EUROPEAN SCIENCE FOUNDATION
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Exploratory Workshops Scheme

Standing Committee for the European Medical Research Councils (EMRC)

Scientific Report

ESF Exploratory Workshop on

Disentangling the Molecular Pathophysiology of Schizophrenia: Developing a Research Road Map for a Multidisciplinary European Team

London, United Kingdom, 26 October 2007

Convened by:

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1. Executive Summary

The meeting entitled “Forward a roadmap for European Schizophrenia Research” gathered members of the best European groups on schizophrenia research at the Institute of Psychiatry in London at 26th of October 2007. The intention of the workshop was bringing together schizophrenia researchers specialised in epidemiology, genetics, animal models, molecular neuropathology, and imaging in order to have a fruitful discussion on future research perspectives in this field. An internationally acknowledged expert summarised the state of the art for each outlined topic and furthermore was asked to outline future research questions in this area which should help to disentangle the molecular etiology of schizophrenia. Each talk was followed by an intense discussion focusing on the basics of future European research on schizophrenia. At the end of each of these discussions the opportunities of receiving efficient funding for the respective section were discussed in order to allow generating pivotal data and make a major contribution in examining one of the major mental disorders of human mankind.

2. Scientific content of the event

As outlined above and can be read in more details in the paper Falkai et al. „A Roadmap to disentangle the Molecular Etiology of Schizophrenia“ (Eur Psychiatry. 2008 Jun 24. [Epub ahead of print]). Members of the leading European schizophrenia research groups gathered in London at the Institute of Psychiatry in order to discuss a roadmap to coordinate research efforts for a better understanding of schizophrenia. Five topics were chosen and each of them was represented by one of the leading researchers by giving a short introduction along the following questions:

1. What do we know in this field?
2. What don’t we know?
3. What do we need to do in the next 5 to 10 years?

Mike Owen from Cardiff, England, summarised the evidence for a genetic transmission of schizophrenia. From other medical disorders can be concluded that “genome-wide association (GWA) studies have resulted in the identification of SNPs which confidently have been associated with for example coronary artery disease, atrial fibrillation, asthma, Crohn’s disease, etc. The success of these studies was based on the use of large patient and control samples and, of vital importance, follow-up analyses in even larger samples. Early GWAs of patients suffering from schizophrenia or bipolar disorder indeed are encouraging, but also underline the need for very large samples. This stresses the lack of knowledge in understanding the interaction and the extent of gene environment interactions in schizophrenia. Finally, Mike Owen denominated another area of ignorance concerning the optimal phenotype by emphasising the importance of checking the criteria of the so called endophenotypes. Actually, the clinical phenotype only poorly offers a suitably way for the identification of risk genes. This is the reason for Mike Owen pleading to continue with large scales GWAs on European level.

Inez Myin-Germeys from Maastricht, the Netherlands, summarised the environmental factors in the etiology of schizophrenia. She pointed at factors like urban upbringing, migrance status, experience of trauma or live events, season of birth and cannabis use as triggers for the disease. Further on she outlined the increasing evidence that the psychosis phenotype is a continuum in nature ranging from normal experiences over mild psychotic symptoms. She outlined the obvious lack of knowledge concerning the dynamics of the onset of the disorder and furthermore the need for refined measurements to define the outline of factors/macro-environment to identify gene-environment, environment x environment interactions in schizophrenia.

Paul Harrison from Oxford, England, in his summary adverted to some core neuropathological findings in schizophrenia concerning its molecular neuropathology. However, problematic is the little consented knowledge to what these findings mean for the disorder. He therefore suggested and presented accordant evidence and demanded that the field should concentrate on identifying the pathophysiological basis of key-risk genes like NRG-1 and others. He sees an urgent need for access to well characterized brain samples in order to have critical progress in this field.

Andras Bilkei-Gorzo from Bonn, Germany, summarised the requirements for animal models in schizophrenia. He pointed out that mouse knockouts of disc-1 and NRG-1 are interesting schizophrenia models as they seem to represent at least some relevant features. For future research he esteems animal models to be helpful in understanding the function of risk-genes in the living human subject. Generations of strains with high and low disease risk allelic variants and comparison of their phenotype will bring research closer to understand their role in the pathogenesis of this severe mental disorder.

Sophia Frangou from London, England, summarised that schizophrenia is associated with replicated structural as well as functional abnormalities in the brain. She continued to outline that there are several important questions which are unanswered yet:
1. Which imaging findings are relevant for schizophrenia?
2. What do the imaging findings mean?
3. Can imaging findings be connected to the symptomatology?
She concluded that within the next 5 to 10 years we want to gain insights about how remote cause or risk factors affect brain circuitry and behaviour in order to connect the etiological factors outlined above. Moreover, the causes for disease expression should be determined more explicitly. In order to retrospectively achieve these goals collected large sets of data should be pooled and in parallel large scale multisided studies should be performed prospectively.

In summary this stimulating scientific workshop brought together different fields in schizophrenia research fostering an intense discussion and nailing down how to pursue in this area in the next 5 to 10 years.

3. Assessment of the results, contribution to future direction of the field

More results of this workshop are summarised in a paper already published in European Psychiatry (Eur Psychiatry. 2008 Jun 24. [Epub ahead of print]) under the title “A Roadmap to disentangle the Molecular Etiology of Schizophrenia”. This paper has actually fostered intense activities around the 7th call of the EU and will lead to strong applications out of this group.

4. Final program

Below you find the final program as it was performed in London at the Institute of Psychiatry:

10.00 – 10.15	**Purpose and goals of the meeting** (P. Falkai / S. Frangou)
10.15 – 11.15	**Genetics** (Introduction by M. Owen for 15 min, followed by 45 min discussion)
11.15 – 12.15	**Epidemiology** (Introduction by I. Germeys for 15 min, followed by 45 min discussion)
12.15 – 13.00	*Lunch break*
13.00 – 14.00	**Molecular neuropathology** (Introduction by P. Harrison for 15 min, followed by 45 min discussion)
14.00 – 15.00	**Animal models** (Introduction by A. Bilkei-Gorzo for 15 min, followed by 45 min discussion)
15.00 – 16.00	**Imaging** (Introduction by S. Frangou for 15. min, followed by 45 min discussion)
16.00 – 16.30	**Summary statements** (S. Frangou / P. Falkai)

5. Statistical information on participants

The meeting was attended by 28 participants, plus one ESF Representative (not included in statistics below).

Gender repartition:

Male 21 Female 7

Geographical repartition (by country of work):

AT	1	FR	2
BE	1	GR	1
CH	1	HU	1
DE	7	IT	2
DK	1	NL	2
EE	1	UK	7
ES	1		

6. The final list of participants

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