Summary of the Consensus Statement drafted by the European Brain Council (EBC) on November 26th 2015: "The need to expand Brain Research in Europe"

Morris RGM[1], Oertel W[2], Gaebel W[3], Goodwin G[4], Little A[5], Montellano P[6a], Westphal M[7], Nutt DJ[8], Di Luca M[1]

[1]Federation of European Neuroscience Societies (FENS); [2]European Academy of Neurology (EAN); [3]European Psychiatric Association (EPA); [4]European College of Neuropsychopharmacology (ECNP); [5]European Federation of Neurological Associations (EFNA); [6]Global Alliance of Mental Illness Advocacy Networks-Europe (Gamian-Europe); [7]European Association of Neurosurgical Societies (EANS); [8]European Brain Council

The complexity of the brain defies our attempts to fully understand how it coordinates the body's functions, knowledge that is fundamental in the search for cures of its malfunction. Indeed, this complexity has long hindered the analysis, diagnosis and treatment of Neurological Disorders, as reflected by the heavy burden they impose on health services and the increasing strain associated with the ageing of the European population. Continued commitment has advanced our understanding of the nervous system, with Europe leading efforts in basic research aimed at understanding the brain, as well as in the practical and clinically application of this knowledge. However, while Brain Research has been considered a priority for European funding, and it has been an important recipient of the European budget for medical research, only through continued and coordinated support can it be hoped that real solutions will be found.

Brain disorders currently affect 179 million individuals in Europe and they will affect one in three Europeans during their lifetime. Indeed, the cost of brain disorders to the European economy and national health budgets is calculated to be nearly €800 billion per annum, 45% of the annual European health budget and comparable to that of cancer, cardiovascular diseases and diabetes together. These figures justify the increase in research funding that we have witnessed this century, yet it is important for such support to be strongly coordinated and well directed. Major developments in non-communicable diseases have demonstrated the immense benefits to be gained from dynamic collaboration between all stakeholders committed to progress, encompassing patient organisations, academics, scientists, medical experts and industry. The **EBC** aims to ensure such achievements are made in the area of Brain Diseases, aligning the funding available with recently identified opportunities (see Annex 1 and full Consensus Document) and escalating progress in this field. One focus will be on establishing closer collaborations that will favour better integration among experimentalists, both in traditional and emerging areas of neuroscience (encompassing computational neuroscience and emerging technologies).

Basic research can yield amazing and sometimes unexpected gains. While there has been a clear shift to ensure that the 'translational' potential of basic science is realized, the path to achieving this is far from straightforward[b]. Progress has been made, yet there is still a clear need to educate researchers in more academic environments as to how to ensure their findings are translated into returns for industry and society. Moreover, to ensure that discoveries in basic neuroscience, and in the diagnosis and treatment of brain disorders, can move swiftly into a clinical setting, the high quality translational workforce in Europe must be enriched, providing benefits to both European Industry and patients alike. It is noteworthy that the healthcare sector accounts for 8% of the European workforce, producing 10% of the EU's GDP. As such, it is imperative for us to not only halt the tendency of pharmaceutical

[a] *The author passed away on the 2nd October 2015*

[b] For a drug to reach market requires more than a decade and hundreds of millions of Euros, with 85% of therapies failing in clinical trials and only half of those that pass ultimately obtaining approval.

companies to move out of Europe for administrative and economic reasons, but we must invigorate the return of the pharmaceutical industry and of other translational health research initiatives to Europe to optimize the pipeline for technology transfer.

Key Facts

Annual European Budget dedicated to diseases affecting the Nervous system	€ 800 billion (45 % of total annual Health budget)
Europeans currently affected by brain disorders	127 million individuals, 35% of the burden of all diseases in Europe.
EU Funding dedicated to brain-related research since 2007 (FP7)	> €3.1 billion (> €300 million/year)
No of EU projects funded since 2007 (FP7)	1,931
The EBC, established in 2002, represents the main European stakeholders in Brain sciences	FENS[c], EAN[d], EPA, ECNP, EFNA, IBRO PERC Gamian-Europe & EANS

The opinion of Europe's most outstanding young neuroscientists and its more senior leading figures in the field provides us with insight into the 'challenges' we are currently facing. While reiterating the clear reliance on fundamental science to achieve clinical progress, a critical need for a more interdisciplinary focus becomes evident, a shift already underway in many instances. There is a strong prevailing desire to maintain European competitiveness in brain research and young scientists still feel Europe leads research into many neurological disorders, especially due to excellent transnational collaborations. However, a feeling persists that European scientists must too often rely on tools, services and data-sharing repositories in the USA. Moreover, and despite the impressive groupings of basic scientists and some new initiatives (e.g., the Francis Crick Centre, London), Europe lacks major life sciences facilities and infrastructures. Thus, efforts must be made to ensure that the research environment in Europe is optimal to retain the best-trained young scientists in this discipline and provide them with the means to flourish.

Conclusions

It is imperative to improve the prevention, treatment and management of brain disorders for humanitarian, medical, scientific, societal, political and economic reasons. Accordingly:

- **We call on European authorities to devise and implement a plan to tackle brain health in an integrated and comprehensive manner in cooperation with all EU member states.**
- **We highlight the need to augment the support for basic and clinical brain research in Europe through current funding platforms, especially to retain promising young neuroscientists.**
- **We recommend the EBC serve as a liaison to optimise support for patients and research, and to ensure funding support is best aligned with today's fundamental challenges and opportunities.**
- **Nevertheless, it is the joint responsibility of all stakeholders to ensure that basic research is adequately translated into concrete applications.**

Only by maintaining brain science high on the political agenda can both basic and clinical research be fortified, and the burden of brain diseases reduced, preventing them from becoming a societal emergency.

[c] FENS in figures: 24,000 members in 42 scientific societies (biannual meetings > 6000 participants).
[d] EAN in figures: 25,000 members in 46 national neurological societies.

Annex 1 – Outline of the major areas where our efforts in brain research should be focused, drawn up on a consensus based on urgency and tractability

Area	Challenge
1. Making the brain: developmental neuroscience	The challenge in developmental neuroscience is to establish bridges with systems neurosciences to define how altered development (pre- and post-natal) affects the adult CNS and the risk or susceptibility of brain disorders (including dyslexia, dyscalculia, attention disorders, autism, schizophrenia and similar complex syndromes). Molecular and biochemical studies into brain development must be complemented by functional studies to make sense of the properties of neural circuits.
2. Understanding the causal mechanisms: linking cellular/molecular mechanisms to complex behaviours and disease states	Bridging multiple spatial and temporal scales is a major challenge in neuroscience (e.g., molecular, genetic and neural), as is understanding how different systems in the body (e.g., immune system, cardiovascular system, etc.) influence the complex behaviour of the brain and nervous system. We must understand how molecular events in neurons affect information processing at the circuit level, and how these circuits are integrated to control behaviour and cognition in both normal and pathological situations. This requires overcoming technical hurdles to simultaneously access the activity of many neurons and to combine single-spine imaging with whole-cell recordings in vigilant animals, beyond the capacity of all but a very few laboratories.
3. Information processing: what the brain does.	The brain controls behaviour through elaborate related mechanisms: sensing the world around us (seeing, hearing, etc…) and the world within (proprioception); transforming this sensory input into object-oriented understanding (perception); associating this knowledge with stored information; and organising actions and habits guided by emotion and motivation. Many aspects of these processes remain a mystery, especially fundamental concepts like numerosity and decision-making, as well as how they are impaired in neurological and mental health disorders.
4. Emerging technologies	Europe must ensure that the imagination of its scientists leads to novel technologies that open new windows on discovery, focusing on: ways to study and non-invasively monitor activity in the human brain; new methods for big data analysis and the integration of multisource, complex data to formulate new theories; optogenetics to measure synaptic plasticity and degeneration; and functional imaging at cellular resolution.
5. Brain and mental health disorders of children and adults	Despite advances in their prevention and treatment, the burden of neurological and psychiatric brain diseases on our society persists, reflecting the need to understand these disorders at the circuit level through novel technologies and enhanced collaboration between European centres of excellence.
6. Computational Neuroscience and data repositories	The exponential growth of the data produced in neuroscience mean that computational approaches are fundamental to make sense of this information, including theoretical modelling and methods for large scale data analysis/integration that are capable of handling and comparing data generated over such diverse timescales (e.g. synaptic versus genetic changes). As such, quantitative theoretical neuroscience must be gradually integrated with mainstream experimental neuroscience.
7. Understanding and Improving Drug Delivery to the Brain	Increasing insight into the pathophysiology of brain diseases has led to the development of many promising drugs, yet their delivery represents an important challenge for agents other than “small molecules”. Thus, a concerted effort is needed to develop technologies for interstitial delivery, either directly or by specific manipulation of the BBB. Furthermore, the pharmaceutical industry must be encouraged to embark on drug development programmes to stall or reverse neurodegenerative processes.