

How will information about the genetic risk of mental disorders impact on stigma?

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Objectives: To suggest ways of testing hypotheses about the impact that information on genetic risk may have on the social stigma of mental disorders and to analyse the implications of these hypotheses for genetic screening for mental disorders.

Method: Literature review and critical analysis and synthesis.

Results: An optimistic view is that information on the genetic risk for mental disorders will reduce blame and social stigma experienced by individuals living with mental disorder. A more pessimists view is that genetic risk information and the use of predictive genetic testing will lead to earlier stigmatization of those at risk of mental disorders. Research is identified that is needed to provide a better understanding of the implications of predictive genetic testing for the stigmatization of different mental health disorders.

Conclusions: It is essential that research on the genetics of mental disorders is accompanied by social science research on the ways in which genetic findings influence the lives of those who are tested.

Key words: ethics, genetic screening, informed consent, mental disorders, stereotyping, stigmatization.

Australian and New Zealand Journal of Psychiatry 2008; 42:214–220

Stigma has been defined as an ‘attribute that is deeply discrediting’, that reduces a person to someone who is ‘tainted’ and ‘discounted’ [1,2]. The consequences of stigma for individuals with mental disorders can be profound. Stigmatization not only limits access to material resources and opportunities (e.g. employment) but via a process of social exclusion it can also act to perpetuate symptoms of the disorder (e.g. inducing a sense of hopelessness) [3]. In

this paper we examine the nature and sources of stigma and identify research priorities for assessing whether future genetic testing for mental disorder will reduce stigma associated with mental disorder or result in progressively earlier forms of stigmatization.

Emerging evidence from twin, family and linkage studies suggest a genetic contribution to mental disorders. Available population-based twin studies suggest a heritability of around 40% [4] for common mental disorders (including depression and anxiety). Twin studies of schizophrenia suggest higher heritability, with some estimates as high as 80% [5]. There have been numerous reports of association between a range of candidate genes and mental disorders such as anxiety and schizophrenia [6,7], but cross-replication has been difficult to achieve in most cases. It appears that interactions between environmental and genetic influences are important. For example, a functional variant within serotonin transporter gene (*5-HTT*) has been shown to moderate the impact of adverse life events and risk of depression and anxiety,

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Received 28 June 2007; accepted 24 October 2007.

although there remains some uncertainty about the direction of effect [8,9].

Genetic risk may not be restricted to inherited DNA sequence changes, but may also involve epigenetic mechanisms [10]. For the purposes of simplicity we use the term ‘genetic testing’ to refer to new technologies that may be capable of assessing both genetic and epigenetic risk. Recent data suggest that difficulties in achieving cross-replication of genetic findings may be due to unmeasured variation in epigenetic processes [11]. Thus predictive genetic tests of the future may well assess both an individual’s genetic and epigenetic characteristics.

Despite the fact that there is still considerable work to be done before reliable predictive genetic tests for mental disorder risk become available, it is essential that we begin an active dialogue about how society should behave once measurement of early genetic risk becomes possible. There is already significant pressure to commercialize tests for functional variants. Genetic testing for the short allele of *5HTTLPR* (the variable number tandem repeats implicated in depression by Caspi *et al.* [8]), for example, is being directly marketed to consumers as a Depression Risk Test (Neuromark, Boulder, CD, USA), at a time well before its reliability in predicting depression risk has been established. A genetic test – nicotest (<http://www.nicotest.com>) – has also been marketed as a way of matching individuals to interventions for smoking cessation [12].

Current opinion about the impact of predictive genetic testing is polarized between optimistic and pessimistic projections [13,14], which seem to depend on the level of genetic determination perceived to be involved [15,16]. The optimistic view is that a future capacity for predictive genetic testing will be a potent weapon against blame and stigma by promoting the view that people who suffer from ‘diseases of the brain’ are not to blame for their condition [17]. A more pessimistic possibility is that early detection of a genetic disposition to mental disorders will stigmatize individuals well before they develop symptoms. We argue that to understand the implications of genetic testing for psychiatric disorders, a more detailed analysis of the nature and sources of social stigma is needed. Moreover, we hypothesize that the complex and multidimensional nature of the stigmatization process will mean that the implications of predictive genetic testing will differ for different types of mental disorders. Describing the disease-specific nature of stigma will provide a basis for judging whether health outcomes for different forms of mental disorders are

likely to be substantially improved by predictive genetic testing or not [17].

Nature and sources of stigma

To understand stigma we need to understand something of the nature of the dominant cultural understandings of mental disorder, and how these conceptual frameworks can adversely affect those living with these disorders. We then need to assess how these cultural paradigms may accommodate or assimilate new knowledge of pre-clinical genetic indicators of a person’s risk of mental disorders. Such steps are important if we are to have a positive effect on changing the way society thinks about, accepts and integrates those at risk or living with a mental disorder. We suggest that stigma and fear are essentially synonymous, and that any intervention to reduce stigma is effectively an intervention to reduce fear. Thus we hypothesize that fear is one of the most fundamental barriers to a healthy assimilation of new knowledge about genetic risk for mental disorder.

There are arguably only two basic forms of threat underlying most fears. The first is threat to physical or emotional security. The second is threat to sense of worth or significance. Fear is a uniquely anticipatory phenomenon that can be aroused independently of objective external threat. We propose that anticipatory fears around threats to personal security or worth are quintessential features of the way psychiatric disorders are stigmatized. In this way stigmatization of mental disorder can be considered almost always anticipatory, largely the result of misinformation, and associated with perceived threats to personal security, sense of worth, or both. Each fear-based dimension of the stigmatization process is discussed now in further detail.

Security-based fears

These have a particular focus on threats to personal security associated with the unpredictable nature of psychiatric symptoms in another, or of the heightened sense of uncertainty that can arise about vulnerability to psychiatric symptoms in oneself (referred to as discomfort anxiety [18]). The perceived threat of disordered behaviour in another, or the fear that one’s own behaviour could become similarly disordered, derives from the anxiety about loss of control in the face of unpredictable threats to personal security. For many people, mental disorder represents

sufferance and deviation from the norm: the familiar, the understandable, and the controllable. Security-based fears can create a societal fear of those with mental disorder (social stigmatization), which in turn can create a fear of self in those with a mental disorder (self-stigmatization).

Sources of unpredictability have changed over time with advancing knowledge. Physical illnesses whose causes we now better understand, such as leprosy, attract much less stigma than they did in the past when their causes were not understood and their course could not be controlled. A century ago cancer was similarly feared, with family members hidden from social view. Now that the causes of cancer are better understood, and more effective treatments have become available, a cancer diagnosis is more likely to elicit compassion than fear. It seems reasonable on this experience to predict that a better understanding of the aetiology of mental illness, and the development of more effective treatments, will reduce the uncertainty and unpredictability of being at increased risk of developing a psychiatric disorder and hence reduce security-based fears.

Shame-based fears

These focus on threats to self-worth through association with an individual with mental health problems, or through social rejection and alienation if one were to develop a mental disorder (referred to as ego anxiety [18]). We suggest that shame-based fears derive from the common human drive for significance and status that creates a second (and powerful) fear centred on shame, rejection and social alienation. Because the symptoms of mental disorders affect our self-consciousness, autonomy and capacity to meet the demands of everyday life, persons with these disorders may be particularly prone to shame-based stigmatization [19]. For example, a common community belief is that people who are depressed or addicted should simply 'pull themselves together' because others have 'coped with worse'. People who are heroin dependent may be seen as lacking in 'moral fibre' or character.

Shame-based stigma is exemplified in the very different attitudes towards the personal disclosure of physical and mental disorders [20]. While people will readily admit to having asthma and coronary problems, they tend to conceal a history of mental disorder. The idea that we could lose our reason and behave irrationally is deeply disturbing and motivates efforts to clearly distinguish ourselves from those

with psychiatric conditions. Common responses include categorical exclusion ('us vs them') and social exclusion (with reduced survival chances for ostracized individuals). We also suggest that shame-based fears have double effects in that they create a societal disdain for those with mental disorder (social stigmatization), which in turn creates a disdain for self among those with a mental disorder (self-stigmatization).

In some instances shame-based-fears prompt avoidance of persons with behavioural manifestations of mental disorder as a way of managing threats to self-worth. Avoidance may be as seemingly benign as walking on the other side of the street to avoid an individual experiencing a florid psychotic disorder, or more active policies of bygone eras that removed disturbed individuals to asylums away from public view.

Implications of social stigma on predictive testing

Advances in genetic knowledge and predictive genetic testing for mental disorders may affect security-based and shame-based sources of stigma in different ways. Two important determinants of the effects on stigma are likely to be (i) the degree of genetic contribution to risk and (ii) the ability to intervene and treat the disorder in question. Thus where the genetic contribution to mental disorder is modest, and there are readily modifiable environmental determinants, information about a genetic predisposition is likely to generate limited security-based stigma. We suggest that this may be true for common conditions such as depression and anxiety. Conversely, for conditions with a stronger genetic contribution, and with few modifiable environmental determinants, knowledge of genetic predisposition may be more likely to increase security-based stigma. We suggest that this may be true for less common and more serious psychiatric conditions such as psychotic depression and schizophrenia.

These concepts can be expressed in two hypotheses about the conditions in which stigma is and is not likely to result from genetic testing: (i) security-based stigmatization will typically occur where a mental disorder is highly genetically determined and is therefore difficult to control should the problem not be averted early in life and develop into a major condition (such as schizophrenia); and (ii) shame-based stigmatization will typically occur when the genetic risk is modest and the actions of the person

play some role in aetiology of the disorder (as in neurotic depression or addiction).

Shame-based and security-based stigma often coexist in those who live with conditions such as schizophrenia, creating a toxic social environment that can perpetuate or worsen the disorder [21]. In order to assess the likely impact of genetic risk information on stigma, we need to understand the contexts in which genetic tests may be performed on healthy asymptomatic people and to identify the circumstances under which such a test is likely to be useful.

Reasons for choosing genetic testing for susceptibility to mental disorder

Psychological benefit

Knowledge of genetic susceptibility in persons with a family history of mental illness has the potential to remove uncertainty and reduce feelings of shame deriving from personal responsibility for perceived weaknesses. As we have suggested, testing could be particularly useful in the context of mental disorders with a considerable environmental component, because in these disorders genetic information may provide guidance on who most needs to reduce their environmental risks. There is a clear role for genetic counselling in this kind of situation.

Improved engagement in preventive interventions

Where a genetic susceptibility to a disorder can be identified, testing could allow for early intervention using cognitive therapy and medication at the first signs of disorder. This could contain the damage wrought by an actual episode of mental disorder [22,23]. Some argue that intervening in a pre-symptomatic period also involves serious risks. Corcoran *et al.*, for example, argue that intervening in 'a period of time that could represent [a child's] best shot at normalcy in the face of what might be a lifelong struggle with mental illness' could reduce quality of life and interfere with functioning [24]. Preventive interventions may reduce the severity of both security-based and shame-based stigma. In the short term though, the initiation of preventive interventions may stigmatize persons who have not yet developed a disorder but who have been identified as being at risk.

Informing reproduction decisions

Where there is a family history of mental illness, some individuals may choose not to reproduce

because of the fear that the illness is hereditary. Choosing not to have children, adopting or using donor gametes, are among the options that genetic counsellors provide to people with a significant chance of passing on an inherited genetic disorder [25]. Unlike genetic tests for Mendelian disorders such as Huntington's disease, future genetic testing for a mental disorder would not be definitive. Indeed for polygenic disorders the risk distribution is likely to be lognormal [26]. This means that most people may have a genetic susceptibility of some degree.

It is possible that reproduction decisions informed by genetic testing may perpetuate stigma. To the extent that they are able, people will make decisions to avoid things they consider harmful or that they fear (e.g. if the risk is great or their fear is great, they may choose not to have children). One study examining predictive testing in the context of psychosis risk suggests that families with a disposition may choose to have fewer or no children [27]. The working party of the Nuffield Council recommends that access to genetic counselling is essential for those who have a family history of mental disorder [14].

In the future it may be possible to use pre-implantation genetic diagnosis to select against embryos with genetic susceptibility to mental disorders but there is as yet insufficient genetic knowledge to do so. Indeed, reliable knowledge for measuring susceptibility may be many years away. Studies that have investigated interest among affected families in genetic testing suggest that this option is unlikely to be taken up [28]. A study of the attitudes of families with two or more members with bipolar disorder found only a limited interest in prenatal testing. Some thought that because 'life involved so many other risks', ruling out bipolar disorder would make 'little difference' [28].

Reasons to avoid genetic testing for susceptibility to mental disorder

Distortion of parents' perceptions of their children

Parents may want to know if their child has a genetic susceptibility to a mental disorder. One risk of identifying a child as being at risk of mental illness is unwitting stigmatization that could occur if testing altered parental perceptions of the child in ways that adversely affected their behaviour towards the child and hence impaired the child's healthy development. This is not a risk peculiar to genetic testing: the same may also occur as a result of parents' knowledge of a family history of mental illness. If a parent's fear

about mental illness in the family is already adversely affecting a child's development then counselling as part of a decision to have genetic testing for susceptibility could be of benefit by providing parents with better information about genetic risk.

Over-interpretation of positive test results

The number of people who are stigmatized may increase with a focus on genetics and testing for susceptibility to mental illness. It may lead to an increase in the number who are seen as being at risk. A positive result from a genetic test indicates only susceptibility and does not mean that a person will develop a mental illness. Nevertheless that person may be stigmatized in much the same way as someone with the disorder. This is a particular risk for anxiety and depressive disorders that have complex genetic and environmental determination. A positive result also does not provide information about whether a condition will be mild or severe or have an early or late onset. A positive result – even for susceptibility – means that family members may become victims of stigmatization as well.

'Folk genetics' – commonly held but false beliefs about the implications of a genetic aetiology of mental disorder [26] – may worsen stigma. Folk genetics includes the idea that a genetic predisposition rules out free will (a genetic predisposition to alcoholism for example does not mean that a person is compelled to use alcohol). It also often includes the mistaken idea that a genetic predisposition to mental disorder rules out the possibility of environmental interventions – overlooking the possibility of effective medications and cognitive behavioural approaches that may prevent the development of or modify the course of a mental disorder. These false beliefs, if uncorrected, may increase security-based stigma. They are less an argument against genetic testing than an argument in favour of better community education about the genetics of common polygenic disorders.

Sense of entrapment

In mental and neurological disorders that are known to be genetically determined, and for which there is no effective form of preventive intervention (such as Huntington's disease), early knowledge of genetic disposition may produce a profound sense of entrapment and loss of control over one's future that increases the risk of poor mental health outcomes. These features of Huntington's disease genetics allow security-based and shame-based stigma to flourish

against individuals with this disorder. Predictive genetic testing for psychiatric disorders may not be useful in this context and this is supported by empirical evidence that shows very little interest in genetic testing among family members of persons with Huntington's disease [29].

Some individuals at risk because of a family history of psychiatric disorder will prefer to know about their risk. For these individuals, an advance directive or autonomously chosen plan of treatment becomes a possibility. Others may want this knowledge so that family burden might be relieved by better future planning. For other individuals, genetic information may have no meaning or be difficult to conceptualize and interpret.

Importance of informed consent

Informed consent is required before an individual submits to predictive genetic testing. In health, law and ethics, moral authority is conferred on the autonomous decisions that competent adults make about their own health. Most predictive genetic testing for mental disorders will be carried out before the onset of symptoms and hence at a time when competence is not compromised by psychiatric symptoms. Predictive testing for a psychiatric disorder is most relevant to children and young people because the age of onset is often late adolescence and early adulthood. An asymptomatic young person who is a 'mature minor' or 'Gillick competent' (i.e. who has 'sufficient understanding and intelligence' to enable him or her 'to understand fully what is proposed'), is also capable of giving informed consent [30]. The informed consent of a competent adult or a Gillick-competent adolescent to undergo genetic testing is sufficient justification to proceed. For younger children, the authority of a parent to decide on behalf of their child is not so clear.

Conclusion

A better understanding of the nature and sources of social stigma will provide clinicians and genetic counsellors with important information about the likely benefits of predictive genetic testing for different kinds of mental disorder. The implications of stigma are significant and create risk for perpetuating emotional distress both within a lifetime and across generations. Knowledge of genetic susceptibility will

carry potentials for both health promotion and harm and these are likely to be disease-specific.

Based on our assessment of the reasons for and the reasons to avoid genetic testing together with the potential benefits and harms of genetic testing, we suggest that the following broad principles be used in dealing with emerging knowledge about genetic susceptibility to mental disorders. Specifically, we predict the following.

1. Predictive genetic testing is most likely to be of use in early life for mental disorders with a high genetic determination and where there are interventions available to reduce that risk.
2. Conditions carrying high risk for social stigmatization require greater justification for genetic screening in early life.
3. Predictive genetic testing for conditions of low genetic determination, for which modifiable environmental processes are important, will necessarily be unreliable predictors of future disease risk and so may be prone to producing unnecessary stigma.
4. A general screen for genetic risk in early life is not warranted for those with no family history of psychiatric disorder, unless there is something inexpensive and low risk that can be done preventively to reduce the risk.
5. Screening for genetic risk of any disorder should be motivated by family history, and permitted where there is a clear capacity to act preventively or where the individual can put in place measures that they perceive as beneficial, provided that the choice is based on clear and current information, and the individual understands the risks and benefits of genetic testing and the stigma associated with particular test results.
6. Genetic testing can be provided for individuals who choose testing when there is a capacity to act preventively in the absence of a family history, provided that the choice is based on clear and current information, and that the individual understands the risks and benefits of genetic testing and the stigma associated with particular test results.
7. Any individual who will be given a genetic test result that is likely to induce social stigma, should be counselled from the outset by trained mental health professionals. This does not necessarily mean one-on-one counselling; for children, peer support groups and less psychiatrically intense interventions may be more developmentally appropriate.

Finally, it is essential that research into the genetics of mental disorders is accompanied by social science research on the ways in which genetic findings influence the lives of those who are tested. Such research is needed to inform community level interventions that aim to develop more tolerant and compassionate societies that will make good use of genetic information about the causes of mental disorders. It could inform efforts like that of the Australian depression initiative (beyondblue; www.beyondblue.org.au) to reduce community stigmatization of depression and improve its diagnosis and treatment.

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