ECNP Targeted Expert Meetings (TEMs)
2-3 September 2011, Paris, France

Report on the TEM Dementia
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The focus of the meeting was on basic molecular mechanisms of neurodegeneration, in particular the role of protein aggregation, the modelling of disease mechanisms and treatment paradigms in transgenic animals, advances in molecular imaging of pathology in humans, and the translation of these findings into concepts of better clinical trial designs for drug development in Alzheimer's disease (AD) or subjects at risk for AD.

Brian Bacskai, USA, expanded on protein aggregation and related toxicity in transgenic mouse models as well as patients with AD with respect to the development of novel therapeutics by active immunisation or antibody transfer. The discussants, Frank Heppner, Germany, and Lawrence Rajendran, Switzerland, pointed to the eminent role of the cellular immune system in amyloid clearance from the brain, in particular glial cells and macrophages, and to the obvious complexity of the molecular and cellular basis of the disease as opposed to the over simplistic amyloid cascade hypothesis.

Chet Mathis, USA, inventor of the Pittsburgh compound B (PiB), which is now in widespread research use to image beta-amyloid in the brain of patients with AD and subjects at risk for dementia, reported on the potential of PiB and other ligands to be used as surrogate markers of clinical trials, along with CSF biomarkers and MRI imaging. Giovanni Frisoni, Italy, and Agneta Nordberg, Sweden, underscored the potential of beta-amyloid imaging in drug trials as well as identification of future converters from MCI to AD, in particular when combined with advanced MRI methods assessing brain morphology, connectivity and function.

Lon Schneider, USA, elaborated on clinical trial designs to test the amyloid hypothesis of Alzheimer's disease. He summarized past successes and failures of AD trials and identified critical areas of the current study designs, e.g. variability of diseases courses, variability of outcome ratings, target identification, patient selection, sample sizes and power, timing of the therapeutic intervention, and use of biomarkers related to expected actions of the drug. Ezio Giacobini, Switzerland, pointed to the limitations of translating results from studies in transgenic mouse models to human patients, and, finally, Jean-Marc Orgogozo, France, stimulated by earlier study designs suggested by Leber, 1999, proposed a parallel group assessment of disease modification in AD, termed 'Natural History Staggered Start Design'.

The presentations were followed by extensive and lively debates by the main lecturers, discussants and participants from more than six European countries and the USA.