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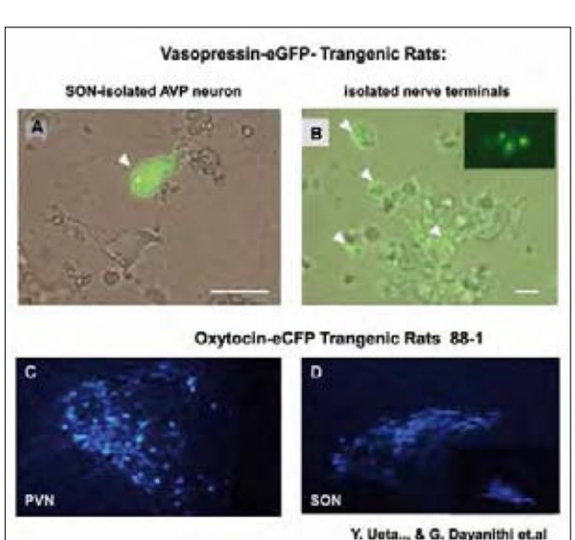
RESEARCH TOPICS

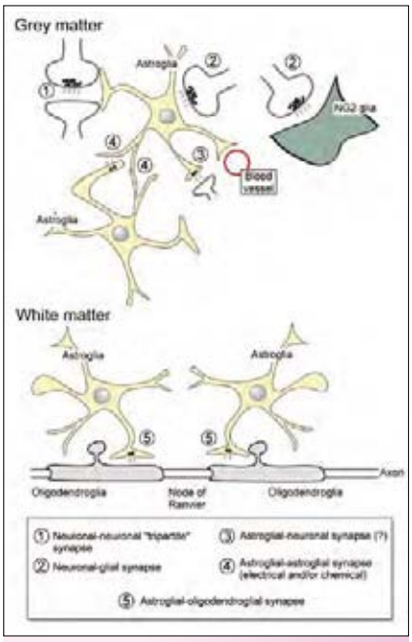
The identification of the cellular and molecular mechanisms of integration in neural networks, through the characterisation of intercellular signalling pathways within neuronal-glial circuits and intracellular signalling mechanisms in neurones and glia under physiological and pathological conditions:

– The role of glutamatergic and purinergic pathways in neuronal-glial signalling in the cortex, hippocampus and spinal cord with a specific emphasis on the glial NMDA and P2X receptors;

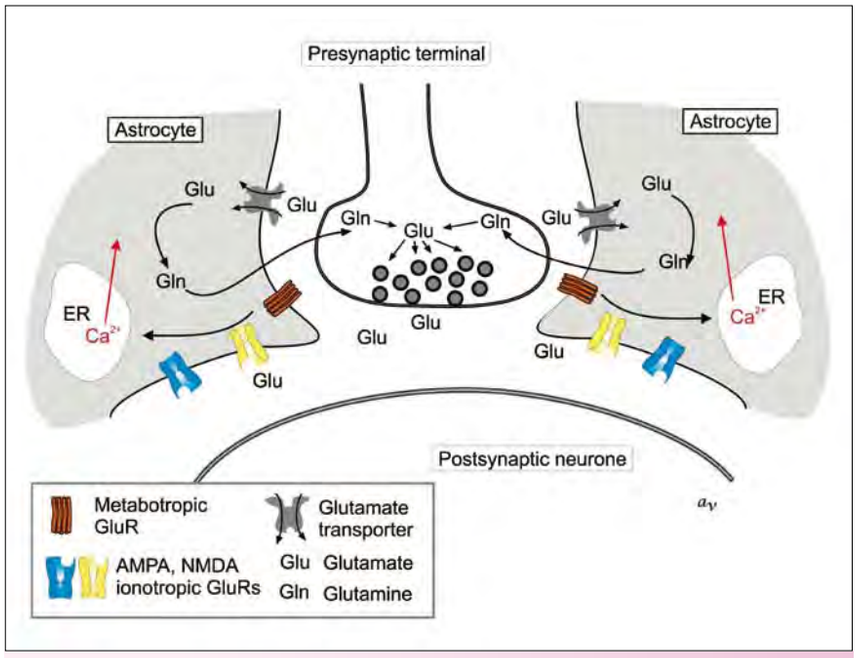
– purinoreceptor-mediated signalling in neurones and glia in the context of their role in sensory transduction and in acute and chronic pain;



Newly generated transgenic rats that express the vasopressin-enhanced green (eGFP) or an oxytocin-enhanced cyan fluorescent protein fusion genes in the HNS. AVP-eGFP fluorescence was observed in the isolated supraoptic nucleus (SON; A) neurons, nerve terminals (B); OT-eCFP in the paraventricular nucleus (PVN; C) and the SON sections (D). Inset is isolated OT neurons from SONs.



Diversity of synaptic contacts between neural cells.
In the grey matter synapses may include (1) classic "tripartite" neuronal-neuronal contacts, enwrapped by an astroglial membrane; (2) neuronal glial synapses (which have already been shown for neuronal-astroglial (Jabs and others 2005) or neuronal-NG2 cell contacts (Lin and Bergles, 2004); (3) astroglial-neuronal synapses (which are yet to be discovered); and (4) astroglial-astroglial synapses, which may exist as electrical/gap junctional or chemical contacts. In the white matter astrocytes may act as presynaptic elements in astroglial-oligodendroglial synapses (5).



Glutamate mediated neuronal-glial signalling.
Synaptically released glutamate activates glial ionotropic (AMPA and NMDA) and metabotropic receptors. Activation of group I metabotropic receptors initiates phospholipase C-dependent synthesis of InsP3, which, in turn, triggers Ca^{2+} release from the endoplasmic reticulum (ER) Ca^{2+} store. The majority (~ 80%) of glutamate released during synaptic transmission is taken up by astroglial Na^+/glutamate transporters; subsequently glutamate is converted into glutamine, which is transported back to neurones, where it acts as a main source of newly synthesised glutamate ("glutamate-glutamine shuttle").

– glial representation of TRP channels and their role in glial signalling;

– ion channels and Ca^{2+} signalling cascades in various types of neural cells at different stages of differentiation;

– *in vivo* imaging of neuronal-glial circuits under physiological and pathophysiological conditions;

– calcium signalling cascades in neurodegeneration and Alzheimer's disease, in particular; the morphology and physiology of glia during normal brain ageing.

Cellular, molecular and morphological changes in neurons and glial cells during pathological states:

– Characterization of events affecting ischemic brain damage, especially astrocytic swelling and the disturbance of Na^+, K^+, Cl^- and Ca^{2+} homeostasis;

– the role of chloride movement in regulatory volume processes in astrocytes during and after oxygen-glucose deprivation;

– characterization of the ischemia-induced time-dependent changes in Ca^{2+} entry carried by TRP channels, ionotropic glutamate and purinergic receptors in glial cells;

– correlation of ischemia-induced changes, such as the onset of reactive gliosis and glial proliferation or apoptosis, with the expression of Na^+ and K^+ ion channels;

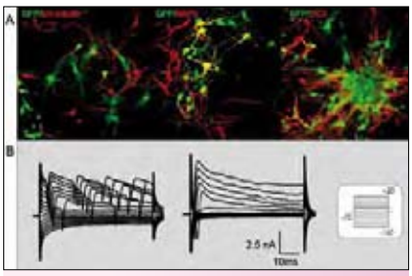
– identification of endogenous neural stem cell migration and differentiation during CNS regeneration – the role of morphogenes and growth factors;

– proliferation, migration and differentiation of region-specific neural stem/progenitor cells *in vitro* as well as after transplantation into the ischemic brain;

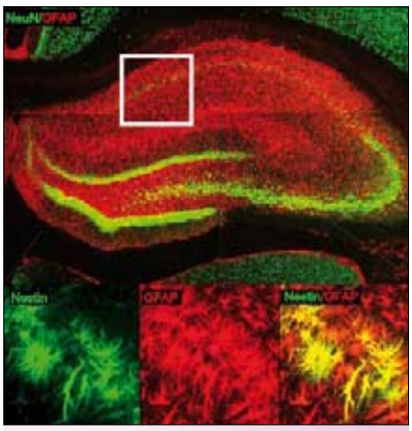
– morphometric measurements and three-dimensional reconstruction of morphological changes of neurons, glial cells and stem cells during pathological states and regeneration.

Laboratory of Molecular Neurophysiology

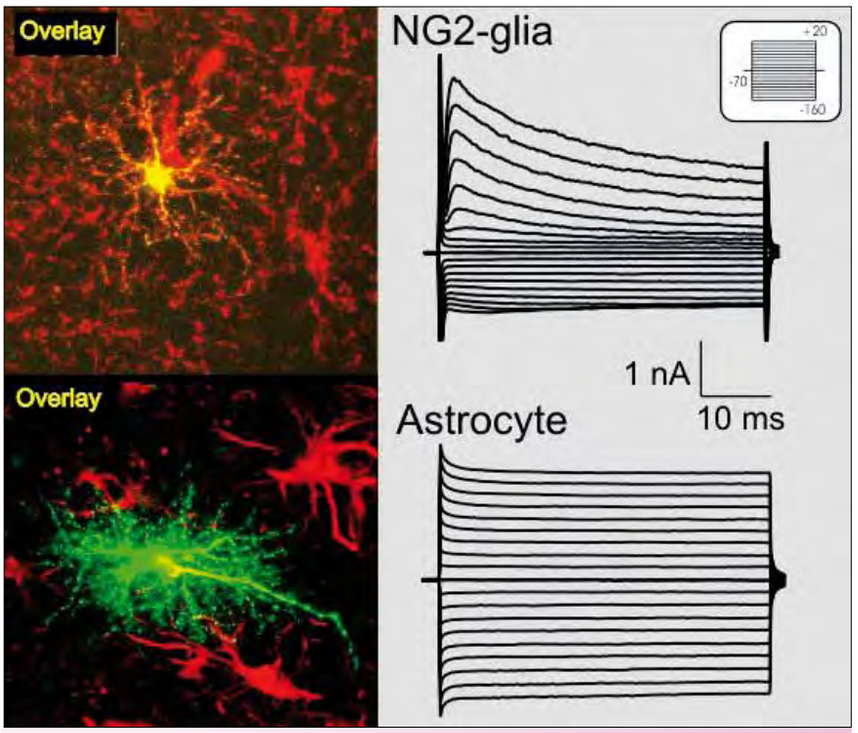
By employing a complex of electrophysiological, video-imaging and molecular biological techniques, we seek to identify the main receptors responsible for calcium signalling pathways and localise the intracellular signalling cascades. Further, we work to develop a complex understanding of information processing in neuronal-glial circuits, thus contributing to a more inclusive theory of brain function, which empha sizes a continuous interplay of discreet neuronal networks with the reticular and internally continuous astroglial web.



Membrane properties of GFP-labeled primary embryonic stem cells during differentiation.
(A) Green fluorescent protein (GFP)-labeled primary embryonic stem cells (D6/GFP) express the typical neuronal markers βIII-tubulin, MAP-2 and DCX (doublecortin), six days after in vitro differentiation. (B) A typical current pattern of D6/GFP-derived neuron-like cells.



Neuronal loss and astrogliosis in the hippocampus after global cerebral ischemia.
Coronal sections of the rat hippocampus 7 days after ischemia/reperfusion. The slices were stained with antibodies against glial fibrillary acidic protein (GFAP) and NeuN or nestin.



Membrane properties of astrocytes and NG2-glia after global cerebral ischemia.
Immunohistochemical identification and electrophysiological characterization of NG2-glia and astrocytes in the rat hippocampus (CA1 region) after bilateral carotid occlusion (left). Typical current patterns of NG2-glia and astrocytes in the rat hippocampus(CA1 region). NG2-glia express a typical complex current pattern of outwardly and inwardly rectifying K^+ currents; astrocytes display predominantly time- and voltage-independent passive K^+ currents (right).

Laboratory of Neurobiology

Research is focused on the cellular, molecular and morphological changes in neurons and glial cells during pathological states such as anoxia and ischemia and during nervous tissue regeneration. In addition, the morphological, electrophysiological and immunohistochemical properties of endogenous stem cells are studied to reveal their possible role in neuroregeneration after injury. Advanced electrophysiological, immunohistochemical and imaging techniques, as well as transgenic animals, are used to identify changes in membrane ionic channels and the expression of cell-type specific markers. Three-dimensional confocal morphometry is used to quantify morphological changes in neurons, glial cells and stem cells.

CURRENT GRANT SUPPORT

GA CR, 309/08/1381, Physiological and pathological potential of astroglial NMDA receptors, 2008–2012.

GA CR, 305/08/1384, Age-related changes in the structure and function of astrocytes, 2008–2010.

GA CR, 309/09/1696, Pathological potential of astroglia in Alzheimer disease, 2009–2011.

GA CR, 305/09/0717, Induction of neuro- and gliogenesis in rat brain after ischemia – the role of morphogenes and growth factors in nervous tissue regeneration, 2009–2011.

Ministry of Education, 1M0538, Research Center: Center of the cell therapy and tissue repair, 2005–2009.

Ministry of Education, LC554, Research Center: Center of Neuroscience, 2005–2009.

SELECTED RECENT PUBLICATIONS

1. Anděrová M, Kubinová S, Jelitai M, Neprašová H, Glogarová K, Prajerová I, Urdzíková L, Chvátal A, Syková E. (2006) Transplantation of embryonic neuroectodermal progenitor cells into the site of a photochemical lesion: immunohistochemical and electrophysiological analysis. J Neurobiol 66: 1084–1010.

2. Chvátal A, Anděrová M, Hock M, Prajerová I, Neprašová H, Chvátal V, Kirchhoff F, Syková E. (2007) Three-dimensional confocal morphometry reveals structural changes in astrocyte morphology in situ. J Neurosci Res 85: 260–271.

3. Neprašová H, Anděrová M, Petřík D, Vargová L, Kubinová Š, Chvátal A, Syková E. (2007) High extracellular K+ evokes changes in voltage-dependent K+ and Na+ currents and volume regulation in astrocytes. Pflugers Arch 453: 839–849.

4. Jelitai M, Anděrová M, Chvátal A, Madarász E. (2007) Electrophysiological characterization of neural stem/progenitor cells during *in vitro* differentiation: a study on an immortalized neuroectodermal cell line. J Neurosci Res 85(8): 1606–1617.

5. Verkhratsky A, Anděrová M, Chvátal A. (2009) Differential calcium signalling in neuronal-glial networks. Front Biosci 14: 2004–2016.

6. Benešova J, Hock M, Butenko O, Prajerová I, Anděrová M, Chvátal A. (2009) Quantification of astrocyte volume changes during ischemia in situ reveals two populations of astrocytes in the cortex of GFAP/EGFP mice. J Neurosci Res 87: 96–111.

7. Rodríguez JJ, Olabarria M, Chvátal A, Verkhratsky A. (2008) Astroglia in dementia and Alzheimer's disease. Cell Death Differ. 16: 378–385.