



editorial

Psychiatric Bulletin (2006), 30, 1–2

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Psychiatric patients and gene-based smoking cessation packages

Psychiatric patients are an important consumer body of cigarettes worldwide, demonstrating an increased smoking prevalence (generally greater than 70%) compared with healthy control individuals (around 30%) (Leonard *et al*, 2001). Schizophrenia (Lohr & Flynn, 1992) and depression (Dierker *et al*, 2002) are the disorders with the clearest evidence of increased prevalence of cigarette smoking and tobacco addiction. Smoking in schizophrenia and depression is thought in part to represent an attempt to self-medicate symptoms of the illness. In particular, troublesome negative symptoms in schizophrenia and low mood in depression. There is also preliminary evidence to support a relationship between eating disorders and smoking, whereby smoking may be used as weight control behaviour (Welch & Fairburn, 1998; Sanchez-Johnsen *et al*, 2005). As clinicians working with a group of individuals with such high smoking rates, we have a duty of care to protect them from the ill effects of tobacco smoke. Our efforts should include informing patients of the best treatments available and directing them to the appropriate services. The recent arrival of gene-based smoking cessation tests should broaden this responsibility.

Gene-based tests

The mainstays of current smoking cessation treatment are nicotine replacement therapy (patches, gum, inhalers, lozenges, spray) and bupropion (Zyban), although behavioural support is also effective. Gene-based tests for smoking cessation are currently marketed privately to smokers via the internet to help inform them as to whether they carry gene variants predisposing them to nicotine addiction. Smokers can buy a genetic test package (retailing around £95), which includes subsequent advice online, and a kit containing a device to take a pin prick of blood which the customer places on an absorbent pad and sends to a laboratory for DNA analysis. The results are given with a personally tailored plan for cessation of smoking, including advice on the pharmacological treatment most appropriate to an individual's genetic make-up. Advice about behavioural

changes, alternative therapies and other ways to succeed in stopping smoking is also offered.

Opinions and issues

The main reason a patient is likely to purchase a gene-based test is to gain personalised scientific information on their likelihood of succeeding in smoking cessation with particular pharmacological treatments (nicotine replacement therapy and/or Zyban). This information will not be available as part of a patient's routine care on a psychiatric ward.

Several issues that are relevant to patients purchasing gene-based smoking cessation tests are discussed below.

Clinical utility of genetic tests

Current tests for predisposition to nicotine dependence and response to treatment draw on evidence from genetic association studies. The difficulty in using such data is that they are inconclusive with regard to our best genetic candidates in the smoking cessation field. A good example is the dopamine D₂ receptor (*DRD2*) gene, which has been reported to be both associated and not associated with alcoholism and drug dependence phenotypes (including nicotine dependence) in several studies over many years. There is only at best modest evidence to support the role of *DRD2* in nicotine dependence. A recent meta-analysis by Munafò *et al* (2004) failed to demonstrate a statistically significant relationship between *DRD2* and nicotine dependence. The only studies on UK populations have found no association between variations in this gene and nicotine dependence (Singleton *et al*, 1998).

What is needed before a recommendation of the introduction of genetic tests is a thorough investigation of potential benefit and harm, especially among general medical and psychiatric patients, including an analysis of specificity and validity. Furthermore, evidence regarding the efficacy of genetically tailored treatments compared with outcomes associated with currently available treatment strategies should be made available.



Psychiatrists' readiness for gene-based tests

Psychiatrists are a key point of contact for patients wanting to give up smoking because of the inflated rates of smoking among individuals suffering from psychiatric illness. Most services will not have access to medical geneticists and the bulk of counselling falls to psychiatrists and other members of the mental health team. Findings from studies among general practitioner groups in the USA indicate that they do not have the knowledge, willingness or training to take on such a role (Shields *et al*, 2005). Recent evidence indicates that such concerns are greater for new genetic tests than other new tests (Freedman *et al*, 2003). The responsibilities of general adult psychiatrists, substance misuse service professionals and general practitioners are already significant without the additional burden of providing counselling for such tests. The cost implications for the National Health Service of this added duty should also be of concern.

Privacy, genetic discrimination and social stigma

Current privacy laws within the UK fail to protect patients from the misuse of genetic information. Many European countries (including France, Spain and Germany) have laws preventing insurers and prospective employers from gaining access to an individual's genetic profile. These worries are enhanced in the context of smoking because of the pleiotropic nature of the genetic loci that are investigated. Genes that have been associated with smoking behaviour or treatment response have been implicated in many other disorders, such as alcohol and cocaine addiction, compulsive sexual activity, pathological gambling and schizophrenia, among other psychiatric conditions. When patients spend money on a genetic test, they are inadvertently generating information about their risk for predisposition to developing or possessing a number of other stigmatising conditions.

Can patients be misled by current gene-based tests?

The majority of individuals who attempt to give up smoking using genetic tests will fail according to accepted success rates from cessation studies using nicotine replacement therapies and bupropion, which are as low as 20% in a year (Department of Health, 2002), even with the best available combination therapies of pharmacological treatment and behavioural support. A real danger is that the information provided to patients from the test may mislead them into thinking that they have a particularly virulent or 'genetic' form of addiction and are never

going to be able to give up. Similarly, the information may lead certain individuals to believe that they will never respond to (for example) Zyban and will avoid it in future.

Conclusion

It is hoped that targeted therapies based on genotype will play a key role in the field of smoking cessation. However, our current knowledge of genetic and pharmacogenetic influences in smoking cessation is, at best, modest. The evidence supporting the use of genetic tests in smoking cessation is preliminary and largely unrepliated. More studies are needed to verify the usefulness of genetic tests for smoking cessation in the clinical setting. Until we have a greater understanding of the genetic influences in nicotine addiction, individuals being cared for in psychiatric services are best advised to avoid such tests.

Declaration of interest

Dr Marcus Munafò has provided consultancy services for G-Nostics Ltd.

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