20th National Meeting of the British Neuroscience Association

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On 19–22 April 2009, the British Neuroscience Association held its 20th National Meeting in the Adelphi Hotel in Liverpool, UK. The conference included seven plenary lectures, 20 symposia, 42 poster sessions, four workshops and one satellite meeting, and attracted almost 600 delegates.

The conference was preceded by a satellite meeting on glutamate receptors, during which Jon Hanley (University of Bristol, UK) explained the importance of the protein PICK1 in AMPA receptor trafficking during ischemia. He proposed that PICK1 regulates the amount of calcium-impermeable AMPA receptors, which contain the selective glutamate receptor (GluR)-2 subunit, by endocytosis in response to NMDA-induced synaptic activity. These receptors are replaced with calcium-permeable GluR2-lacking AMPA receptors, which could lead to the delayed cell death seen in cerebral ischemia. Giles Hardingham (University of Edinburgh, UK) described the fine balance between NMDA receptor signals influencing neuronal survival or death. NMDA receptor activity can mediate neuroprotection from oxidative stress and apoptotic insults, by suppressing elements such as cytochrome C, caspases and prodeath genes. Conversely, NMDA receptor signaling via JNK and p38 can cause neuronal cell death. He explained that neuroprotection can be achieved by using a combination of p38 (TAT-NR2B9c) and JNK (D-JNKI1) inhibitors.

The conference opened with a plenary lecture from Dick Passingham (University of Oxford, UK) who discussed the benefits and limitations of brain imaging. Many studies have used functional MRI to investigate correlations between specific brain areas during tasks, but the future of brain imaging lies in uncovering the mechanisms that underlie these correlations and understanding how the system works as a whole using computational models.

In the first symposium, devoted to steroid hormones and neuroprotection, Hilary Carswell (University of Strathclyde, UK) highlighted the gender-dependent susceptibility to cerebral ischemia. Premenopausal women have a decreased risk of stroke, but equal risk to that of males in postmenopausal years, suggesting that estrogen is neuroprotective. Interestingly, studies involving women receiving hormone-replacement therapy demonstrated a varied risk for stroke. Exogenous estrogen has been shown to be neuroprotective in a wide range of ischemic models, yet the mechanism by which this occurs is still unknown. A link with ApoE has been proposed since estrogen loses its neuroprotective effects in ApoE-knockout (KO) mice. Claire Gibson (University of Leicester, UK) presented progesterone as a potential therapeutic treatment for stroke. Progesterone reduced ischemic brain injury in rodents, which was accompanied by better outcome. She proposed that progesterone acts directly on nuclear receptors and GABA receptors to reduce necrosis, and indirectly by reducing edema. Progesterone reduced the production of nitric oxide as well as IL-1β. A Phase III clinical trial has recently been launched at 17 centers across the USA to investigate the neuroprotective effects of progesterone following traumatic brain injury.

In a symposium on neural stem cells (NSCs), Victoria Chistie from the spin-out company Reinnervate (Durham University, UK) demonstrated that neurodifferentiated H9 cells are electophysiologically active (as measured by GABA- or glutamate-induced Ca^{2+} influx). The company is also involved in development of small and more stable analogues of retinoic acid to induce differentiation of NSCs. Using patch-clamp studies, Bob Halliwell (Pacific, USA) demonstrated that NSCs express all ion/receptor channels. Glutamate, glycine, GABA and NMDA are able to induce Na^{2+} and K^{+} currents in NSCs with very similar

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pharmacokinetic properties to those observed in primary neurons. Excitotoxicity also occurs in NSCs in the presence of excess glutamate. Last, Saga Johansson (King's College London, UK) demonstrated that immunosuppression, which is required to promote NSC survival after administration, is mainly dependent on expression of MHC class I and II (from NSCs and the host). Cyclosporin-induced immunosuppression is required to reduce lymphocyte infiltration that is triggered by graft.

One highlight of the symposium on neural basis of drug addiction was a talk by Jonathan Lee (University of Birmingham, UK) who presented evidence that drug addiction is memory related and can be managed through manipulating memory reconsolidation. The transcription factor Zif268 is upregulated during memory reconsolidation and knocking down Zif268 reduced the levels of cocaine self-administration in rats, demonstrating that Zif268 could therefore be important in drug addiction.

In a symposium on neuronal G-protein-coupled receptor (GPCR) trafficking, Tristan Bouschet (University of Bristol, UK) highlighted the importance of calcium-sensing receptors (CaSR), a class III GPCR, in calcium signaling and homeostasis, and presented data on the trafficking pathway of CaSR. By using pH-sensitive green fluorescent protein molecules (Super Ecliptic pHluorins) tagged to CaSR (SEP-CaSR), he demonstrated that receptor activity-modifying proteins (RAMPs) are required for CaSR translocation through the secretory pathway for delivery to plasma membranes. RAMPs mediate removal of endoplasmic reticulum-retention motifs from CaSR, allowing transport to the cell surface. Kumlesh Dev (Trinity College Dublin, Ireland) presented recent work on the mechanisms of action of a sphingosine-1-phosphate (S1P) receptor agonist, FTY720, which is a potential new oral treatment for multiple sclerosis (currently in a Phase III clinical trial). Binding of FTY720 to S1P receptors expressed by autoreactive T cells mediates internalization of these receptors rendering the T cells unresponsive to chemotaxis. Subsequently, these autoreactive T lymphocytes are retained in peripheral lymph nodes and do not infiltrate the brain.

A very interesting symposium was on sleep and circadian dysfunction in neurological disorders, during which Michael Hastings (University of Cambridge, UK) and Eus Van Someren (Netherlands Institute for Neuroscience, The Netherlands) highlighted the importance of the circadian system in dementia. Emphasizing that the primary cause of dementia in patients entering nursing homes was restlessness during the night, they suggested that breakdown of the body's 24-h clock correlates with cognitive decline. This circadian breakdown occurs due to a reduction in the number of vasopressin-expressing cells that promote sleep. Van Someren explained that his method of exposing rats to bright lights to increase the number of vasopressin cells had successfully been moved to the clinic, with light-treated patients not only showing an improvement in their sleep patterns but also in the depression, agitation and cognitive deterioration associated with dementia.

The Wolstencroft Lecture was delivered by Nancy Rothwell (University of Manchester, UK) who presented IL-1 as a key mediator of inflammatory responses to acute brain injury. A truly translational story began with the finding that IL-1 mediates brain injury and its naturally occurring antagonist (IL-1RA) massively reduces brain damage in experimental models. She demonstrated the neuroprotective effects of IL-1RA in a small Phase II clinical trial, and the future aim is to conduct a full pharmacokinetic study of IL-1RA in patients with subarachnoid hemorrhage.

In a symposium on prion diseases, Hugh Perry (University of Southampton, UK) demonstrated that microglial activation (induced by engulfment of previously injected misfolded prion protein) correlates with cognitive deficit. He showed that this activation is accompanied by expression of a robust anti-inflammatory profile (TGF-β, prostaglandin E_2), and showed that neurodegeneration occurs at the synapses.

In a symposium on neuron–glia interaction in plasticity and pathology, Arthur Butt (University of Portsmouth, UK) demonstrated that astrocytes couple cerebral blood flow to neuronal activity by mediating the communication between vascular cells and neurons. NG2-expressing glia and pericytes are undifferentiated cells that are also involved in this communication system.

In the symposium on the biology of myelination, David Lyons (Stanford University, CA, USA) demonstrated that *Kif1b* is required for the transport of myelin-specific proteins from the trafficking machinery to the myelin sheath. Zebra fish with disrupted *Kif1b* displayed hypomyelination as well as ectopic

myelination, which was attributed to the failure of myelin basic protein to localize in the myelin sheath. Evidence presented suggests that *Kif1b* is required for mRNA localization of myelin-forming proteins to ensure normal rates of myelin formation, and specific myelination to prevent the formation of an ectopic myelin sheath.

Casper Hoogenraad (Erasmus Medical Center, Rotterdam, The Netherlands) presented, during a symposium on synaptic plasticity, elegant experiments using EB3–green fluorescent protein fusion protein that allows visualization of polymerizing ends of microtubules. He showed by live imaging that polymerizing microtubules enter into dendritic spines promoting β-actin filament formation, leading to enlargement of dendritic spines and therefore increasing synaptic plasticity.

The meeting ended with two plenary lectures. David Porteous (University of Edinburgh, UK) described how one Scottish family has helped unravel some of the genetic mysteries of mental illness disorders, such as schizophrenia and depression. Damage to the novel Disrupted in Schizophrenia 1 (*DISC1*) gene on chromosome 1 was found in members of the family who suffered from mental illness. Malcolm Brown (University of Bristol, UK) discussed the issue of whether recognition memory is a process located in one or several regions of the brain. The focus of his research is to understand the mechanisms of neural plasticity in the perirhinal cortex that is responsible for the familiarity element of recognition memory. His team is now able to make stable recordings from perirhinal neurons while rats are given visual stimuli, and they are currently identifying the signaling mechanisms that regulate recognition memory.

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