

European Brain Policy Forum 2009: Depression and the European Society

European Brain Council*

The European Brain Policy Forum was inaugurated by the European Brain Council in 2008, as a forum in which all stakeholders in a given brain disease—patients, clinicians, basic scientists, health economists, industry representatives and policymakers—could come together to try to shape future policy with regard to that disease and its impact on society. The second of these events took place in Brussels over 25-26 February 2009, and focused on depression.

Sooner than expected, depression has become Europe's most debilitating disease. In the mid-1990s, the World Health Organization predicted that in 2020, it would rank second after ischaemic heart disease among the leading causes of disability-adjusted life years (DALYs), where a DALY is a time-based measure that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health [5]. But depression has already overtaken heart disease in the European Union, and now accounts for 9.2% of DALYs in the region [12]. Untreated severe depression is a major risk factor for suicide, of which there were at least 59,000 cases in the EU in 2006 [3]. Depression is also the most expensive of all brain diseases, costing the EU €118 billion in 2004 [8].

The European Commission's Seventh Framework Programme of research (2007-2013) has made brain diseases a priority, and the brain is also one of the five priorities of the Innovative Medicines Initiative, a public-private partnership between the EC and the pharmaceutical industry. But the EC only accounts for 5% of the public budget for R&D, and the public budget only represents 21% of total R&D funding in Europe [9]. National governments need to invest more in brain diseases in general, and in depression in particular.

Of the total costs of depression, 90% are indirect and result from lost productivity [10], though regulatory authorities whose role it is to assess the cost-effectiveness of prevention and treatment strategies tend only to take into account the direct (mainly healthcare) costs. Moreover, lost productivity is measured largely in terms of absenteeism, and does not generally include the costs of staff turnover, or of "presenteeism", low productivity of employees who remain at work despite being ill.

The cost and burden of depression fall mainly on the shoulders of families, employers and social services, who should therefore be mobilised to help reduce them. If employers need an incentive, it is that for every euro invested in supporting an employee with depression, he or she can expect a sixfold return in terms of regained productivity [12]. Where should that investment be targeted? The statistics offer some clues: the disease is twice as prevalent in women as in men, and women who marry and have children double their risk of developing it, unless they return to work [12]. Men with depression, on the other hand, are far less likely to seek help.

The stigma associated with this most common of diseases is still such that it prevents people from seeking help, and when they do seek help there is often a delay before they are correctly diagnosed. Relatives or carers are often the first to contact the healthcare services. Better education is needed for both patients and their families, and the media have a role to play in this. Carers and relatives themselves are vulnerable to depression and need attention and support.

Overcoming stigma and increasing investment are not enough, however. A new intervention agenda is required. Too much burden is placed on primary care doctors, and stimulating the self-help infrastructure alone won't alleviate it. Though GPs would benefit from more training in recognising and treating the symptoms of depression, more mental health specialists are required. Early targeted intervention of high risk groups is probably more effective than general prevention strategies, and policymakers should bear this in mind when drawing up voluntary codes of practice, such as the 2008 European Pact for Mental Health and Well-being [2].

How should high risk groups be identified? A number of clinical and biological markers of vulnerability to depression are being investigated. For example, there is preliminary evidence that brain imaging correlates of emotional responses to facial expressions could provide a surrogate marker for the condition [1]. Reduced numbers of 5HT_{1A} receptors in the brain may be another vulnerability marker, since these do not increase with recovery [6], while working memory deficits correlate with lifetime history of depression, rather than with present mental health status, providing some indirect evidence for the hippocampal atrophy model of the disease [7].

Treatment adequacy needs to be improved, with an emphasis on starting sooner and improving continuity, to prevent recurrence. Depression is a disease of long duration, and it has a cumulative effect, becoming more severe with each subsequent episode. It is also a heterogeneous disease, and its heterogeneity presents an obstacle to the development of more effective drugs. New ratings scales are required, which allow clinicians to identify subgroups within depression that respond differently to therapies, and for which animal models can then be developed.

Existing anti-depressants are only partially effective, even when adequately prescribed. The US National Institute of Mental Health (NIMH)-funded STAR*D trial found that only a third of patients achieved remission after a maximum of 12 weeks' anti-depressant treatment [11]. Novel anti-depressant agents, including combinations of agents, are needed which have a faster onset, greater efficacy and fewer side-effects.

Many studies have shown that cognitive behavioural therapy (CBT) works as well as anti-depressant medication. Among the newer, non-pharmacological therapies for depression, deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS) have both shown efficacy for severe forms of the disease, but TMS has not yet reached the clinic and little is known about either of their mechanisms of action.

Electroconvulsive therapy (ECT) has such a negative image that patients with refractory depression have been known to opt for invasive DBS surgery rather than consider this non-invasive alternative. Yet ECT is still the most effective treatment for severe depression in some patients, and its rapid onset of action—one of the unmet needs in depression therapy—merits further preclinical investigation, which could in turn be used to guide the design of faster-acting anti-depressants and new psychotherapeutic approaches.

More epidemiological research is needed. The incidence of depression in the under-18s and over-65s has not been well-studied, though limited evidence suggests that in children it is equally prevalent in boys and girls at between 2-4%, rising to twice that in adolescence, with the gender difference first emerging at puberty [12]. Data are lacking on the comorbidity of depression with conditions such as stroke and cardiovascular disease, and on other high risk groups such as the children of depressed parents, carers of those with brain diseases, and women in the pre-, peri- and postnatal period.

Patient-doctor communication must be improved. One way to do this involves harnessing new technologies. Information Technology Aided Relapse Prevention in Schizophrenia (ITAREPS) is a successful initiative which involves patients and carers regularly sending completed questionnaires by SMS to a web-based interface where psychiatrists can access them [4]. ITAREPS could potentially be applied to depression, too.

In terms of treatment, clinicians should consider the person behind the disease, as well as the disease, bearing in mind its psychosocial dimension and the need for rehabilitation. Finally, the architects of clinical trials should be more inclined to consult patients when it comes to determining the endpoints of those trials. Better communication is ultimately the key to overcoming stigma, and to accelerating the diagnosis and treatment of depression.

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