Preface

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This meeting constituted the 4th International Conference on Brain Energy Metabolism, the previous meetings having been held in Carcassonne, France, 1993; Blaubeuren, Germany, 1995; Waterville, New Hampshire, USA, 1997. It was also sponsored by the Biochemical Society as the 49th Harden Conference and the International Society of Neurochemistry (ISN) as a satellite meeting to the ISN/ESN meeting in Berlin. It took place August 14–18, 1999, at the idyllic setting of Eynsham Hall (see picture) in the Cotswold country near Oxford, UK, and was dedicated to Derek Williamson, who had participated in the first meeting of this series and had agreed to be a keynote speaker at this meeting, but who had sadly died just prior to the meeting. The theme of the meeting was 'Functional Aspects of Energy Metabolism in Brain', concentrating particularly on brain development and neurodegenerative diseases. Nineteen speakers from 10 countries from around the globe gave plenary contributions, whilst a further 10 participants took the lead in 2 workshops; one upon 'Non-Invasive Techniques for Analysing Brain Energy Metabolism' and a second addressing 'Infant Nutrition – Brain Development and Disease in Later Life'. Forty-five poster presentations related to the themes of the conference were held in a session for this purpose on the second day of the conference; posters were on display throughout the meeting for viewing and discussion during coffee/tea recess. Approaching 100 scientists, clinicians and dieticians attended the meeting and enjoyed the good food, superb setting and relaxed atmosphere which has become the hallmark of these conferences.

David Barker of the MRC Epidemiology Unit (UK) set the scene highlighting in particular why prenatal brain-sparing and subsequent accelerated linear growth may be harmful, resulting in a predisposition for cerebrovascular disease. Norbert Herschkowitz (Switzerland) lent a paediatrician's view to early brain development, highlighting the propensity that premature infants have for serious cerebral damage, whilst Tony Costello of the Institute of Child Health, London (UK), discussed the importance of adequate glucose homeostasis as evidenced by his work in Nepal. This was subsequently complimented by Sylvia Salvati (Italy) who explored the crucial role dietary lipids play in myelinogenesis.

In a plenary session designed to introduce the first workshop, Graham Kemp (UK) gave a lucid theoretical talk on the valuable role MRS could potentially play as a non-invasive monitoring system. This was amply illustrated by John Wyatt (UK), who described his work in infants with acute perinatal asphyxia, which has shown that secondary impairment of oxidative phosphorylation is highly correlated with adverse neurodevelopment, whilst protection can in part be afforded by applying moderate cerebral hypothermia. MRS as well as other methods, particularly the potential utility of near infrared spectroscopy, were discussed in depth during the first evening's workshop, which despite a gruelling ISN meeting the previous week, and it being Sunday, went on late into the evening.

Day two of the meeting focussed upon the mechanisms associated with perinatal hypoxic/ischaemic brain damage. Following discussion of those changes seen in neo-

Eynsham Hall, near Oxford (UK). Location of the meeting (with thanks to June Smalley).

nates (Waney Squier, UK), Bob Vannucci (USA) described his rat model and suggested that glutamate excitotoxicity is a late event in this condition, whilst further proposing that even in mature neurons, a cellular energy debt is a necessary prerequisite for excitotoxic cell death. Neil Sims (Australia) using the same model illustrated that increased intramitochondrial calcium is an early event in ischaemia/hypoxia and results in the opening of the mitochondrial permeability transition pore giving rise to redistribution of cellular glutathione. In an elegant presentation, Sten Orrenius (Sweden) linked these findings to the release of cytochrome c from mitochondria and activation of the caspase system and apoptosis. He contrasted this to necrotic cell death which would be expected to be seen if diminution of the mitochondrial membrane potential and subsequent ATP depletion occurred. Bruce Kristal (New York) showed how metabolites known to accumulate in various neurodegenerative conditions could open the mitochondrial transition pore. He particularly focussed up the ganglioside GD3, as well as the aldehyde products of MAO metabolism of epinephrine and dopamine, DOPEGAL and DOPAL, compounds known to be raised in the brains of patients suffering from Alzheimer's and Parkinson's diseases, respectively.

The third day focussed primarily on intracellular signalling mechanisms and was set off to a flying start by Regino Perez-Polo (USA). He described the reversal of cognitive and cholinergic deficits in rats by nerve growth factor (NGF). In addition, he showed how a number of other genes whose transcription is regulated by NF- κ B, an agent that is particularly sensitive to oxidative stress, can be modulated by NGF. The theme of oxidative

stress, and in particular the symbiotic relationship between neurones and astrocytes with respect to glutathione was taken up by Ralf Dringen (Germany) and Simon Heales (UK). Both illustrated, using a neurone astrocyte co-culture system, how glutathione released from astroglial cells is subsequently split by the astroglial ectoenzyme γ GT to generate the dipeptide CysGly, which serves as a precursor of neuronal glutathione. Dringen went on to show that catalase is another important neuronal antioxidant system, whilst Heales suggested superoxide dismutase released from the astrocyte served to protect, for neuronal use, astroglial released glutathione, and that reduced neuronal mitochondrial GSH levels in response to oxidative stress could result in impaired neuronal energy metabolism.

This latter theme was taken up by Mark Mattson (USA) when he considered Alzheimer's disease and the pro-oxidant activities of A β peptide. He illustrated how in addition to mitochondrial damage, significant inhibitory effects upon the glucose and glutamate carriers of the neuronal plasma membrane were caused by A β -induced oxidative stress. Eric Shoubridge (Canada) reminded us all that mitochondrial dysfunction was central to a wide range of mitochondrial encephalomyopathies. He also presented some recent data illustrating disease based upon abnormalities of the assembly factor for Complex IV (Surfl), illustrating for us the structural and vectorial complexity of the respiratory chain. Finally, his discussion of the complex topic of genotype-phenotype relationships in mitochondrial disease was a perfect platform for Jean-Pierre Mazat (France) to present his ideas upon threshold effects and tissue specificity.

After three hard days of science, interrupted only by a short break for some leisure activities including horse riding and getting to grips with the carding, spinning and weaving of wool, there remained the Karger Lecture. This was given by Prof. John Edmond of the University of California at Los Angeles. He highlighted quite beautifully from his studies of several years, how the brain is autonomous in terms of lipogenesis and that this could be considered a mechanism to spare and protect the integrity of the developing brain.

Prof. John Clark (UK) presented John Edmond with a plaque from his friends and colleagues, marking the outstanding contribution that he has made to neurochemical science. Delegates then adjourned to the farewell conference dinner: a Bar-B-Que, accompanied by an excellent local jazz quartet. At last they were able to enjoy the splendour of the venue and reflect that the meeting had been a fitting tribute to Derek Williamson.

This special issue presents papers which reflect the proceedings of the energy conferences from either the plenary or poster presentations. The editors express their gratitude to the many reviewers who gave of their time and expertise to ensure a thorough evaluation of the manu-

scripts. Each manuscript was subjected to the regular and expected review accorded all manuscripts that are submitted to *Developmental Neuroscience*.

The organisers of this conference – the three Johns – are grateful to their advisory committee, Nancy Auestad (Columbus, Ohio), Mary McKenna (Baltimore, Md.), Bill Nicklas (Piscataway, N.J.) and Neil Sims (Adelaide, Australia), for their help in drawing up the programme and seeking sponsors. We are particularly grateful to the Biochemical Society, whose meeting office under the stewardship of Sheila Mills, Katrina Light and Kate Harris undertook all the administrative tasks associated with this conference as well as supporting us financially. Other sponsors who generously supported us financially were: Clinical Reference Laboratories Inc., Kans., USA; Guarantors of Brain; ISN; Martek Biosciences Corporation, USA; Milupa GmbH & Co, KG, Germany; Nestlé SA, Switzerland; Ross Products Division, Abbott Labs, USA; S. Karger AG and Scotia Pharmaceuticals plc.

We are now looking forward to the next conference in this series to be organised by Ursula Sonnewald and Arne Schousboe in Trondheim, Norway, 19–23 May, 2001.