws on experience of relatively simple single gene disorders, such as phenylketonuria, Huntington's disease and fragile X syndrome.

**Ethical issues**

The Working Party adopted a broad ethical and humanistic perspective which considered two ethical requirements as basic: the limitation of harm and suffering to all humans and respect for human beings and human dignity.

Genetic disorders are distinctive because they affect not merely individuals (as do all diseases), or groups of unrelated persons (as with epidemics), but groups of related individuals. Genetic information about one individual may reveal either certain, or more commonly probabilistic, information about their relatives, including any future children. Yet genetic information can be obtained by testing or treating a single individual. Both individuals and their doctors will then have to decide whether sharing information with relatives to whom it pertains, or its non-disclosure, is the better course of action.

Even in cases where it is relatively clear whether disclosure or non-disclosure would better limit suffering, it is often difficult to decide which would better express respect for persons. Would withholding knowledge from relatives about the possibility that they too might have a genetic mutation that could lead to a disorder be acceptable? Relatives might use that information in making decisions about their lifestyle or their medical treatment, or about whether to have children. Would withholding information be a form of paternalism that denied them the possibility of making their own well-informed decisions? In that case, would respect for others require relatives or doctors to communicate what they knew about the results of genetic tests, or other genetic information? Or should genetic test results be treated as confidential to individuals, like other medical information? Can we think of a ‘right to know’ – or of a ‘right not to know’ – in purely individualistic terms in the case of genetic knowledge? Or does genetic knowledge challenge the basis of our usual individualistic understanding of medical confidentiality? Does respect for others require doctors or
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researchers to seek consent for genetic investigation from all who might be affected? Even if these questions can be resolved, and they are legal as well as ethical questions, showing proper respect for persons may make complex demands in seeking consent for investigation and treatment of genetic conditions.

The range of ethical issues raised by genetic information expands when the information concerns mental disorders. Some of these additional issues cluster around the notion of personal wellbeing, of how one views oneself and is viewed by others; others concern reproductive decisions and some arise from the fact that mental disorders are often stigmatised. Genetic information which might be used to diagnose, or suggest susceptibility to a mental disorder, might raise questions about an individual's ability to function as a whole person and about their personal relationships. It might also undermine or weaken a person's sense of integrity and well-being, even when they are not suffering from any manifest difficulty or disorder.

A second area in which information about genetic susceptibility to mental disorder might raise difficult questions is that of reproductive choice. Even in the absence of genetic information, reproductive decisions can be hard for people with mental disorders. For a few, rare single gene disorders, prenatal testing may provide definite information about the fetus; if information is both certain and adverse and the law permits it, termination is possible, and sometimes chosen. However, where genetic influences are slight (as for many mental disorders) and prenatal tests cannot provide accurate predictions, the relevance of genetic tests to reproductive decisions may also be slight. Nevertheless, concerns have been expressed that new genetic technologies could be used for eugenic purposes. The possibility that genetic information relevant to mental disorders might be misused to influence reproductive choices, or for other forms of genetic abuse, cannot be simply dismissed.

A third distinctive group of ethical problems raised by mental disorders is that those afflicted often have to suffer not only their disease, but also the associated stigma. Many mental disorders are a matter of shame for those affected and for their relatives and, far from attracting sympathy, are a source of avoidance, criticism or even of blame by others. It is important, therefore, to consider whether the availability of genetic information will increase or decrease the stigma associated with mental disorders, and whether fear of stigma will affect reproductive decisions.

What do genetic studies of mental disorder tell us?

Given that our understanding of normal brain function is still quite limited, it is not surprising that it has been very difficult to study the abnormal function of the brain in mental disorders. The attraction of genetics is that it enables functionally important components to be identified without any pre-existing knowledge of how the brain works. The Working Party noted, but did not accept, the concerns of some that genetic research into mental disorders is methodologically flawed. We would emphasise, however, that genetic research has so far yielded little practical help in limiting the suffering of those with mental disorder. The difficulty of identifying reproducible gene localisations in common mental disorders represents a key scientific discovery in its own right. It indicates that they are rarely, if ever, caused by simple dominant or recessive mutations analogous to Huntington's disease or phenylketonuria. This has crucial implications for clinical practice. However, methodology for genetic research is progressing rapidly and there seems little doubt that over the next ten years, susceptibility genes will be identified and some of these will hold up to robust scientific scrutiny.
Clinical applications

Classification and diagnosis

The discovery of gene mutations associated with single gene disorders has had profound implications for their diagnosis. But the Working Party concluded that genetic tests will not be particularly useful in diagnosing mental disorders with more complex causes. Similarly, it is unlikely that genetic tests will be useful in prenatal diagnosis or for general population screening for susceptibility to common mental disorders. It is more probable that identifying genes involved in susceptibility to common mental disorders will improve our understanding of abnormal processes and hence lead to the development of useful biochemical diagnostic tests.

Genetic counselling

Genetic counsellors will only be able to offer very precise figures about the risk of recurrence for a few single gene disorders such as Huntington’s disease. The Working Party concluded that it is essential that counsellors make clear to individuals the current limitations of scientific knowledge about the majority of mental disorders and, in particular, our limited understanding of the interaction of different environmental and genetic factors. Furthermore, the Working Party concluded that, where risk is slight, it is particularly important that genetic counselling is not urged on individuals who do not wish to have it.

Where mental illness is concerned, genetic counselling has the potential to affect family dynamics adversely and to trigger anxiety and even illness. Stress may arise when counselling cannot predict a precise level of risk. There is as yet little evidence about the effects of counselling for mental disorders and caution should therefore be exercised. The Working Party recommends that research is undertaken to clarify the appropriate aims and outcomes of genetic counselling for mental disorders and to assess the response of individuals and families to counselling. Such research should investigate the expertise and training needed by those undertaking counselling for various conditions and purposes.

The future demand and need for genetic information and counselling is difficult to predict but, as more knowledge about genetics becomes available, demand may well increase. Psychiatric nurses trained in genetic counselling would be well placed to provide a link between primary care teams and genetic clinics offering specialist counselling. The Working Party recommends that the British Society for Human Genetics and the Royal Colleges of General Practitioners, Nursing, Psychiatrists and Physicians consider arrangements for the education, training, and support both of primary health care teams providing genetic information about mental disorders and of those providing specialist genetic counselling.

Genetic testing

One outcome of initial clinical consultation or of genetic counselling may be that a patient is advised, and chooses, to seek genetic testing. At present, the number of conditions for which tests are available is small, as is the number of people taking tests. The stigma associated with mental disorders, however, may lead to exaggerated demands for, or fear of, genetic testing.

For most mental disorders, genetic tests are likely to have limited value for the diagnosis or prediction of individual risk. In the case of late onset Alzheimer’s disease, one or two copies
of the apoE4 allele will only result in a small alteration in risk which cannot take into account the other genetic and environmental variation between individuals. Given the very low predictive power of apoE4 tests, the Working Party endorses the position that testing for apoE4 alleles to provide predictive or diagnostic input for Alzheimer’s disease is currently inappropriate. It recommends that genetic testing for susceptibility genes providing predictive or diagnostic input of certainty comparable to, or lower than, that offered by apoE tests for Alzheimer’s disease should be discouraged unless and until the information can be put to effective preventive or therapeutic use.

Genetic testing may reveal additional medical information about the patient. This will become more likely as increasing numbers of genes are identified which confer susceptibility to more than one condition. The possibility that additional information will be revealed should be discussed with the patient before the test is undertaken. The Working Party recommends that the duty of physicians to discuss and disclose any possible increase in risk revealed by genetic tests for conditions other than that under investigation be considered equivalent to the duty to do so for other, non-genetic, types of information.

The potentially large numbers of people carrying susceptibility genes for common disorders may lead to commercial pressure for the promotion of testing for susceptibility genes even where this would not be advisable or appropriate. The Advisory Committee on Genetic Testing discourages directly marketed tests other than for carrier status for inherited recessive diseases. The Working Party endorsed this position but concluded that the present voluntary system of approval is likely to prove insufficient. The Working Party recommends that the Advisory Committee on Genetic Testing monitors the uptake of directly marketed tests and the consequences of their use. If, in the light of such monitoring, adverse consequences become apparent, it recommends that the UK government seeks national or international regulation of directly marketed tests.

**Consent and impaired capacity**

Most people with mental disorders will be competent to consent on their own behalf to genetic counselling and any further procedures, including genetic tests. Obtaining genuine consent requires health care professionals to do their best to communicate accurately, and in an understandable and appropriate way, the purposes and implications of the procedure as well as its risks. For a person deemed mentally incompetent to make his or her own treatment decisions, a doctor must act in that patient’s best interests even though there are difficulties in translating from the general principle to the specific case.

**The genetic testing of children**

For children deemed able to give consent to medical treatment, the issues raised by genetic testing are comparable to those for adults. For genetic testing that cannot be considered as medical treatment, it is unclear whether children below 16 would be regarded as able to give valid consent on their own behalf. For the child unable to give valid consent, the consent must be given by the child’s parent (or, rarely, the Court). The guiding criterion is the best interests of the child.

*Diagnostic testing:* When a condition begins during childhood, deciding whether genetic testing for diagnostic purposes is in the best interests of the child is not in principle any different to a decision about any other medical treatment.

*Predictive testing:* For genetic tests which offer some degree of predictive certainty professional opinion amongst clinical geneticists has been against the testing of children for
adult onset conditions on the grounds that this has no benefit for the individual during childhood and denies him or her the chance of making their own choice as an adult, and could lead to discrimination within the family. Some parents and patient groups have argued, to the contrary, that parents have a right to know about their children’s genetic make-up. Whatever the ethical arguments, such testing, if not carried out explicitly to serve the best interests of the child, would not be permissible in law. **The Working Party recommends that, for children unable to give consent, predictive genetic testing should be strongly discouraged unless there are implications for clinical intervention in childhood.**

*Carrier testing:* The use of genetic tests to determine the carrier status of young children denies them the possibility of making their own decisions about being tested at a later stage. For the law these ethical arguments translate into the question posed earlier: whether it would be in the child’s best interests to carry out the test? It is not immediately obvious that it would be. **The Working Party recommends that children should not be tested for carrier status for mental, or indeed other, disorders until they are competent to make their own decisions.**

*Directly marketed tests:* Despite guidance to the contrary from the Advisory Committee on Genetic Testing, the direct marketing of tests to the public may result in the inappropriate testing of children since it is not clear how a company would determine whether a sample had in fact come from a child under 16. This emphasises the importance of monitoring the uptake of directly marketed tests.

*Adoption:* Genetic testing of children might also be considered during adoption. **The Working Party recommends that, given the importance and complexity of the issues, the Health Departments, in consultation with the appropriate professional bodies, provide guidance on the pre-adoption use of genetic testing.**

**Genetic information and reproductive decisions**

Where the common mental disorders are concerned, genetic information will not be particularly helpful in making reproductive decisions. The predictive certainty of genetic tests will be slight in the majority of cases making prenatal testing and termination less relevant and acceptable to parents. It will also be less likely to meet the criteria of S.1.(1)(d) of the Abortion Act. Even within this framework, what one woman or couple will see as a sufficient reason for abortion, another will see as quite insufficient. **The Working Party recommends that people making reproductive decisions in the light of a family history of a mental disorder should have access to genetic counselling.**

The ideal of non-directiveness in genetic counselling is widely endorsed. There is accumulating evidence, however, that non-directiveness is rarely achieved. The Working Party questioned the appropriateness of non-directiveness as a universal aim in genetic counselling and felt that, in some circumstances, it would be inappropriate and unhelpful. It has emphasised, however, how important it is that genetic counselling and testing are undertaken voluntarily, and that individuals are enabled to make their own decisions at each stage of the process. **The Working Party notes the need for further debate about the appropriateness of non-directiveness in genetic counselling and recommends that further research to establish appropriate aims and outcomes for genetic counselling is undertaken.**
Confidentiality and disclosure

The duty of medical confidentiality is not absolute. When genetic screening reveals information which may have serious implications for relatives, ‘health professionals should seek to persuade individuals, if persuasion be necessary, to allow disclosure of relevant information to other family members’. For the common mental disorders, problems of non-disclosure are likely to be rare since genetic information is unlikely to lead to such significant modification of risk that non-disclosure would have serious consequences. It is, nevertheless, necessary to be wary of breaking confidentiality in those cases where an individual opposes disclosure of information about his or her condition. The Working Party recommends that the confidential nature of genetic information should be maintained. The Working Party can conceive of exceptional circumstances in which, in the absence of the consent of the individual, disclosure to close family members might be justified, if there are serious implications for them. Such decisions should be judged on a case by case basis.

Particular concern has been expressed about the confidentiality of the information contained in genetic registers. The Working Party concluded that clear guidelines are needed. The Working Party recommends that the British Society for Human Genetics explores mechanisms for the development of guidelines for the establishment and maintenance of genetic registers in the new NHS.

Wider uses of genetic information about mental disorders: ethical and legal issues

Stigma

The issues raised by genetic information about mental disorders go beyond the clinical context. The Working Party considered the implications of genetic information for the stigma that mental disorders evoke. It concluded that proper treatment of those with mental disorder must include efforts to eliminate both the injury which stigma constitutes and the harm which it causes and it noted that the former may be deeper and less easy to rectify. Genetic information could, in principle, decrease stigma by increasing the understanding of mental disorders, putting them on a par with conditions thought of as physical and countering notions that some mental disorders reflect weakness of character. Similarly the stigma suffered by families may decrease if genetic information provides evidence for a biological component to some mental disorders. Genetic information could, however, be interpreted in different ways; as indicating that people with mental disorders are fundamentally different from others or that parents are to blame for having affected children in the first place. Genetic information may also serve, therefore, to increase stigma.

This emphasises the importance of combating stigma and ensuring that additional genetic information decreases, rather than increases stigma. There is no simple way, no single institution and no simple piece of legislation which can eliminate the stigma of mental disorder; only long-term changes in public understanding of, and support for, those with mental disorders will improve matters. The Working Party welcomes, therefore, the current Respect campaign by MIND to oppose discrimination on mental health grounds and the newly launched campaign against stigma by the Royal College of Psychiatrists. The Working Party recommends that campaigns to reduce stigma emphasise that it constitutes harm as well as causing it.
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Insurance

The Working Party noted that the use of genetic information relevant to mental disorders for insurance purposes is likely to be fairly limited and specific. The Working Party concluded that it is doubly important that insurers do not exaggerate the actuarial implications of genetic test results relevant to mental disorders, where the risk of stigma and its effects is high. It is important to have systems in place that can monitor whether insurers are discriminating unfairly on the basis of genetic test result. The Working Party recommends that the Government, in consultation with the insurance industry, makes arrangements for monitoring insurers’ use of genetic tests for mental disorders, and for reporting on any tendency to load premiums excessively, any actuarially unwarranted refusal of insurance and any other forms of unfair discrimination.

Employment

In view of the employment difficulties and discrimination faced by those with mental disorders, the Working Party considered it important to consider how the use of genetic information might improve or worsen matters. With respect to genetic screening of employees for increased occupational risks, although the Working Party has not learnt of any genetic sensitivities to chemical or biological agents which are associated with an increased risk of mental disorder, other features of some working environments might represent greater risk factors for mental disorder for individuals with relevant susceptibility genes. This adds force to the recommendation in the Council’s previous report, Genetic Screening: Ethical Issues, that genetic screening of employees for increased occupational risks should occur subject to strict safeguards and only after consultation with a co-ordinating body. The Working Party recommends that the Human Genetics Advisory Commission, in its consideration of genetics and employment, determines which is the appropriate body to monitor any introduction of genetic screening programmes for increased occupational risks.

It is possible to envisage the use of genetic tests for mental disorders for reasons other than identifying occupational risks; possibly even to exclude some people from employment on health grounds. The Working Party welcomes the forthcoming consideration of genetics and employment by the Human Genetics Advisory Commission and recommends that, in view of the special significance of stigma in mental disorder, the Commission pays particular attention to the implications of testing for genetic factors relevant to mental disorders for employment purposes.

Education

The Working Party noted that in some cases a genetic test might be useful in identifying a specific educational approach; in others it might be of doubtful value. In the latter case there would be prima facie grounds for relying on conventional tests. Even in the former case, reliance on genetic tests should not, we believe, become automatic in educational assessment since testing itself may have other, possibly adverse, implications. The Working Party does not endorse any wider use of genetic tests to assess individual or group potential of any sort.
Genetic research into mental disorders: ethical and legal issues

For most people with a mental disorder, arrangements about consent for research need not and should not be any different from those required for other people. While the mental capacity of many individuals with mental disorders varies, it is desirable, and almost always possible, to involve them in relevant genetic research at a time when they are competent to consent on their own behalf. The Working Party recommends that individuals who are intermittently competent should only be approached about participation in research when competent. Although genetic research tends to be of minimal physical invasiveness, the Working Party recommends that written consent for participation should be the general rule.

The intermittent nature of some mental disorders and the confinement of some patients to institutions are two aspects of mental disorders which suggest that special safeguards are needed when obtaining informed consent to research participation. The Working Party concluded that where potential participants in research are confined in an institution, special care is needed to ensure that no form of coercion is used to secure participation. In particular, the use of payment must be carefully considered. The Working Party recommends that any proposed payment for participation in research should always be carefully considered by research ethics committees and by grant-giving bodies. The Working Party also noted that the validity of consent should not be assumed when the potential participant’s capacity to consent changes during the course of the research. Proposed contingencies to deal with such a situation should be presented to a research ethics committee and discussed with the patient at the outset.

Most genetic research into mental disorders is unlikely to lead to any immediate benefit to patients lacking the capacity to consent to participation and is therefore of doubtful legality. In the case of children, provided that there is an important interest served by the intervention, a parent may consent on the child’s behalf. It is unlikely, however, that progress can be made in the treatment of mentally incapacitated patients without research and most relevant research is probably only possible if it involves individual patients. The Working Party considers that genetic research holds out important prospects of advances in understanding and treatment of mental disorders and that restrictions on participation are not in the patient’s best interests. The Working Party recommends therefore that non-therapeutic research involving people lacking the capacity to consent to participation on their own behalf should be considered ethically acceptable, subject to strict safeguards. The Working Party recognises that there should be legislative backing for and controls over nontherapeutic research involving mentally incapacitated patients. It recommends that further consideration be given to the details of legislation and regulation to safeguard the interests of people with mental incapacity with respect to participation in research.

The Working Party concluded that additional specialist ethics committees to consider research involving those unable to give consent on their own behalf were not necessary or desirable. It considered that such committees might increase the stigma suffered by potential participants and diminish the skills of regular ethics committees. Rather, the Working Party recommends that every research ethics committee should include at least one member who has experience in the area of competence in decision making about research participation.

It is not uncommon for researchers to discover, using DNA samples collected for research purposes, information of clinical significance to the individual donor of the sample. An ethical difficulty arises because the process of obtaining the informed consent required for research
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does not usually include consent for disclosure of identifiable data to clinics outside the strict environs of the research, nor the kind of genetic counselling that would be required for an individual seeking a genetic test for clinical purposes. To provide an individual with information from a research study about gene mutations they might or might not carry, could be to give them information they would choose not to have, and/or information for which they or other members of the family are not prepared or cannot understand in terms of its implications. A further difficulty is that quality controls and procedures used for clinical testing may be different and sometimes more rigorous than those used in research studies. For these reasons the Working Party recommends that, as a general rule, those who consent to take part in research should be told that individual information derived from analysis of their DNA will not be given to them. A summary of the overall findings of the research can be provided if the participant wishes. The Working Party further recommends that, in any research study that could yield genetic information which is clinically relevant to a research participant and/or their relatives, consent to that research should make it clear whether or not such information would be made available.

In relation to the additional use of research samples or data, the Working Party recommends that, when an individual participant is regarded as competent, any further use of data in the longer term should be discussed with him or her as part of the consent procedure; new research should, as a minimum, be submitted for approval to a research ethics committee before proceeding. When a person is considered to be incompetent to make his or her own decision about participation in research, data collected for non-therapeutic research purposes should not be used for any other research purpose.

While debate about the use of clinical genetic information by outside agencies continues, information that is obtained within a research context and is not being used for clinical purposes is clearly distinct. The Working Party recommends that genetic information obtained during participation in research should not be made available to organisations such as insurers or employers.