ERA-Net Neuron

NEWSLETTER 6

Italy UK Finland Romania Germany Israel France Austria Luxemburg Poland Spain Sweden Canada

News from ERA-Net NEURON

ERA-Net NEURON chose "mental disorders" as the focus of the third joint call, to be published early 2010.

The review process of the proposals submitted in response to the second joint call on "Development and advancement in methods and technologies towards the understanding of brain diseases" was finalized. Ten applications were recommended for funding by the scientific review board and approved by the participating funding agencies. Detailed information on the funded projects will be published soon.

On June 2009, ERA-Net NEURON published a call for applications entitled "Awards for Excellent paper in Neuroscience". The awardees for 2009 are Heidi Nousiainen from Finland and Asya Rolls from Israel. The awards will be given in a ceremony to be held during the next FENS conference on July 5th, 2010 in Amsterdam.

We are glad to announce that the organizations 'Canadian institutes of Health Research' (CIHR) and the 'Québec Health Research Funding Agency' (FRSQ) joined ERA-Net Neuron as full partners.

Scientific Workshop
Mental illness and neural dysfunction
Paris (France), May 4 - 5th, 2009

Foreword - Alexis Brice, France

Psychiatric disorders place a huge and underestimated burden on society. Treatment and research into these disorders face numerous difficulties due to the complexity of the nervous system, limitations of current classifications of psychiatric disorders and paucity of relevant animal models. The variability of neuropsychological manifestations and the complex interactions between gene and environment result in further challenges.

In this workshop, four major psychiatric disorders, namely bipolar disorder, schizophrenia, autism, and drug addiction were explored by eight experts. These presentations help delineate the challenges facing the scientific community, and define the priorities for research into neurodegenerative and mental illnesses.

German Aerospace Centre, Project Management Agency

Federal Ministry of Education & Research (BMBF), Germany

Austrian Scuence Fund (FWF), Austria

National Authority for Scientific - Ministry of Education, Researc and Youth (ANCS - MECT), Romania

Ministry of Health (MOH), Italy

Academy of Finland (AKA), Finland

Ministry of Science and Innovation (MICINN), Spain

National Research Agency (ANR), France

National Center for Scientific Research (CNRS), France

National Institute for Medical Research (INSERM), France

Chief Scientist Office, Ministry of Health(CSO-MOH), Israel

National Research Fund (FNR), Luxemburg

The National Centre for Research and Development (NCBIR), Poland

Institute of Health Carlos III (ISCII), Spain

Swedish Research Council (SRC), Sweden

Medical Research Council (MRC), UK

National Centre For Programmes Management, Romania

Québec Health Research Funding Agency

Canadian institutes of Health Research, Canada

Funded by the European Commission

More information can be found in our web page
http://www.neuron-eranet.eu/index.php

Scientific Workshop

Neurogenetic mechanisms of Schizophrenia

Andreas Meyer-Lindenberg
Central Institute of Mental Health, Mannheim, Germany

Schizophrenia is largely genetic, and a novel approach is to link gene variants associated with the risk for schizophrenia with abnormal brain mechanisms. One heritable change is a thinner and functionally abnormal prefrontal cortex, and abnormal prefrontal-hippocampal circuitry. Prefrontal dysfunction is coupled to striatal dopamine disinhibition in schizophrenic patients. Indeed, the Val allele of the COMT gene, linked to schizophrenia, results in reduced dopamine in the prefrontal cortex, affects working memory and prefrontal signal to noise. Drugs that inhibit COMT thus improve cognitive function in Val/Val subjects specifically. A variant of KCNH2, a gene encoding a potassium channel, also confers risk for schizophrenia and affects hippocampal activity. COMT and GRM3, a metabotropic glutamate receptor shows an epistatic interaction in the prefrontal cortex. A partial agonist of GRM2/3 is proving to be an effective antipsychotic with no dopaminergic side effects.

Schizophrenia, a neurodegenerative disorder?

Celso Arango
Hospital General Universitario Gregorio Maranon, CIBERSAM, Madrid, Spain

Schizophrenia is associated with progressive degenerative brain changes. Within 5 years of the first episode, a significant decrease of grey matter is observed, especially in the frontal and temporal lobes. The extent of some of these changes seems to be determined genetically, but also by the duration of psychosis. It is not clear what is the role of the antipsychotics in these progressive changes. Degenerative changes, however, may also precede external manifestations of the disease. Generally, such changes are seen also in non-schizophrenic psychoses, but a decrease in volume of the left middle frontal gyrus may be specific for schizophrenia, as are degenerative changes in the left dorso-lateral prefrontal cortex. Such changes may be precipitated by an inflammatory processes or oxidative stress. Indeed, in schizophrenia and bipolar patients, antioxidant levels are significantly lower than in controls and levels of oxidative stress markers are higher.

Scientific Workshop

Neurocognition and functional outcome in bipolar disorder

Eduard Vieta
Clinical Institute of Neuroscience, Barcelona , Spain

Bipolar disorder (BD) is intimately linked with long lasting disability, with 89% of patients experiencing some occupational impairment. Whereas clinical symptoms are effectively treated, after the first episode less than 40% of patients return to their previous occupational status. Even in euthymic patients, BD is linked to cognitive impairment, mainly in processing speed and attention, which is worse for people carrying mutations in neurodevelopment genes LIS1 and PAFR. In contrast, as children, people who developed DB later on in life had better motor and cognitive skills than healthy peers, hinting that a neurodegenerative process is taking place, possibly due to changes in levels of cortisol and neurotrophins. Grey matter loss is also seen, and its extent is correlated with the number of episodes and the level of cognitive impairment. Overcoming this negative cycle requires mood stabilizers, psychoeducation and cognitive remediation.

Evidence based psychological interventions for psychosis: individual cognitive behavioural therapy and family intervention

Elizabeth Kuipers
King's College London, United Kingdom

Psychosis is associated with reduced employment, ill health and increased mortality. First line of treatment is medication but up to 40% of people show limited improvement. Psychological interventions now have an evidence base, showing that CBT can help improve persistent symptoms, and family intervention reduces relapse. These approaches stem from cognitive models positing that vulnerable individuals make pathological appraisals leading to the persistence of positive psychotic symptoms. Bio-psycho-social vulnerability is triggered by stressful events leading to misinterpreted unusual experiences that are appraised as worrying, and it is this that leads to symptoms. Recent research confirms that psychosis is part of a continuum in that specific symptoms, such as psychotic thoughts and paranoid ideas, exist also in the general population. Finally there is overlap between psychosis and emotional problems, such as depression, low self esteem, and obsessive compulsive disorder. This understanding has helped develop these psychological approaches.

Scientific Workshop

Bipolar disorder: neurobiology, challenge of early detection and treatment

Guy Goodwin
University of Oxford, United Kingdom

Bipolar disorder (BD) afflicts at least 4-5% of the population, but it remains largely undiagnosed, particularly due to difficulties in distinguishing it from major depression. In addition, initial diagnosis is often delayed, thereby postponing essential treatment. The disorder ranges from so called manic depression to people who experience only depression. Within this spectrum, the definition of hypomania holds the key to differentiating between BD and unipolar depression, potentially influencing treatment and genetic studies. In fact, experiencing manic symptoms appears to be an early risk factor that may help trigger BD, but not depression. From screening 19 years old students for manic symptoms, it seems that 2-4% of students suffer from BD, almost all undiagnosed. Finally, an understanding of the neurocognitive mechanisms moderating the impact of provoking mechanisms may be critical for accurate diagnosis and for developing better drugs and psychological treatments.

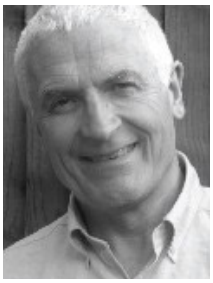
Questions about addictions that can or should be addressed by experimental research. Experimental research on drug addiction: a turning point

Véronique Deroche-Gamonet
Neurocentre Magendie, Bordeaux, France

The mechanisms underlying transition from occasional drug use to addiction are poorly understood, despite 40 years of research efforts. Unadaptation of experimental preparations to a drastic conceptual change in the clinical vision of addiction could help explaining this situation. A decisive step has been taken five years ago when pertinent animal models were developed. Two disctinct vulnerable phenotypes were revealed to lead to addiction. A “drug prone” phenotype facilitates the shift from occasional to sustained drug use. An “addiction prone” phenotype promotes addiction in a reduced proportion of the sustained users. The “drug prone” phenotype involves interactions between glucocorticoids and the meso-accumbens dopaminergic transmission. The transition from regular use to addiction is still biologically poorly characterized, but the preliminary data revolutionize the common perception. Addiction would be less the result of drug-induced alterations than the inability to counteract drug-induced alterations.

Epidemiology of mental illnesses

Paul Bebbington
University College London, United Kingdom



Epidemiology is a powerful tool, capable of generating valuable information for neuroscience. The key concept in epidemiology is the case, identifiable by case and syndrome definitions. Such specifications are difficult to formulate, and must be validated empirically. It seems, for example, that current definitions fail to adequately encompass the complexity of schizophrenia. The difficulties in psychiatric diagnosis led to somewhat arbitrary operationalisation and standardisation, reducing the validity of case identification. Current case identification instruments include fully structured questionnaires (CIDI and CIS-R), and semi-structured interviews (SCAN). These instruments underlie large psychiatric surveys, sometimes leading to very disparate results between countries. Thus, the global relevance of such surveys is questionable. In addition, these enormous data sets are under-analyzed. Finally, we should consider inserting neurocognitive tests and collecting genetic material in such surveys, to enable more sophisticated data analyses.

Synaptic and clock genes in autism spectrum disorder

Thomas Bourgeron
Institute Curie, Paris, France

Autism spectrum disorder has a strong, but complex, genetic basis. In an effort to elucidate the connection between autism and genes controlling neuronal signalling, three gene families were isolated: neuroligins, SHANK3 and neurexin. The neuroligins are post-synaptic cell-adhesion proteins, and mutations in these genes may lead to Asperger syndrome or delayed speech. SHANK3 is a scaffolding protein located at glutamatergic synapses. In this case, one normal gene copy leads to almost complete absence of speech, whereas 3 wild type copies lead to Asperger syndrome. These genes lead to defects in synaptogenesis, and knock-out mice are defective in social interactions. Another axis of the research focused on circadian rhythm, showing that Autism is correlated with low levels of melatonin and with defects in the ASMT gene coding for the last enzyme of the melatonin synthesis pathway.