

making

sense of

# MENTAL ILLNESS

biology, medicine &amp; society



A summary of the talks and discussions presented at the 12th EMBO | EMBL Science & Society conference Making Sense of Mental Illness – Biology, Medicine and Society, Heidelberg, 4–5 November 2011. The conference highlighted the biological, medical and societal aspects of brain diseases and behavioural disorders. An audience of more than 400 participants and 19 speakers from a wide range of disciplines explored the implications of mental disorders for individuals and for society; the speakers also presented the latest scientific knowledge about their causes and treatments. The conference participants discussed a number of relevant issues such as the definition of mental disorders, financial interests in their diagnosis and treatment and controversial therapies.

12th joint  
EMBO | EMBL conference  
on Science & Society

4–5 November 2011  
EMBL Heidelberg, Germany

## Introduction

The 12th EMBO | EMBL Science & Society conference Making Sense of Mental Illness highlighted the biological, medical and societal angles of brain diseases and behavioural disorders. An audience of more than 400 participants and 19 speakers from a wide range of disciplines explored the implications of mental disorders for individuals and for society; the speakers also presented the latest scientific knowledge about their causes and treatments. The conference participants discussed a number of relevant issues such as the definition of mental disorders, financial interests in their diagnosis and treatment and controversial therapies.

## Epidemiology and economic burden

According to a study by the European College of Neuropsychopharmacology (ECNP) and the European Brain Council (EBC), led by Hans-Ulrich Wittchen from the Technical University of Dresden, Germany, 164,8 million (38,2 percent) Europeans suffer from a mental disorder (MD) each year. Wittchen further detailed in his presentation that anxiety is the most prevalent disorder, suffered by 14 percent of Europeans, followed by insomnia, unipolar depression, attention deficit hyperactivity disorder (ADHD) in the young and dementia. The World Health Organization estimates that worldwide 25 percent of individuals develop one or more mental disorders in their lifetime; depression is among the leading causes of disability, affecting about 121 million people.

These diseases are highly disabling because they typically manifest early in life, are chronic and prone to relapse, and often poorly

diagnosed and treated: on average there is a lapse of 15,6 years between the manifestation of first symptoms and treatment.

Women have a higher risk of developing mental disorders than males, and persons of lower social-economic position are generally at higher risk.

These figures indicate an ongoing epidemic of mental disorders, but the numbers of people affected in Europe has remained stable during the past decade. The total increase from 2005 is caused by the inclusion of more disorders and more nations in the study (the EU 27 member states plus Switzerland, Iceland and Norway).

The study also highlighted that mental disorders are substantially more costly than other chronic diseases, such as coronary heart disease, cancer and diabetes: the total cost in the EU-30 is estimated to be 674 billion euro annually. Addressing the “economic burden” of mental disorders is therefore a core challenge of the 21st century. Although the direct costs—treatment, inpatient stays, outpatient visits—are less than 20 percent of the total costs, most prevalent mental disorders cause substantial indirect costs through lost workdays and productivity.

But most of all, mental disorders have dramatic effects on the lives of the individuals affected and their families, not only because of the consequences of the disease itself, but also due to widespread prejudices against mental illness. According to a study presented by Wulf Rössler from the Psychiatric University Hospital in Zurich, many consider the mentally ill as dangerous, unpredictable and unreliable. These stigma create a vicious cycle of discrimination leading to social isolation, unemployment, homelessness, drug abuse and long-lasting institutionalization.

Rössler presented studies showing that even mental health professionals have similar attitudes towards their patients. However,

empowering patients by involving them actively in the decisions about their treatment is an essential step towards a successful treatment, asserts Donna Franceschild, TV writer and dramatist, who is affected by bipolar disorder.

The fact that stigma and discrimination present a major obstacle to successful treatment of mental disorders has started to be recognized, said Rössler, and campaigns to help fight them have been organized in many European countries, directed mainly to general public, schools and police officers, but more needs to be done.

The main reason for the social and economic burden, according to Wittchen, is the ineffective use of existing resources. The majority of cases remain untreated and only 2 to 9 percent of patients receive minimum adequate treatment. At the same time, funding for brain research, health care and education at medical schools are disproportionately small in all EU states. To reduce size and cost burden, Wittchen suggested a coordinated public health effort to provide better primary prevention; prevent recurrence and secondary disorders; slow down disease progression; and reduce associated psychosocial impairment.

## Causes of mental disorders

During the past two decades, neuroscience and psychiatry have made major progress in understanding the molecular and physiological causes of many brain diseases. One outcome of new knowledge and technologies to analyze brain function and brain morphology has been a redefinition of mental disorders as disorders of the brain. At the same time, the importance of external factors for brain functions has also become evident: experience, education and social interactions affect the brain and can establish stable and lasting changes.

The notion that it's all in the brain or it's all in the environment has therefore been abandoned in favour of a new model that embraces different kinds of interactions between genetic and environmental factors as Michael Rutter, King's College London, and Steven Rose, emeritus professor of the Open University, UK, stressed in their talks. Another important discovery has been the unexpected plasticity and adaptability of brain structures throughout life. Mental disorders therefore develop over longer time periods and the underlying molecular and cellular changes start much earlier in life long before the disease becomes manifest.

Despite this progress, the pathophysiology of brain disorders is still not clear—only a small group of disorders, which includes Huntington Disease and Fragile X Syndrome, are caused by the mutation of a single gene. Diagnosis is therefore still based on clinical observation and on the description of symptoms by patients.

The identification of the gene responsible for Huntington Disease initially raised hopes that it would be possible to identify the genes related to other mental disorders. But many years of research have shown that many genes are involved in the development of mental disorders, most of which play only a minor role.

So far, research has concentrated on a few well-understood pathological processes, such as the beta amyloid cascade in Alzheimer's Disease (AD) or dopamine production in schizophrenia. However, in light of public expectations, scientists are often inclined to overstate new findings and their potential therapeutic use, which, in the long run, may damage the public view of science, according to Nikolas Rose, social scientist at the London School of Economics.

Moreover, many biologists have largely ignored the role of the social environment in the development of mental disorders. They also ignored the potential contribution of the social sciences in understanding the onset of mental illness. In fact, various studies e.g. on the societal impacts of urban living, would help neuroscientists to better understand the role of societal factors in brain disease.



As Steven Rose concluded, it is time to move on from genetic studies and stop hunting for genetic factors. Instead, research should start with the epidemiology and ask questions such as why are more women and more poor people and ethnic minorities affected? Rose also cited the World Health Organization's Grand Challenges for mental disorders: the first challenge is to identify modifiable social and biological risk factors across the life course; understand the impact of poverty, violence, war, migration and disaster; and identify biomarkers in order to identify root causes, risk and protective factors.

Moreover, we need to better understand the pathophysiology of the disease before designing, testing and using psychiatric drugs, according to Simon Lovestone from King's College London. It would also mean recognizing the limitations of existing animal models and to design better methods to study brain function in humans.

But most of all, we need new ideas, Michael Rutter and Steven Rose stressed. We need to consider the brain as an organ embedded in both the body and in the environment that is also affected by other bodily functions such as the neuroendocrine system or immune system.

## Treatments

During the past two decades, new psychiatric drugs became available to replace older, largely ineffective drugs against a range of psychiatric diseases—notably depression, schizophrenia or attention deficit disorders. However, the development of more and better drugs has stalled during the past years. An obstacle remains proving efficacy in clinical trials compared to placebo, which has turned out to be a major hurdle. Merely visiting a doctor, entering a clinic or enrolling in a trial is known to result in improvement at least of some symptoms. The molecular mechanisms of placebo are not clear, but studies are ongoing.

Moreover, the molecular pathophysiology of most mental disorders is not clear, which further impedes the search for efficient compounds. At the same time, the costs to develop and bring a new drug to market have increased tremendously, showed Andreas Meyer-Lindenberg, Director of the Central Institute of Mental Health, Germany. From 2008 to 2011, the average costs have increased from US\$0.8 billion to about US\$4 billion. Many pharmaceutical companies have therefore reduced their investments in developing psychiatric drugs. Roche is one of the companies that are still active in the field; Luca Santarelli, Head of Roche Neuroscience Disease Translational Area, presented the company's research efforts that concentrate on major diseases with a good understanding of the pathophysiology, such as Alzheimer, autism spectrum disorder, and schizophrenia.

Another strategy to improve the efficiency of drug development is private/public partnerships between pharmaceutical companies and academic research to share data, material and information in the development stage. Roche is also engaged in various partnerships such as the European Innovative Medicine Initiative (IMI) and the NEWMEDS project. NEWMEDS is funded by IMI and aims at finding new methods for the development of drugs for schizophrenia and depression.

Tim Kendall from the UK National Institute for Health and Clinical Excellence (NICE), highlighted the persistent problem of selective publication of drug trials in mental health: 85 percent of published drug trials are funded by the drug companies that manufacture them, and mainly report positive findings whereas negative effects are rarely published. Although this affects all research fields, it seems to be particularly relevant for psychiatric drugs and it leads to overestimating their benefits and underestimating the negative side effects. Kendall, and Richard Smith, former editor of the British Medical Journal, therefore suggested a few possible solutions including public funding of drug trials, and publishing the results of clinical trials in publicly accessible databases.

However, some developments are underway that could rekindle the interest of pharmaceutical companies in developing psychoactive drugs. Personalized medicine for instance would enable doctors to use existing drugs more effectively in patients who could benefit from them. On the research side, better animal models and *in silico* psychopharmacology could greatly improve the drug development process. Even more ambitious is the Human Brain Project, which aims to model the whole human brain.

According to Mathias Berger from the University Medical Centre in Freiburg, Germany, psychotherapy has been improving more rapidly than psychoactive drug development. New and disorder-tailored psychotherapies, such as Cognitive Behavioural Analysis System of Psychotherapy (CBASP) for chronic depression, or Interpersonal Psychotherapy (IPT) and Cognitive Behavioural Therapy (CBT) for episodic depression show very good results. Psychotherapies are more effective on a large group of disorders including anxiety, post-traumatic stress disorder, obsessive-compulsive disorders, substance abuse, but less so to treat diseases such as schizophrenia that have a strong neurodevelopmental component. For some diseases (as ADHD in adults) a combination of pharmacotherapy and psychotherapy seems to work best.

However, as Berger pointed out, in Germany alone exist at least 350 different 'schools' of psychotherapy—all of which are based on different theories and assumptions, which creates conflicts and decreases efficiency. A related problem is the lack of evaluation of efficacy of the therapies regarding morbidity, life quality and mortality. Still, the situation is improving also with the advent of neuropsychotherapy or neurobehavioural therapy, which is a combination of psychotherapy and neuroscience. In addition, more neuroscientists and psychiatrists are starting to work together to use combinations of psychotherapy and psychopharmaceuticals to increase the efficiency of both.

Another example of multidisciplinary collaboration is the ongoing revision of the Diagnostic and Statistic Manual of Mental Disorders, DSM-5, the standard classification of mental disorders used worldwide by clinicians to assist diagnosis and treatment. David Kupfer, chair of the task force in charge of the changes, explained that the new manual will incorporate the latest scientific knowledge and, in particular, the new developmental view of mental disorders by adding measures to assess the degree of severity of symptoms and focusing on issues of development across the life span for all mental disorders. Hopefully this will result in more accurate diagnosis and treatment.

## What remains to be done

### To reduce size and cost burden

- Optimize existing resources to improve primary prevention, prevent recurrence and secondary disorders, slow down disease progression, and reduce associated psychosocial impairment (Hans-Ulrich Wittchen)

### To reduce stigma and discrimination

- Increase public awareness via campaigns targeted at specific groups (Wulf Rössler)
- Improve patients' rights (Nikolas Rose)
- Empower patients to participate in decisions about treatments (Donna Franceschild and Nikolas Rose)

### To improve understanding of the causes of mental disorders

- Include the social environment in research on the causes of mental disorders (Nikolas Rose)
- Diversify research on the possible biological factors that contribute to the development of mental illness (Michael Rutter and Steven Rose)
- Remove the limitations of existing animal models and design better methods to study brain function in humans (Andreas Meyer-Lindenberg)

### To improve treatment

- Start more industry-academia partnerships to develop new effective drugs (Andreas Meyer-Lindenberg and Luca Santarelli)
- Develop public funding of drug trials, and encourage publication of clinical trial results in publicly accessible databases (Tim Kendall and Richard Smith)
- Evaluate efficacy of psychotherapies in a systematic way (Mathias Berger)
- Promote collaborations between neuroscientists, psychiatrists, psychologists and sociologists (Nikolas Rose, Mathias Berger)

## Further reading

The Size and Burden of Mental Disorders in Europe:  
[www.ecnp.eu/en/publications/reports/sizeandburden.aspx](http://www.ecnp.eu/en/publications/reports/sizeandburden.aspx)

WHO Global Burden of Disease 2004:  
[who.int/healthinfo/global\\_burden\\_disease/GBD\\_report\\_2004update\\_part3.pdf](http://who.int/healthinfo/global_burden_disease/GBD_report_2004update_part3.pdf)

WHO Grand Challenges in Global Mental Health:  
<http://grandchallengesgmh.nimh.nih.gov/>

NEWMED – Novel Methods Leading to New Medications in Depression and Schizophrenia:  
[www.newmeds-europe.com/en/news.php?hs=id3&display=block](http://www.newmeds-europe.com/en/news.php?hs=id3&display=block)

Diagnostic and Statistical Manual of Mental Disorders (DSM-5)  
[www.dsm5.org/Pages/Default.aspx](http://www.dsm5.org/Pages/Default.aspx)

For more information on the conference, videos of the talks and interviews with the speakers:  
[www.embo.org/science-policy/science-society/conferences/2011.html](http://www.embo.org/science-policy/science-society/conferences/2011.html)

