The Berlin Neuroscience Forum 2006 is sponsored by

Schering AG Berlin
Fine Science Tools GmbH Heidelberg
Harry Fein - World Precision Instruments

This meeting is a joint activity of

SFB „Die Bedeutung nicht-neuronaler Zellen bei neurologischen Erkrankungen“

SFB „Theoretische Biologie“

SFB „Entwicklungsstörungen im Nervensystem“

GRK „Zelluläre Mechanismen von Lernen und Gedächtnis-konsolidierung in der hippocampalen Funktion“

GRK „Functional Insect Science“

GRK „Neuropsychiatrie und Psychologie des Alters“

GRK „The Impact of Inflammation on Nervous System Function“

Berlin Neuroimaging Center

Klinische Forschergruppe „Molekulare Mechanismen der Opioidanalgesie bei Entzündungsschmerz“

Studiengang „Medizinische Neurowissenschaften“

Promotionskolleg „Computational Neuroscience“

Bernstein Center for Computational Neuroscience

Table of Contents

Program Committee

Ingolf Blasig
Ulrich Dirnagl
Gabriel Curio
Carsten Duch
Karl Einhäupl
Ralf Engbert
Uwe Heinemann
Andreas Herz
Isabella Heuser
Helmut Kettenmann
Reinhold Kliegl
Harald von Keyserlingk
Dietmar Kuhl
Robert Nitsch
Randolf Menzel
Jochen Pflüger
Werner Sommer
Christoph Stein
Werner Reutter
Arno Villringer
Bernd Walz
Bertram Wiedenmann

Organization

Prof. Dr. Helmut Kettenmann
Meino Alexandra Gibson
Max-Delbrück-Centrum für Molekulare Medizin (MDC) Berlin-Buch
Zelluläre Neurowissenschaften
Robert-Rössle-Str. 10
13092 Berlin
Tel.: +49 30 9406 3336
Fax: +49 30 9406 3819
EMail: gibson@mdc-berlin.de

Homepage

http://bnf2006.glia.mdc-berlin.de

General Information

Registration	Thursday, June 8, 2006	**12.00 - 15.00**
Office Hours	Thursday, June 8, 2006 Friday, June 9, 2006 Saturday, June 10, 2006	**12.00 - 19.30** **8.00 - 19.00** **8.00 - 13.00**
Office Phone **Office Fax**	0160 90218506 +49 33054 871 87	
Poster Boards	Height : 120 cm Width: 100 cm	
Poster Sessions	**Poster Session I** Thursday, June 8, 2006 Poster No. 1- 60	**16.05 – 18.00**
	Poster Session II Friday, June 9, 2006 Poster No. 61 - 115	**10.00 – 12.00**
Duration of Oral Presentations	**Invited Speakers**	45 min (talk) 15 min (disc.)
	Welcome to Berlin Presentations	15 min (talk) 5 min (disc.)
	Young Investigator Presentations	10 min (talk) 5 min (disc.)

Scientific Program

Thursday, June 8, 2006

12.00 – 15.00 Arrival and Registration

15.00 – 15.05 Welcome: Helmut Kettenmann

15.05 – 16.05 Lecture I
Chair: Isabella Heuser
Rainer Goebel
Department of Cognitive Neuroscience, Maastricht University, The Netherlands
Gaining conscious control of local brain activity using real-time fMRI neurofeedback

16.05 – 18.00 Poster Session I and Coffee Break

18.00 – 19.40 **Welcome to Berlin Session**
Chair: Carmen Birchmeier und Klaus Obermayer

Matthias Riepe
Klinik für Psychiatrie, Campus Benjamin Franklin, Charité Berlin
Alzheimer disease: early markers in mouse and man

Ines Ibanez-Tallon
Max Delbrück Center for Molecular Medicine (MDC)
Optimizing tethered toxins for cell-autonomous inactivation of ion channels

Thomas Jentsch
Zentrum für Molekulare Neurobiologie, Universität Hamburg
Overview of research activities: CLC, KCNQ, and KCC proteins

Ferdinand Le Noble
Max Delbrück Center for Molecular Medicine (MDC)
Common molecular mechanisms involved in guidance of blood vessels and nerves

Michael Brecht
University Medical Center Rotterdam, The Netherlands
Head-anchored whole-cell recordings in freely moving animals

20.00 **Dinner and Informal Get-together**

Friday, June 9, 2006

8.00 – 9.00 **Breakfast**

9.00 – 10.00 **Lecture II**
Chair: Uwe Heinemann
Michael Häusser
Wolfson Institute for Biomedical Research, University College London, UK
A dendritic switch for synaptic plasticity in neocortical pyramidal cells

10.00 – 12.00 **Poster Session II and Coffee Break**

12.00 – 13.00 **Young Investigator Presentations Session I**
Chair: Ingolf Blasig & Dietmar Kuhl

Anja Bräuer
Center for Anatomy, Charité
Phospholipids and PRG-1 control synapse stabilization and axon growth

Sven Hendrix
Center for Anatomy, Charité
T helper cells induce axonal outgrowth in vitro and in vivo by neurotrophin receptor upregulation

Tim Hucho
Max Planck Institute for Molecular Genetics
Estrogen controls PKC-Epsilon-dependent mechanical hyperalgesia through direct action on nociceptive neurons

René Jüttner
Developmental Neurobiology, Max Delbrück Center for Molecular Medicine (MDC)
Function of Caleb in regulating synaptic connectivity

13.00 – 14.00 **Lunch**

14.00 – 17.00 **Excursion**

17.00 – 18.00 **Lecture III**
Chair: Arno Villringer
Martin Lauritzen
Glostrup Hospital and University of Copenhagen, Glostrup, Denmark
Coupling brain function to blood flow and oxygen consumption: control mechanisms related to signalling in cerebral grey matter

18.00 – 19.00 **Young Investigator Presentations Session II**
Chair: Randolf Menzel & Christoph Stein

Juliane Klehmet
Experimental Neurology, Charité
Autoreactive phenomena induced by ischemic brain injury

Volker Kunzmann
Neurology, Campus Benjamin Franklin, Charité
The Berlin Brain-Computer Interface (BBCI) - Single-trial classifications of phantom movements of arm amputees

Alexander Luborzewski
Clinic for Psychiatry, Campus Benjamin Franklin, Charité
Metabolic alterations in the dorsolateral prefrontal cortex after treatment with high-frequency repetitive transcranial magnetic stimulation in patients with unipolar major depression

Sebastian Major
Experimental Neurology, Charité
Combined inhibition of Na, K-ATPase and NO synthase cause cortical spreading ischemia in the rat cortex

19.00 – 20.00 **Dinner**

20.00 – 21.00 **Lecture IV**
Chair: Hans-Joachim Pflüger
Stephan Sigrist
European Neuroscience Institute Göttingen, Germany
In vivo formation of synapse structure and function

21.00 **Disco Night**

Saturday, June 10, 2006

8.00 – 9.00 **Breakfast**

9.00 – 10.00 **Lecture V**
Chair: Robert Nitsch
John Parnavelas
Department of Neuroanatomy, University College London, UK
Cell and molecular mechanisms involved in the migration of cortical interneurons

10.00 – 10.15 **Coffee Break**

10.15 – 11.15 Young Investigator Presentations Session III
Chair: Gabriel Curio & Bertram Wiedenmann

Roland Schaette
Institute for Theoretical Biology, Humboldt University
Predicting Tinnitus Pitch with a Computational Model for the Development of Neuronal Hyperactivity after Hearing Loss

Ruth Schubert
Department of Neurology, Charité
How you feel it – now you don´t: ERP correlates of somatosensory awareness

Stefan Schumacher
Institute of Cell Biology and Neurobiology, Center for Anatomy, Charité
Functional analysis of CALEB/NGC in mouse brain development by in utero electroporation

Stefan Britsch
Max Delbrück Center for Molecular Medicine (MDC)
The zinc finger transcription factor Bcl11a controls dendrite formation and layer-specific connectivity in the dorsal spinal cord

11.15 – 12.15 **Lecture VI**
Chair: Andreas Herz
Ad Aertsen
Institute for Biology, University of Freiburg, Germany
Cortical network dynamics – precision in a noisy environment?

12.15 – 12.30 **Poster Prize Awarding**

12.30 **Lunch and Departure**

Poster Presentations - Session I

1. EXPRESSION PATTERN OF OPA1 PROTEIN ISOFORMS IN MOUSE BRAIN
Akepati, V.R.; Otto, A.; Müller, E.C.; Alexander, C.
Neurodegeneration, Max Delbrück Zentrum für Molekulare Medicin (MDC), Berlin

2. ANTICONVULSANT EFFECTS OF BILATERAL INJECTION OF N^6-CYCLOHEXYLADENOSINE INTO THE CA1 REGION OF THE HIPPOCAMPUS IN AMYGDALOID KINDLED RATS
Alasvand Zarasvand, M.; Mirnajafi-Zadeh, J.; Fathollahi, Y.
Physiology Department, Medical Sciences University of Kurdestan, Sanandaj

3. A PROTEOMICAL APPROACH OF THE EFFECT OF BRAIN TRAUMA ON BBB
Aspeslagh, S.; Haseloff, R.; Lohrberg, D.; Mikotheit, K.; Blasig, I.
FMP, Berlin-Buch

4. SEVOFLURANE BUT NOT NITROUS OXIDE ENHANCES GABAERGIC PRESYNAPTIC IA-INHIBITION IN HUMANS
Baars, J.H.; Benzke, M.; Dincklage, F. von; Reiche, J.; Rehberg, B.
Klinik für Anästhesiologie und Intensivmedizin, Charité Campus Mitte, Berlin

5. A PSYCHOPHYSIOLOGICAL MODEL OF ELEMENTARY COLOR SENSATIONS IN MAN
Backhaus, W.G.K.
Theoretical and Experimental Biology, Bioinformatics, Free University Berlin and Technical University Berlin

6. EFFECT OF NOISE EXPOSURE ON HIGHER AUDITORY STRUCTURES
Basta, D.; Tzschentke, B.; Ernst, A.
Otolaryngology, Unfallkrankenhaus Berlin

7. INVOLVEMENT OF $GABA_A$ –MEDIATED TRANSMISSION IN STIMULUS-INDUCED SHARP WAVE-RIPPLE COMPLEXES IN HIPPOCAMPAL AREA CA3 *IN VITRO*
Behrens, C.J.; van den Boom, L.P.; Richter, J.P.; Heinemann, U.
Neurophysiology, Center for Physiology, Berlin

8. POSTSYNAPTIC 5-HT_{1A} RECEPTOR FUNCTIONS REVEALED IN TRANSGENIC MICE
Bert, B.; Rex, A.; Voigt, J.-P.; Fink, H.
Institute of Pharmacology and Toxicology, School of Veterinary Medicine, Freie Universität Berlin

9. RESONANCE PROPERTIES OF RAT HIPPOCAMPAL INTERNEURONS IN STRATUM ORIENS *IN VITRO*
Boehlen, A.; Herz, A. V. M.; Heinemann, U.
Institut für Neurophysiologie, Johannes-Müller-Institut, Berlin

10. NEURONAL CALCIUM SENSOR (NCS) PROTEIN VILIP-1 MODULATES CGMP SIGNALLING BY REGULATING RECEPTOR GUANYLYL CYCLASE B CELL SURFACE EXPRESSION AND ACTIVITY IN NEURAL CELLS AND HIPPOCAMPAL NEURONS
Brackmann, M.; Buck, N.; Anand, R.; Behr, J.; Braunewell, K.-H.
Signal Transduction Research Group; Neuroscience Research Center, Charité, University Medicine Berlin

11. CLINICAL PREDICTORS OF EARLY RESPONSE TO ECT AND RTMS
Brakemeier, E.-L.; Quante, A.; Luborzewski, A.; Röpke, S.; Bajbouj, M.
Department of Psychiatry and Psychotherapy, Charité Universitätsmedizin, Campus Benjamin Franklin, Berlin

12. TWO PHOTON IMAGING OF INTERACTIONS BETWEEN IMMUNE CELLS AND NEURAL CELLS IN MODELS OF MULTIPLE SCLEROSIS
Brandt, A.U.; Radbruch, H.; Hahner, A.; Siffrin, V.; Asselborn, N.; Pohl, E.; Infante-Duarte, C.; Aktas, O.; Zipp,F.
Institute of Neuroimmunology, Charité Universitätsmedizin Berlin

13. CALEB/NGC REGULATES DENDRITIC TREE COMPLEXITY
Brandt, N.; Nitsch, R.; Schumacher, S.
Center of Anatomy, Charite University Hospital Berlin, Institute of Cell- and Neurobiology, Berlin

14. THE OPTIMAL VIEWING POSITION EFFECT NEW EVIDENCE FROM EYETRACKING RESEARCH
Braun, M.; Hutzler, F.; Vo, M.; Engl, V.; Jacobs, A.M.
Erziehungswissenschaften und Psychologie, Freie Unviversität Berlin

15. GENETIC ANALYSIS OF THE ZINC FINGER TRANSCRIPTION FACTOR BCL11B IN THE POSTNATAL HIPPOCAMPUS
Brylka, H.; Jones, K.R.; Copeland, N.; Birchmeier, C.; Britsch, S.
AG C. Birchmeier, Max-Delbrück-Zentrum für Molekulare Medizin, Berlin

16. THE CONTRIBUTION OF COLD-SENSITIVE TRP CHANNELS TO COLD ALLODYNIA AND NEUROPATHIC PAIN
Caspani, O.; Heppenstall, P.
Anesthesiology, Charité, Campus Benjamin Franklin, Berlin

17. RESPONSE OF MICROGLIA TO GABAERGIC STIMULATION IN EARLY POSTNATAL CORPUS CALLOSUM
Cheung, G.; Färber K.; Kettenmann, H.
Cellular Neuroscience, Max-Delbrueck-Center, Berlin

18. DEVELOPMENTALLY REGULATED EXPRESSION PATTERN OF CALEB, AN EGF-LIKE PROTEIN RESTRICTED TO THE CENTRAL NERVOUS SYSTEM
Craveiro, R.B.; Jüttner, R.; Babich, A.; Rathjen, F.G.
Developmental Neurobiology, Max-Delbrück-Centrum für Molekulare Medizin, Berlin

19. FROM BURST ENCODING TO TIME-WARP INVARIANCE
Creutzig, F.; Wohlgemuth, S.; Benda, J.; Stumpner, A.; Ronacher, B.; Herz, A.V.M.
Institute for Theoretical Biology, HU Berlin, Berlin

20. EFFICIENT ESTIMATION OF HIDDEN STATE DYNAMICS FROM SPIKE TRAINS
Danóczy, M.; Hahnloser, R. H. R.
ITB, HU Berlin

21. LAMOTRIGINE EFFECTS ON HUMAN NEOCORTICAL NEURONES IN SLICES FROM EPILEPSY SURGERY TISSUE
Deisz, R.A.; Lehmann, T.-N.; Meencke, H.-J.; Nitsch, R.
Cell- and Neurobiology, Center for Anatomy, Berlin

22. EVIDENCE FOR A VASCULAR CORRELATE OF THE BEREITSCHAFTPOTENTIAL USING NEAR-INFRARED SPECTROSCOPY
Drenckhahn, J.C.W.; Obrig, H.; Steinbrink, J.; Duemmler, J.; Kohl-Bareis, M.; Villringer, A.; Dreier, J.P.
Department of Experimental Neurology, Charité Campus Mitte, Berlin

23. FOLATE DEFICIENCY, HYPERHOMOCYSTEINEMIA AND BASE EXCISION REPAIR: ARE THE NEUROPATHOLOGICAL AND BEHAVIORAL CONSEQUENCES RELATED TO ALTERED NEUROTROPHIN LEVELS?
Eckart, S.; Kronenberg, G.; Endres, M.; Hörtnagl, H.; Hellweg, R.
Department of Psychiatry, Charité-University Medicine Berlin, Campus Benjamin Franklin, Berlin

24. THE ECTONUCLEOTIDASE *CD39*/ENTPDASE1 MODULATES PURINERGIC-MEDIATED MICROGLIAL MIGRATION AND MICROGLIAL RESPONSES TO CEREBRAL ISCHEMIA
Färber, K.; Markworth, S.; Pannasch, U.; Prinz, V.; Kronenberg, G.; Endres, M.; Enjyoji, K.; Robson, S.C.; Kettenmann, H.
Cellular Neuroscience, Max-Delbrueck-Center for Molecular Medicine, Berlin

25. MECHANISM OF INTRACELLULAR CA^{2+} OSCILLATIONS
Falcke, M.; Skupin, A.
Department Theory, Hahn-Meitner-Institut, Berlin

26. LONG-TERM DEPRESSION IN BURST AND REGULAR FIRING NEURONS OF THE SUBICULUM
Fidzinski, P.; Behr J.
Institute of Neurophysiology, Charité Universitätsmedizin Berlin

27. LOSS OF OPA1 (OPTIC ATROPHY 1) LEADS TO EARLY DEATH DURING GASTRULATION IN THE MOUSE
Fiket, M.; Seeliger, M.; Alexander, C.
Neurodegeneration, Max Delbrück Zentrum für Molekulare Medizin (MDC), Berlin

28. REGULATION OF NOCICEPTOR HEAT SENSITIVITY BY THE C-KIT/STEM CELL FACTOR SIGNALLING SYSTEM
Frahm, C.; Milenkovic, N.; Gassmann, M.; Birchmeier, C.; Lewin, G.R.; Garratt, A.N.
Department of Neurosciences, Max-Delbrueck-Center for Molecular Medicine, Berlin

29. SLOWNESS LEADS TO PLACE CELLS
Franzius, M.; Sprekeler, H.; Wiskott, L.
Institute for Theoretical Biology (ITB), HU-Berlin

30. SMOKING AND STRUCTURAL BRAIN DEFICITS: A 3 TESLA VOLUMETRIC MR INVESTIGATION
Gallinat, J.; Staedtgen, M.; Kalus, P.; Heinz A.
Klinik für Psychiatrie und Psychotherapie, Charité, CCM, Berlin

31. BACE1 CLEAVAGE AND RELEASE OF NEUREGULIN-1 DETERMINES THE ENSHEATHMENT FATE OF AXONS
Garratt, A.N.; Willem, M.; Rabe, L.; Novak, B.; Rittger, A; Saftig, P.; Dorner-Ciosek, C.; De Strooper, B.; Birchmeier, C.; Haass, C.
Department of Neurosciences, Max-Delbrueck-Center for Molecular Medicine, Berlin

32. PROMOTER ANALYSIS OF THE PLASTICITY RELATED GENE-1
Geist, B.; Trimbuch, T.; Ninnemann, O.; Nitsch, R.
Institute of Cell- and Neurobiology, Center of Anatomy, Charité, Berlin

33. PRIMARY MICROCEPHALY WITH A SEVERE CHROMOSOME CONDENSATION PHENOTYPE CAUSED BY A NOVEL MISSENSE MUTATION, W75R, IN THE BRCT DOMAIN OF MICROCEPHALIN
Ghani Kakhki, M.; Morlot, S.; Neitzel, H.
Chromosomal Diagnostics, Institute of Human Genetics, Berlin

34. SPIKE PRECISION AND RELIABILITY IN AUDITORY RECEPTOR NEURONS OF THE LOCUST
Glauser, S.; Herz, A.V.M.; Benda, J.
Institute for Theoretical Biology, Humboldt Universität zu Berlin, Berlin

35. IDENTIFICATION AND CHARACTERIZATION OF TWO NOVEL TUBULIN-BINDING MOTIFS LOCATED WITHIN THE C-TERMINUS OF TRPV1
Goswami, Ch.; Hucho, T.; Hucho, F.
Max Planck Institute for Molecular Genetics, Berlin

36. MAPPING COMPLEX OLFACTORY LEARNING TASKS WITHIN THE HONEYBEE BRAIN BY PROCAINE INJECTIONS
Grünewald, B.; Seifert, S.; Blunk, A.; Podufall, J.; Papouin, T.; Giurfa, M; Devaud, J.-M.
Institut für Biologie – Neurobiologie, FU Berlin

37. KNOCKDOWN OF *FOXP2* IN ZEBRA FINCH AREA X IMPAIRS SONG LEARNING
Haesler, S.; Licznerski, P.; Georgi, B.; Osten, P.; Scharff, C.
Verhaltensbiologie, FU Berlin

38. THE ROLE OF CX_3CR1-EXPRESSING NK CELLS IN MULTIPLE SCLEROSIS
Hamann, I.; Prozorovski, T.; Zipp, F.; Infante-Duarte, C.
Institute of Neuroimmunology, Charité - Universitätsmedizin Berlin

39. DOES THE FREQUENCY OF THE ANTECEDENT NOUN AFFECT THE RESOLUTION OF PRONOMINAL ANAPHORS? AN EEG STUDY
Heine, A.; Tamm, S.; Hofmann, M.; Hutzler, F.; Jacobs, A.M.
Dept. of Psychology, Freie Universität Berlin

40. CHRONIC ETHANOL EXPOSURE OF SH-SY5Y CELLS IMPAIRS RETINOIC ACID-INDUCED NEURONAL DIFFERENTIATION INVOLVING ERK-1/2 RESPONSIVENESS TO BDNF AND RAF KINASE INHIBITOR PROTEIN
Hellmann, J.; Wernicke, C.; Rommelspacher, H.
Dept. of Psychiatry, Charité-University Medicine Berlin

41. DISENTANGLING NEURAL PROCESSES ON A MICRO-SECOND TIME SCALE DESPITE MILLI-SECOND SPIKE-TIME VARIABILITY
Herz, A. V. M.
Inst. of Theoretical Biology, Humboldt University, Berlin

42. MECHANOSENSITIVE CHANNELS IN THE NEURITES OF CULTURED SENSORY NEURONS
Hu, J.; Lewin, G.R.
Neuroscience, MDC, Berlin

43. EFFECTS OF MITOCHONDRIAL COMPLEX I INHIBITION DURING BRAIN DEVELOPMENT
Huchzermeyer, C.; Schuelke, M.; Kann, O.
Institut für Neurophysiologie, Charité-Universitätsmedizin Berlin

44. ELECTROPHYSIOLOGICAL ANALYSIS OF NEURONAL PROPERTIES IN DIFFERENT LAYERS OF THE MOUSE AUDITORY CORTEX
Huggenberger, S.; Deisz, R. A.; Vater, M.
Institute for Biochemistry and Biology, University of Potsdam, Golm

45. ADEQUATE ANTIPSYCHOTIC TREATMENT NORMALIZES NERVE GROWTH FACTOR SERUM CONCENTRATIONS IN SCHIZOPHRENIA WITH AND WITHOUT CANNABIS OR ADDITIONAL SUBSTANCE ABUSE
Jockers-Scherübl, M.C.; Rentzsch, J.; Radzei, N.; Danker-Hopfe, H.; Schürer, F.; Bahri, S.; Hellweg, R.
Psychiatry and Psychotherapy, Charité, CBF, Berlin

46. THE NOVEL PROSPERO-RELATED HOMEODOMAIN TRANSCRIPTION FACTOR PROX2 IDENTIFIES A SUBPOPULATION OF PLACODE-DERIVED VISCEROSENSORY NEURONS
John, A.; Petrova, T. V.; Alitalo, K.; Birchmeier, C.; Britsch, S.
AG Prof. Carmen Birchmeier, MDC Berlin

47. BLOCK OF DRUG TRANSPORTER ACTIVITY AND EFFICACY OF ANTIEPILEPTIC DRUGS IN HUMAN EPILEPTIC HIPPOCAMPUS
Kim, S.; Leite Antonio, L.; Kovács, R.; Päsler, D.; Raue, C.; Heinemann, U.; Gabriel, S.; Lehmann, T.-N.
Institute for Neurophysiology, Charité University Medicine, Berlin

48. CONTRIBUTION OF NITRIC OXIDE TO INITIATION OF SEIZURE-LIKE EVENTS IN THE LOW $[MG^{2+}]$ MODEL OF EPILEPSY
Kovács, R.; Rabanus, A.; Otahal, J.; Heinemann, U.; Kann, O.
Mitochondrial Physiology and Pathology, Institute for Neurophysiology, Charité, Berlin

49. MODULATION OF PREFRONTAL CORTEX ACTIVATION BY EMOTIONAL WORDS IN RECOGNITION MEMORY
Kuchinke, L.; Jacobs, A.M.; Võ, M.; Conrad, M.; Grubich, C.; Herrmann, M.
Allgemeine Psychologie, Freie Universität Berlin

50. MODELING THE ACTIVITY OF THE AUDITORY NERVE AFTER HEARING LOSS
Kuokkanen, P.T.; Schaette, R.; Kempter, R.
Institute for Theoretical Biology, Humboldt Universität zu Berlin

51. RECORDING OF PATHOPHYSIOLOGICALLY RELEVANT PARAMETERS NON-INVASIVELY USING SIMULTANEOUS MAGNETOENCEPHALOGRAPHY AND NEARINFRARED SPECTROSCOPY
Leistner, S.; Sander, T.; Liebert, A.; Wabnitz, H.; Burghoff, M.; Macdonald, R.; Curio, G.; Trahms, L.; Mackert, B.M.
Department of Neurology, Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin

52. FAIR-MRI BLOOD FLOW IMAGING IN A MOUSE MODEL OF STROKE: COMPARISON WITH 14C-IODOANTIPYRINE AUTORADIOGRAPHY
Leithner, C.; Gertz, K.; Villringer, A.; Dirnagl, U.; Lindauer, U.; Endres, M.; Royl, G.
Experimentelle Neurologie, Charité Universitätsmedizin Berlin

53. INFLAMMATORY PAIN INSENSITIVITY IN THE AFRICAN NAKED MOLE-RAT (HETEROCEPHALUS GLABOR)
Lewin, G.R.; Lu, Y.; Hu, J.; Brand, A.; Anirudhan, G.; Heppenstall, P. A.; Milenkovic, N.; Erdmann, B.; Wetzel, C.; Laurito, C.E.; Wilson, S. P.; Park, T.J.
Neuroscience, MDC, Berlin

54. LONG LASTING DETERIORATION OF SPATIAL NAVIGATION ON REPETITIVE INHIBITION OF ENERGY METABOLISM – AGE MATTERS
Lohmann, P.; Riepe, M.W.
Department of Psychiatry, Charité University, Berlin

55. A NEW TECHNIQUE FOR ENRICHMENT OF CLAUDINS AND CLAUDIN ASSOCIATED PROTEINS
Lohrberg, D.; Winkler, L.; Piontek, J.; Haseloff, R.F.; Krause, E.; Schümann, M.; Blasig, I.E.
Signaltransduktion, Leibniz-Institut für Molekulare Pharmakologie (FMP), Berlin

56. HIGH TONIC CL^- CONDUCTANCE IN DEVELOPING HIPPOCAMPAL NEURONS OVEREXPRESSING A HIGH-AFFINITY GLYCINE RECEPTOR RESULTS IN ALTERED DENDRITE MORPHOLOGY DUE TO CHANGES IN THE E/I RATIO OF SYNAPTIC INPUT
Meier, J.C.; Kirischuk, S.; Grantyn, R.
Developmental Physiology, Johannes Müller Centrum, Berlin

57. A NOVEL APPROACH TO STUDY NEUROPROTECTIVE GENES
Mergenthaler, P.; Freyer, D.; Muselmann, C.; Dirnagl, U.; Meisel, A.
Experimental Neurology, Charité Universitaetsmedizin Berlin

58. VAGUS NERVE STIMULATION IMPROVES RESTLESS LEGS SYNDROME ASSOCIATED WITH MAJOR DEPRESSION: A CASE REPORT
Merkl, A.; Brakemeier, E.L.; Danker-Hopfe, H.; Bajbouj, M.
Psychiatry, Charité, CBF, Berlin

59. SCREENING FOR NOCICEPTOR SPECIFIC GENES
Milenkovic, N.; Lewin, G.R.
Neuroscience, MDC, Berlin

60. SPECIFICATION AND DIFFERENTIATION OF DORSAL SPINAL CORD INTERNEURONS
Müller, Th.; Wildner, H.; Bröhl, D.; Treier, M.; Birchmeier, C.
Medical Genetics, Max-Delbrück-Center for Molecular Medicine, Berlin

List of Poster Presentations – Session II

61. TOWARDS MODELLING THE FUNCTION OF TOP-DOWN VISUO-SPATIAL ATTENTION
Naito, A.; Kraft, A.; Brandt, S.; Wiskott, L.
Neurology, Charité, Campus Mitte, Humboldt University, Berlin

62. TWO METHODS FOR TIME-RESOLVED INTER-SPIKE INTERVAL ANALYSIS
Nawrot, M.; Benda, J.
Neuroinformatics and Theoretical Neuroscience, Free University Berlin

63. SELECTIVE ANTERIOR CINGULATE CORTEX DEFICIT DURING CONFLICT SOLUTION IN SCHIZOPHRENIA: AN EVENT-RELATED POTENTIAL STUDY
Neuhaus, A.H.; Koehler, S.; Opgen-Rhein, C.; Urbanek, C.; Hahn, E.; Dettling, M.
Psychiatry, Charité University Medicine Berlin, Campus Benjamin Franklin, Berlin

64. MOLECULAR INTERACTIONS OF THE COXSACKIEVIRUS AND ADENOVIRUS RECEPTOR (CAR), A NEURAL CELL-ADHESION PROTEIN
Patzke, C.; Dorner, A.; Behlke, J.; Henning, M.; Müller, E.C.; Otto, A.; Schmidt, H.; Kröger, S.; Rathjen, F.G.
Developmental Neurobiology, Max-Delbrück-Centrum, Berlin

65. ALZHEIMER-DISEASE-LIKE PATHOLOGY ALTERS ASTROCYTE PROPERTIES IN SITU
Peters, O.; Phillips, A.; Haas, B.; Pannasch, U.; Wang, L.-P.; Schipke, C.G.; Kettenmann, H.
Department of Psychiatry, Charité – CBF, Berlin

66. FUNCTIONAL INVESTIGATION OF THE SECOND EXTRACELLULAR LOOP OF CLAUDIN-5 IN TIGHT JUNCTION FORMATION
Piehl, C.; Winkler, L.; Piontek, J.; Blasig, I.E.
Leipniz-Forschungsinstitut für Molekulare Pharmakologie, Berlin

67. DRUG TRANSPORTERS AND PHARMACORESISTANCE IN EPILEPSY: REGIONAL AND CELLULAR DISTRIBUTION OF MRP1, MRP2 AND PGP IN HUMAN HIPPOCAMPUS
Raue, C.; Leite Antonio, L.; Päsler, D.; Heinemann, U.; Gabriel, S.; Lehmann, T.-N.
Institute for Neurophysiology, Charité University Medicine, Berlin

68. ANTICONVULSANT ACTIVITY OF DELPHINIUM DENUDATUM ON EPILEPTIFORM ACTIVITY INDUCED BY COMBINED APPLICATION OF BICUCULLINE AND 4 AMINOPYRIDINE IN RAT HIPPOCAMPAL ENTORHINAL CORTEX SLICES
Raza, M.; Shaheen, F.; Choudhary, M.I.; Gabriel, S.; Heinemann, U.
Physiology, School of Medical Sciences, Tarbiat Modares University, Tehran

69. PREATTENTIVE INFORMATION PROCESSING IN SCHIZOPHRENIA WITH CANNABIS ABUSE: AN ERP STUDY
Rentzsch, J.; Penzhorn, A.; Wolf, T.; Jockers-Scherübl, M.
Charité - Universitätsmedizin Berlin, Psychiatrische Klinik, Berlin

70. EFFECTS OF 8-OH-DPAT ON HIPPOCAMPAL NADH FLUORESCENCE *IN VIVO* IN ANAESTHETISED RATS
Rex, A.; Fink, H.
Institute of Pharmacology and Toxicology, Freie Universität Berlin

71. APOPTOSIS ONSET AND BAX PROTEIN DISTRIBUTION IN SPINAL MOTONEURONS OF NEWBORN RATS FOLLOING SCIATIC NERVE AXOTOMY
Rezaie M.J.; Tirihi, T.
Departments of Anatomical Sciences and Histology, Medical Sciences University of Kurdestan, Sananadaj

72. ROLE OF THE MOUSE TEASHIRT HOMOLOGUES IN DEVELOPMENT AND FUNCTION OF THE NERVOUS SYSTEM
Rocca, E.; Frahm, C.; Griffel, C; Birchmeier, C; Garratt, A.N.
Max-Delbrück-Centrum für Molekulare Medizin (MDC), Berlin

73. HOW TO SWITCH FROM AN INTEGRATOR TO A RESONATOR IN GENERAL NEURONAL MODELS
Roehner, U.; Benda, J.
ITB, HU, Berlin

74. ANALYZING THE TOXIC EFFECTS CYCLOHEXIMIDE HAS ON CELL CULTURES
Roland, T.
Neuroscience, Charité, Berlin

75. IMPROVED REPERFUSION AND NEUROPROTECTION BY CREATINE IN A MOUSE MODEL OF STROKE
Royl, G.; Prass, K.; Lindauer, U.; Freyer, D.; Megow, D.; Dirnagl, U.; Stöckler-Ipsiroglu, G.; Wallimann, T.; Priller, J.
Department of Experimental Neurology, Charité, Berlin

76. MICRORNA EXPRESSION AND FUNCTION DURING MOUSE CNS DEVELOPMENT
Rybak, A., Smirnowa L.; Fuchs, H., Wulczyn, G.; Nitsch, R.
Center for Anatomy, Institute of Cell Biology and Neurobiology, Berlin

77. DC-MAGNETOENCEPHALOGRAPHY TECHNIQUE FOR THE STUDY OF NEURO-VASCULAR COUPLING
Sander, T.H.; Burghoff, M.; Trahms, L.
AG 8.21, Physikalisch-Technische Bundesanstalt, Berlin

78. THE EFFECT OF INTERVENING TASKS ON RESPONSE PREPARATION. AN ERP STUDY
Sangals, J.; Sommer, W.
Biological Psychology / Psychophysiology, Institut für Psychologie, Humboldt Univ. zu Berlin

79. CALEB/NGC MEDIATES DENDRITIC SPINE COMPLEXITY
Schadt, H.; Brandt, N.; Nitsch, R.; Schumacher, S.
Institute of Cell Biology and Neurobiology, Center for Anatomy, Charité University Hospital, Berlin

80. ASTROCYTIC CALCIUM ACTIVITY IS SUFFICIENT TO INDUCE LONG-TERM SYNAPTIC DEPRESSION OF CA1 SCHAFFER COLLATERAL SYNAPSES
Schipke, C.G.; Serrano, A.; Lacaille, J.-C.; Robitaille, R.
Université de Montréal, Département de Physiologie, Canada

81. ATYPICAL NEUROLEPTIC (OLANZAPINE) INCREASES EFFICACY OF THE PREFRONTAL CORTEX IN SCHIZOPHRENIA
Schlagenhauf, F.; Wrase, J.; Wüstenberg, T.; Koslowski, M.; Filonov, D.; Gallinat, J.; Juckel, G.; Heinz, A.
Department of Psychiatry, Charité -Universitätsmedizin Berlin

82. DIFFERENTIAL REGULATION OF NEUROTROPHINS AND SEROTONERGIC FUNCTION IN MICE WITH GENETICALLY REDUCED GLUCOCORTICOID RECEPTOR EXPRESSION
Schulte-Herbrüggen, O.; Hörtnagl, H.; Chourbaji, S.; Ridder, S.; Brandwein, C.; Gass, P.; Hellweg, R.
Psychiatry and Psychotherapy, Charité, Campus Benjamin Franklin, Berlin

83. ROLE OF KININ RECEPTOR 1 (B1) IN THE PATHOGENESIS OF EAE
Schulze Topphoff, U.; Smorodchenko, A.; Mori, M.; Nowakowski, N.; Prozorovski, T.; Radbruch, H.; Bader, M.; Zipp, F.; Aktas,O.
Institute of Neuroimmunlogy, Charité, Berlin

84. FUNCTION OF THE MOUSE STOMATIN-LIKE PROTEIN-2 (MSLP2) DURING DEVELOPMENT AND IN MATURE SENSORY NEURONS
Seifert, A.C.; Heppenstall, P.A.; Riethmacher, D.; Lewin, G.R.
Growth Factors and Regeneration Group, Max-Delbrück-Centrum für Molekulare Medizin, Berlin

85. AMCREB RESPONSE TO CA^{2+}-STIMULATION OF CULTURED HONEYBEE KENYON CELLS AND TO INDUCTION OF LONG TERM MEMORY IN VIVO
Seifert, S.; Froese, A.; Grünewald, B.; Eisenhardt, D.
Institut für Neurobiologie, Freie Universität Berlin

86. PHYSIOLOGICAL CHARACTERIZATION OF THE KV 1.1 $^{-/-}$ MICE
Seo, E.Y.; Milenkovic, N.; Lewin, G.R.
Growth Factors and Regeneration Group, Max Delbrück Center for Molecular Medicine, Berlin

87. STOCHASTIC CHANNEL BEHAVIOUR DRIVES INTRACELLULAR CA^{2+} OSCILLATIONS
Skupin, A.; Falcke, M.
Department Theory, Hahn-Meitner-Institut, Berlin

88. REGULATION AND FUNCTION OF *LET-7* MICRORNA DURING NEURAL DIFFERENTIATION
Smirnova, L.; Rybak, A.; Fuchs, H.; Nitsch, R.; Wulczyn, G.
Charité University Hospital, Center for Anatomy, Institute of Cell and Neurobiology, Berlin

89. AXONAL OUTGROWTH IS CONTROLLED BY PLASTICITY-RELATED GENE-1 – RAS-SPECIFIC EXCHANGE FACTOR 2 INTERACTION
Soriguera, A.; Swiercz, J.M.; Offermanns, S.; Bhumika, S.; Rosemarie, G.; Nitsch, R.; Bräuer, A.U.
Institute of Cell Biology and Neurobiology, Center for Anatomy, Berlin

90. ANALYTICAL DERIVATION OF COMPLEX CELL PROPERTIES FROM THE SLOWNESS PRINCIPLE
Sprekeler, H.; Wiskott, L.
Institute for Theoretical Biology, HU Berlin

91. ANALYSIS OF AXONAL PATHFINDING ERRORS IN MICE DEFICIENT FOR CGKI SIGNALING BY AN IMPROVED DII TRACING METHOD
Stonkute, A.; Schmidt, H.; Jüttner, R.; Rathjen F.G.
Developmental Neurobiology, Max Delbrueck Center for Molecular Medicine, Berlin

92. FIGHTING PANIC: FROM A BETTER UNDERSTANDING OF FEAR CIRCUIT MECHANISMS TO MORE EFFECTIVE PSYCHOLOGICAL TREATMENT
Ströhle A.
Department of Psychiatry and Psychotherapy, Campus Charité Mitte, Charité - Universitätsmedizin Berlin

93. ANALYZING OLFACTORY CODING USING EXTRACELLULAR RECORDINGS FROM MUSHROOM BODY-EXTRINSIC NEURONS IN THE HONEYBEE
Strube, M.; Nawrot, M.P.; Grün, S.; Menzel, R.
Neurobiologie, Freie Universität Berlin

94. GENERATION OF CONDITIONAL KO-MICE FOR PRG-1 AND PRG-2 USING RED RECOMBINATION TECHNOLOGY
Trimbuch, T.; Geist, B.; Ninnemann, O.; Nitsch, R.
Institute of Cell- and Neurobiology, Charité - University Hospital Berlin

95. MISSENSE MUTATIONS IN GAP JUNCTION PROTEIN ALPHA 12 ARE ASSOCIATED WITH SEVERE CNS HYPOMYELINATION IN HUMANS
Uhlenberg, B.; Weschke, B.; Gärtner, J.; Hübner, C.
Neuropediatrics, Charité Children's Clinic, Berlin

96. LIPID PHOSPHATE PHOSPHATASES PROMOTE NEURITE OUTGROWTH
Velmans, T.; Savaskan, N.E.; Moolenaar, W.; Nitsch, R.; Bräuer, A.U.
Institute of Cell Biology and Neurobiology, Centrum of Anatomy, Berlin

97. THE FUNCTIONAL ROLE OF NEUROMODULATORY CELLS IN THE MOTOR SYSTEM OF *MANDUCA SEXTA*
Vierk, R.; Pflüger, H.-J.
Biology/Chemistry/Pharmacy Department, Institute for Neurobiology, Berlin

98. LUMBAR SPINAL CORD NEURONAL CELL LOSS IN CHRONIC NEUROINFLAMMATION
Vogt, J.; Aktas, O.; Müller-Wielsch, K.; Nitsch, R.; Zipp, F.
Institute of Cell and Neurobiology, Charité, Berlin

99. DYNAMICS OF NEURONAL DEVELOPMENT IN THE ADULT HIPPOCAMPUS
Vollmar, I.; Klempin, F.; Kronenberg, G.; Kempermann, G.
Max-Delbrück-Centrum für Molekulare Medizin (MDC), Berlin

100. SUBCORTICAL CONTRIBUTIONS TO THE SYNTACTIC ANALYSIS OF PHRASES
Wahl, M.; Marzinzik, F.; Hahne, A.; Kupsch, A.; Friederici, A.D.; Curio, G.; Saddy, D.; Klostermann, F.
Department of Neurology, CBF, Charité - University Medicine Berlin

101. ROLE OF MYOSIN XV IN SENSORY MECHANOTRANSDUCTION
Wang, R.; Lewin, G.R.
Department of Neuroscience, Max Delbrück Center for Molecular Medicine, Berlin

102. CHARACTERIZATION OF THE IMPAIRMENT IN CONGENITAL PROSOPAGNOSIA BY COMBINED ELECTROPHYSIOLOGICAL AND BEHAVIOURAL DATA
Weber, J.E.; Sander, T.; Carbon, C.C.; Grueter, T.; Grueter, M.; Trahms, L.; Curio, G.; Lueschow, A.
Department of Neurology and Neurophysiology, Charité Campus Benjamin Franklin, Berlin

103. ANALYSIS OF MAFA AND C-MAF FUNCTION IN MOUSE EMBRYONIC DEVELOPMENT
Wende, H.; Reuter, K.; Rhode, E.; Birchmeier, C.
MDC, Berlin

104. INVESTIGATIONS OF PATHOMECHANISMS OF PARKINSON'S DISEASE AND SEARCH FOR NEUROPROTECTIVE THERAPIES
Wernicke, C.; Gille, G.; Lehmann, J.; Pavlovic, S.; Schulze, G.; Rommelspacher, H.
Klinische Neurobiologie, Klinik und Hochschulambulanz für Psychiatrie und Psychologie, Charité - Universitätsmedizin Berlin

105. SLP3 IS A MAMMALIAN STOMATIN-DOMAIN PROTEIN ESSENTIAL FOR TOUCH RECEPTOR FUNCTION
Wetzel, C.; Mannsfeldt, A.; Hu, J.; Riethmacher, D.; Harder, L.; Lewin, G.R.
Growth Factor and Regeneration Group, MDC, Berlin

106. PROPERTIES OF HYPERPOLARIZATION-ACTIVATED INWARD CURRENTS OF HUMAN NEOCORTICAL NEURONES IN SLICES FROM EPILEPSY SURGERY SPECIMEN
Wierschke, S.; Huggenberger, S.; Lehmann, T.-N.; Meencke, H.-J.; Nitsch, R.; Deisz R.A.
Institute of Cell- and Neurobiology, Center for Anatomy, Berlin

107. DISTINCT ROLES FOR SELENOPROTEINS IN NEURONAL DEVELOPMENT AND FUNCTION
Wirth, E.; Bharathi, S.; Conrad, M.; Brielmeier, M.; Tessarollo, L.; Hatfield, D.; Köhrle, J.; Schweizer, U.
AG Neurobiologie des Selens, Charité, Berlin

108. ELECTROPHYSIOLOGICAL CORRELATES OF CRAVING AFTER VISUAL AND AUDITORY CUE-EXPOSURE IN ALCOHOLISM
Wölfling, K.; Grüsser, S.M.
Interdisciplinary Research Group on Addiction, Institute for Medical Psychology, Charité - University Medicine, Berlin

109. DYSFUNCTION OF THE REWARD SYSTEM CORRELATES WITH ALCOHOL CRAVING IN DETOXIFIED ALCOHOLICS
Wrase, J.; Schlagenhauf, F.; Kienast, T.; Wüstenberg, T.; Beck; A.; Kahnt, T.; Knutson, B.; Heinz, A.
Psychiatry, Charité Campus Mitte, Berlin

110. IN VIVO MRIMAGING OF TRIGEMINAL NERVE ROOT INFLAMMATION IN A MOUSE MODEL OF MULTIPLE SCLEROSIS
Wuerfel, J.; Tysiak, E.; Aktas, O.; Prozorowski, T.; Smorodzenko, A.; Mueller, S.; Schnorr, J.; Taupitz, M.; Zipp, F.
Institute of Neuroimmunology, Charité, Berlin

111. COMPETITION AND COOPERATION BETWEEN TENASCIN-R, LECTICANS AND CONTACTIN 1 REGULATE NEURITE GROWTH AND MORPHOLOGY
Zacharias, U.; Rauch, U.; Rathjen, F.G.
Developmental Neurobiology, MDC, Berlin

112. HIGH THROMBOPOIETIN CONCENTRATIONS IN THE CEREBROSPINAL FLUID OF NEONATES WITH SEPSIS AND INTRAVENTRICULAR HEMORRHAGE MAY CONTRIBUTE TO BRAIN DAMAGE
Zhang, J.; Reinhold, A.; Gessner, R.; Felderhoff-Mueser, U.; Obladen, M.; Dame, Ch.
Department of Neonatology, Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin

113. THE INVOLVEMENT OF THE NEURONAL CALCIUM SENSOR (NCS) PROTEIN VILIP-1 IN HIPPOCAMPAL PATHOPHYSIOLOGY IN SCHIZOPHRENIA: REGULATION OF EXPRESSION BY MGLURS IN HIPPOCAMPAL INTERNEURONS
Zhao, C.J.; Gierke, P.; Brackmann, M.; Bernstein, H.-G.; Braunewell, K.-H.
Signaltransduction Research Group, Neuroscience Research Center, Charité - Universitätsmedizin Berlin

114. NEURAL REPRESENTATION OF SURFACE WAVE PARAMETERS IN THE AQUATIC PREDATOR XENOPUS LAEVIS
Ziehm, U.; Branoner, F.; Zhivkov, Z.; Behrend, O.
Institute of Biology, Humboldt University Berlin

115. DEFINING A FUNCTION FOR THE ION CHANNEL TRPA1
Zurborg, S.; Yurgionas, B.; Caspani, O.; Heppenstall, P.A.
Klinik for Anästhesioloigie, CBF, Charité, Berlin

Abstracts of Lectures

CORTICAL NETWORK DYNAMICS – PRECISION IN A NOISY ENVIRONMENT?

Ad Aertsen

Neurobiology and Biophysics, Institute of Biology III, and Bernstein Center for Computational Neuroscience Albert-Ludwigs-University, Freiburg, Germany

Studies of cortical network function on the basis of multiple single-neuron recordings have revealed neuronal interactions which depend on stimulus and behavioral context. These interactions exhibit dynamics on several different time scales, with time constants down to the millisecond range. Mechanisms underlying such dynamic network organization are investigated by experimental and theoretical approaches. Our current research focuses on two interrelated aspects: *variability*[1] and *precision*[2] of cortical network activity. Extending previous model work[3] in which we investigated conditions for the occurrence of precise joint-spiking events in cortical network activity, I will present recent findings from ongoing experimental and theoretical work in our laboratory[4-9], undertaken to test and expand some of the model predictions. Specifically, I will discuss new findings regarding the feasibility and constraints of precise synchronization dynamics in cortical networks, resulting from a critical evaluation of biological constraints from cortical connectivity and *in vivo* physiology, and dynamical constraints from large-scale cortical network simulations.

Supported by GIF, DFG-GraKo, EU-FACETS, and BMBF (Grant 01GQ0420 to BCCN-Freiburg). Further information at www.brainworks.uni-freiburg.de and www.bccn.uni-freiburg.de

1. Arieli A, Sterkin A, Grinvald A, Aertsen A (1996) Dynamics of ongoing activity: explanation of the large variability in evoked cortical responses. *Science* 273:1868–1871

2. Riehle A, Grün S, Diesmann M, Aertsen A (1997) Spike synchronization and rate modulation differentially involved in motor cortical function. *Science* 278:1950–1953

3. Diesmann M, Gewaltig MO, Aertsen A (1999) Stable propagation of synchronous spiking in cortical neural networks. *Nature* 402: 529–533

4. Kuhn A, Rotter S, Aertsen A (2003) Higher-order statistics of input ensembles and the response of simple model neurons. *Neural Computation* 15: 67-101

5. Mehring C, Hehl U, Kubo M, Diesmann M, Aertsen A (2003) Activity dynamics and propagation of synchronous spiking in locally connected random networks. *Biol Cybern* 88: 395-408

6. Kuhn A, Aertsen A, Rotter S (2004) Neuronal integration of synaptic input in the fluctuation-driven regime. *J Neurosci* 24: 2345-2356

7. Léger J-F, Stern EA, Aertsen A, Heck D (2005) Synaptic integration in rat frontal cortex shaped by network activity. *J Neurophysiol* 93: 281-293

8. Morrison A, Mehring C, Geisel T, Aertsen A, Diesmann M (2005) Advancing the boundaries of high connectivity network simulation with distributed computing. *Neural Computation* 17: 1776-1801

9. Boucsein C, Nawrot MP, Rotter S, Aertsen A, Heck D (2005) Controlling synaptic input patterns *in vitro* by dynamic photo stimulation. *J Neurophysiol* 94: 2948-2958

GAINING CONSCIOUS CONTROL OF LOCAL BRAIN ACTIVITY USING REAL-TIME FMRI NEUROFEEDBACK

Rainer Goebel

Universiteit Maastricht, Department of Cognitive Neuroscience, Maastricht, The Netherlands

We explored a novel type of neurofeedback for fMRI signals which allows scanning two subjects simultaneously while they compete in a simple video game (ping pong). Subjects saw the same screen depicting the tennis field, the moving ball and the two rackets. Each subject was instructed to move her racket to the correct position using the BOLD signal. The fMRI measurements were performed on two MRI scanners (Siemens 1.5 T Sonata and 3 T Trio). For real-time data analysis and synchronized stimulus presentation, we developed a novel brain-computer interface, which allows the experimenter to observe the ongoing brain activity of the two subjects as well as to select the BOLD signal in selected regions-of-interest (ROIs) for neurofeedback. Before running the pong game, each of the participating subjects was trained to modulate regional brain activity to reach specific target levels and to adapt to the hemodynamic response delay. The ROI with the best modulation results was selected in each subject for controlling the racket in the subsequent video game. Subjects succeded in controlling the up and down movement of the racket by regulating voluntarily the activity in the selected ROIs achieving a hit rate of 60 to 80 %. Subjects reported that playing a game with another subject was highly motivating to practice the otherwise effortful brain modulation process. The results revealed that with extensive practice, subjects learned to reach and maintain intermediate levels of brain activity with high accuracy. This study demonstrates that it is possible to simultaneously measure two subjects engaged in joined attention during social interactions and to use subjects brain activity in real-time during these interactions. Our work might inspire further fMRI studies investigating the neural substrate of social cognitive processes.

A DENDRITIC SWITCH FOR SYNAPTIC PLASTICITY IN NEOCORTICAL PYRAMIDAL CELLS

Michael Häusser

Wolfson Institute for Biomedical Research, University College London, UK

Pyramidal neurons in the cerebral cortex span multiple cortical layers. How the excitable properties of pyramidal neuron dendrites allow these neurons to both integrate activity and store associations between different layers is not well understood, but is thought to rely in part on dendritic backpropagation of action potentials. I will discuss work that shows that the sign of synaptic plasticity in neocortical pyramidal neurons is regulated by the spread of the backpropagating action potential to the synapse. This creates a progressive gradient between LTP and LTD as the distance of the synaptic contacts from the soma increases. At distal synapses, cooperative synaptic input or dendritic depolarization can switch plasticity between LTD and LTP by boosting backpropagation of action potentials. This activity-dependent switch provides a mechanism for associative learning across different neocortical layers that process distinct types of information.

COUPLING BRAIN FUNCTION TO BLOOD FLOW AND OXYGEN CONSUMPTION: CONTROL MECHANISMS RELATED TO SIGNALLING IN CEREBRAL GREY MATTER

Martin Lauritzen

Glostrup Hospital and University of Copenhagen, Glostrup, Denmark

The brain is uniquely dependent on continuous energy supply. Brief disruptions lead to permanent loss of function, and energy failure is a common cause of cell death in major neurodegenerative diseases. In the normal brain, energy turnover varies with activity. Brain function emerges from signalling in and between neurons and associated astrocytes, organized in large-scale synaptic networks. The energy turnover associated with this activity is linked to increased metabolism and blood flow in the regions involved. This is the basis for the powerful neuroimaging techniques that have revolutionized the study of human brain function in recent years.

I will present recent data that examine mechanisms that couple activity-dependent changes in tissue metabolism and blood flow to signalling. Our findings suggest that the dendritic processing of excitatory synaptic inputs correlates more closely than the generation of spikes with the brain imaging signals, vascular as well as metabolic. We suggest that transient changes in cerebral blood flow and oxygen metabolism are produced by intracellular signal transduction mechanisms mainly in neurons. This is linked to the opening of ligand- and voltage-gated channels in the activated nerve cells, while the extent generation of spikes with the brain imaging signals, vascular as well as metabolic. We suggest that transient changes in cerebral blood flow and oxygen metabolism are produced by intracellular signal transduction mechanisms mainly in neurons. This is linked to the opening of ligand- and voltage-gated channels in the activated nerve cells, while the extent to which astrocytes are involved is unknown. We suggest that the intrinsic properties of neurons and the balance between synaptic excitation and inhibition control the amplitude of vascular and oxygen signals. Our new knowledge of cerebral blood flow and oxygen metabolism point to interrelated control mechanisms.

CELL AND MOLECULAR MECHANISMS INVOLVED IN THE MIGRATION OF CORTICAL INTERNEURONS

John Parnavelas

Department of Neuroanatomy, University College London, UK

The molecular mechanisms that guide the migration of the GABA-containing interneurons from their origin in the ganglionic eminence in the ventral telencephalon, around the corticostriatal notch, and into the cortex are the subject of intensive investigations at present. Numerous transcription factors, motogenic factors, neurotrophic factors, and other molecules have already been demonstrated to play a role. My colleagues and I have investigated the role of the LIM-homeodomain gene, Lhx6, which has been localized in neurons of the medial ganglionic eminence (MGE), including those destined for the developing cortex. The expression of this transcription factor in these neurons has prompted speculation that it plays a role in their neurochemical identity and migration. We performed loss of function studies for Lhx6 in mouse brain slices and dissociated MGE neuronal cultures using Lhx6-targeted siRNA. We found that silencing Lhx6 impeded the migration of interneurons into the cortex, although it did not obstruct their dispersion within the ganglionic eminence. Blocking Lhx6 expression in dissociated neurons taken from the MGE did not interfere with the production of GABA or the expression of GAD65/67 in these cells. These results indicate that Lhx6 does not specify the neurochemical identity of interneurons, but regulates their migration to the cortex.

Studies by Marin and colleagues (Marin et al., 2001) have suggested that cortical interneurons express neuropilin (Npn) receptors that enable them to respond to chemorepulsion produced by class 3 semaphorins in the striatal mantle. Their data further suggested that the repulsive activity of semaphorins in the developing striatum creates an exclusion zone for migrating interneurons and channels them into adjacent paths, leading to the formation of their migratory routes into the cortex. We have been investigating the role of Slit signalling in cortical interneuron migration by examining the forebrains

of Robo1 and Robo2 knockout mice generated by targeted deletion. We have found that Robo1 is required to keep the cells originating in the MGE clear of the striatum on their way to the cortex. However, it has been reported that neurons avoid the striatal area in Slit1/Slit2 double mutant mice, indicating that this may be a Slit independent event. Taken together, these observations suggest that both Npn/Sema and Robo1 signalling are required to steer interneurons around the striatum and into the cortex. Our analysis has also shown that more interneurons migrate into the cortex of Robo1 null mice, particularly in the rostral and middle cortical areas. This differential increase may be due to a recent finding (Yozu et al., 2005) that the sources and mechanisms of migration of interneurons that populate these areas are different from those destined for caudal cortical regions. We are also investigating the possibility that the increase in interneuron numbers in the rostral and middle cortical areas is due to a differential increase in proliferation in different parts of the ganglionic eminence. Finally, I shall present results of ongoing work on the role of Robo2 in the guidance of interneurons from their origin in the ventral telencephalon to the neocortex.

IN VIVO FORMATION OF SYNAPSE STRUCTURE AND FUNCTION

Stephan Sigrist

European Neuroscience Institute Göttingen, Germany

Aim of our work is to study formation and activity-dependent remodeling of synapses in native settings. Primary model system are glutamatergic synapses of the *Drosophila* neuromuscular junction, which are similar to glutamatergic CNS synapses of mammals in terms of ultrastructure and molecular composition but genetically easily accessible.

Recent work on hippocampus synapses suggested that regulating the mobility of non-NMDA type glutamate receptors can control synapse efficacy over shorter time periods. So far, however, glutamate receptor mobility had not been studied in the context of naturally occurring synapse formation. Confocal imaging on intact *Drosophila* larvae expressing fully functional GFP-labeled glutamate receptors allowed to follow individual postsynaptic densities over extensive time *in vivo*. We could show that new glutamate receptor fields form exclusively *de novo*, and reach their mature size in within several hours. The *in vivo* mobility of glutamate receptors was further analyzed with photo-bleaching and photo-activation protocols. It was found the incorporation rate of glutamate receptor directly controls the assembly of postsynaptic specializations, qualifying glutamate receptors as key organizers of postsynaptic assembly in this system.

Synaptic vesicles fuse at specialized active zone membranes often associated with electron dense projections (e.g. ribbons, T-bars). However, functional role and assembly of active zones remains to be characterized. Evidence will be presented showing that *Drosophila* Bruchpilot (BRP), a large coiled coil domain protein with homologies to mammalian CAST/ERC/ELKS proteins, is essential for the adequate composition of the active zone to ensure efficient vesicle release. BRP was found to form ring-like structures centered at the active zones of *Drosophila* neuromuscular synapses. In *brp* mutants defective active zone membranes, a complete loss of presynaptic dense bodies, and depressed evoked but sustained spontaneous vesicle release was observed. Elevated sensitivity for the Ca^{2+}-buffer EGTA together with untypical short-term facilitation indicated that this release defect was caused by an increased distance between Ca^{2+}-channels and vesicle docking sites. Correspondingly, Ca^{2+}-channels were not appropriately clustered at *brp* mutant synapses. Thus, dense body formation, Ca^{2+}-channel localization, and vesicular release probability are linked molecularly, and active zone assembly via BRP might well control plastic changes of synapses *in vivo*.

Abstracts of Oral Presentations

PHOSPHOLIPIDS AND PRG-1 CONTROL SYNAPSE STABILIZATION AND AXON GROWTH

Bräuer AU[1], Soriguera A[1], Singh B[2], Savaskan NE[3], Kieselmann O[1], Henneberger C[2], Swiercz J[4], Offermanns S[4], Nitsch R [1] and Grantyn R[2]

1. PRG Research Group, Molecular Neurobiology, Institute of Cell Biology and Neurobiology, Center for Anatomy, Charité – Universitätsmedizin Berlin, Philippstr. 12, D-10098 Berlin
2. Sensory and Developmental Physiology, Johannes Müller Institute for Physiology, Charité – Universitätsmedizin Berlin, Tucholskystr. 2, D-10117 Berlin, Germany
3. Division of Cellular Biochemistry, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands
4. Institute of Pharmacology, University of Heidelberg, Im Neuenheimer Feld 366, D-69120 Heidelberg, Germany

Phospholipid-mediated signaling on neurons provokes diverse responses such as neurogenesis, pattern formation and neurite remodeling. We have uncovered a set of molecules in the mammalian brain, named plasticity-related genes (PRGs), which regulates phospholipid signaling and is involved in mechanisms of activity-dependent and structural plasticity in the brain. PRG-1, the first member, was identified as a membrane-associated, brain- and vertebrate-specifically expressed protein, which belongs to a novel subclass of the LPP-family. First functional studies revealed that PRG-1 expression attenuates LPA-induced axon collapse in neuronal cells via modulation of extracellular LPA. LPA mediates its multiple cellular effects through G protein-coupled receptors (LPA_{1-3}/EDG).

Our new findings revealed that the LPA effect in primary neurons is more intrinsic compared to the drastic phenomenon of the retraction in cell lines. We found that the application of LPA to primary neurons leads to a destabilization on synaptic terminals, predominantly triggered through the LPA2 receptor. Detailed analysis revealed a loss of glutamatergic synapses, whereas GABAergic synapses are unaffected. Electrophysiology analysis confirmed this data and showed a significant reduction of mEPSC, but not mIPSC frequency. Overexpression of PRG-1 protects primary neurons against LPA-induced loss of glutamatergic synapses. Further morphological analyses revealed no changes in dendrites, but some in axon length. In overexpression of PRG-1 in primary neurons, axon length is decreased, whereas in PRG-1 knock down using siRNA, axon length is comparable to controls.

Signal transduction assays indicate that PRG-1 interacts intracellularly with regulators of the Ras signaling pathway, thereby inhibiting N-RAS, an outgrowth-promoting protein. Here I will discuss our findings with emphasis on LPA and PRG-1 involvement in the control mechanism governing axon and synapse stability.

HEAD-ANCHORED WHOLE-CELL RECORDINGS IN FREELY MOVING ANIMALS

Michael Brecht

Erasmus MC, University Medical Center Rotterdam, Department of Neuroscience, The Netherlands

Intracellular recording, which allows direct measurements of the membrane voltage and currents of individual neurons, requires a mechanically very stable preparation. Intracellular recording has thus been limited to *in vitro* and head-immobilized *in vivo* experiments. This restriction constitutes a major obstacle for linking cellular and synaptic physiology with animal behavior. To overcome this limitation we have developed a method for performing whole-cell recordings in freely moving rats. We use a miniature head-mounted device, with mechanical stabilization achieved by cementing the recording pipette in place after the whole-cell configuration has been established. This method allows long duration (average >20 minutes, maximum 60 minutes) recordings in freely moving animals that are remarkably insensitive to mechanical disturbances, followed by reconstruction of the cell. This technique could allow a wide range of new studies involving detailed measurement and manipulation of the physiological properties of identified cells during natural behaviors.

THE ZINC FINGER TRANSCRIPTION FACTOR BCL11A CONTROLS DENDRITE FORMATION AND LAYER-SPECIFIC CONNECTIVITY IN THE DORSAL SPINAL CORD

Anita John1, Heike Brylka1, Pentao Liu2, René Juettner1, E. Bryan Crenshaw3, Neal Copeland2, Carmen Birchmeier1 and Stefan Britsch1

1Max Delbrück Center for Molecular Medicine (MDC), 13125 Berlin-Buch, Germany
2Mouse Cancer Genetics Program, Center for Cancer Research, National Cancer Institute, Frederick, Maryland 21702, USA
3Mammalian Neurogenetics Group, Center for Childhood Communication, The Children's Hospital of Philadelphia, PA 19104, USA

The ability of the dorsal spinal cord to process somatosensory information resides in a heterogeneous population of sensory neurons organized in discrete layers within the dorsal spinal horn, and critically depends on the generation of layer-specific neuronal connections between primary sensory neurons and their spinal targets. The molecular mechanisms underlying layer formation and the generation of connectivity in the dorsal spinal cord are poorly understood. Here we show the zinc-finger transcription factor Bcl11a to be essential for

these processes. Conditional ablation of Bcl11a in the spinal cord results in disrupted layer formation in the superficial dorsal horn and the failure of spinal neurons to form complex dendrites. As a consequence, TrkA-positive primary sensory neurons do not project onto their specific spinal targets and synaptic input of mutant spinal neurons is reduced. Furthermore, we provide genetic evidence *in vivo* that the principle molecular architecture of the dorsal spinal horn is established independently of sensory input. Together, our findings demonstrate Bcl11a as a key molecule in the control of dendrite formation and the establishment of layer-type specific connectivity in the dorsal spinal horn.

T HELPER CELLS INDUCE AXONAL OUTGROWTH *IN VITRO* AND *IN VIVO* BY NEUROTROPHIN RECEPTOR UPREGULATION

Hendrix S, Sallach S, Hechler D, Lüdecke D, Kwidzinski E, Peters EM, Brandt C, Nitsch R

Institute of Cell Biology and Neurobiology, Center for Anatomy, Charité – Universitätsmedizin Berlin

After brain injury, invading T cells may support neuroregeneration by influencing axonal outgrowth. In the present study, we have studied the effects of T helper cells type 1 (Th1) and type 2 (Th2) on axonal outgrowth *in vitro* and *in vivo*. We have used murine entorhinal cortex explants (ECs) in a collagen matrix to quantify axonal outgrowth, as well as a coculture of EGFP-expressing ECs and wildtype hippocampi to investigate the growth of EGFP-positive nerve fibers into the wildtype target tissue. Furthermore, we have analysed *in vivo* the effect of locally injected Th2 cells on axonal outgrowth in the entorhinal cortex lesion model. Here, we report that activated Th2 cells play a decisive role in stimulating axonal outgrowth after brain lesion *in vitro* and *in vivo*. Axonal outgrowth was stimulated by activated MBP-specific, OVA-specific or ConA-stimulated Th2 cells but not by naïve T cells. Th2-induced axonal outgrowth is mimicked by recombinant interleukin (IL)-4 and abolished by inhibitory antibodies against IL-4. Th2 cells upregulate the expression levels of the NT receptors (NTRs) TrkA, TrkB and TrkC on cortical neurons in organotypic brain slices. After entorhinal cortex lesion intracerebral injection of Th2 cells upregulated NTRs on hippocampal-entorhinal neurons of the lesioned hemisphere. Th2-induced axonal outgrowth is significantly reduced by inhibitory antibodies against all NTRs and eliminated by the pan-Trk inhibitor K252a. Our results provide strong evidence for a novel mechanism by which Th2 cells and their marker cytokine IL-4 promote axonal outgrowth via upregulation of neuronal NTR expression after brain injury.

ESTROGEN CONTROLS PKC-EPSILON-DEPENDENT MECHANICAL HYPERALGESIA THROUGH DIRECT ACTION ON NOCICEPTIVE NEURONS

T. Hucho*, O. Dina, J. Kuhn, J. Levine

*NIH Pain Center at the UCSF, San Francisco, USA, *now at MPI für Molekulare Genetik, Berlin*

PKC-epsilon is an important intracellular signaling molecule in primary afferent nociceptors, implicated in acute and chronic inflammatory as well as neuropathic pain. In behavioral experiments the inflammatory mediator epinephrine produces PKC-epsilon-dependent hyperalgesia only in male rats. The mechanism underlying this sexual dimorphism is unknown. We show that the hormone environment of female rats changes the nociceptive signaling in the peripheral sensory neuron. This change is maintained in culture also in the absence of a gender-simulating environment. Addition of estrogen to male-derived DRG neurons produces a switch to the female phenotype, namely abrogation of beta$_2$-AR-initiated activation of PKC-epsilon. Estrogen interferes downstream of the beta$_2$-AR with the signaling pathway leading from Epac to PKC-epsilon. The interfering action is fast indicating a transcription-independent mechanism.

As in other systems, estrogen has a dual effect. If applied minutes before beta$_2$-AR or Epac stimulation, estrogen abrogates the activation of PKC-epsilon. In contrast, estrogen applied alone leads to a brief translocation of PKC-epsilon. Also *in vivo* the activity of estrogen depends on the stimulation context. Intradermal injection of an Epac activator as well as estrogen alone induces mechanical hyperalgesia through a PKC-epsilon-dependent mechanism. In contrast, injection of estrogen preceeding the activation of Epac completely abrogates the Epac-induced mechanical hyperalgesia.

Our results indicate that gender differences in nociception do not reflect the use of generally different mechanisms. Instead, the contribution of a common set of signaling pathways can be modulated by hormones.

OPTIMIZING TETHERED TOXINS FOR CELL-AUTONOMOUS INACTIVATION OF ION CHANNELS

Ibañez-Tallon, I., Stürzebecher, A., Liehl B., Medic B.

Lab. Molecular Neurobiology, Max Delbrück Center, Berlin Germany, Lab. Molecular Biology, HHMI-The Rockefeller University, New York

Venom toxins have been widely used to investigate the properties of neurotransmitter receptors and ion channels. Their high affinity and capability to discriminate between different subunit combinations has allowed a better understanding of the structure, function and physiology of ion channels and receptors. Based on the mode of action and

similarities of the mammalian prototoxin lynx1 and bungarotoxins, we have recently shown that tethering these toxins to cell membranes using the GPI anchor of lynx1, targeted and cell-autonomous inactivation of specific receptors and ion channels can be achieved. Here, we have extended these studies to a number of conotoxins, spider, scorpion and sea anemone toxins and characterize their action on nicotinic acetylcholine receptors, voltage gated sodium and calcium channels and acid sensitive channels. While for some receptor/channel combinations a tethered toxin with a short linker preceding the GPI tether was sufficient to achieve total inactivation of currents, other receptor combinations required tethered toxins with linkers of increased length. In addition we have generated tethered toxin isoforms fused to different transmembrane domain containing proteins and shown their activity when coexpressed with different ion channels. Altogether these studies provide proof of the wide possible use of this approach to manipulate many different ion channels. Moreover, by varying the linker length and type of tether, these structure-function studies using tethered toxins offer a new tool to investigate receptor/ion channel-toxin interfaces.

OVERVIEW OF RESEARCH ACTIVITIES: CLC, KCNQ, AND KCC PROTEINS

Thomas J. Jentsch

ZMNH (Zentrum fuer Molekulare Neurobiologie Hamburg), Hamburg University, Germany

Our lab is interested in various ion transport processes, in particular in CLC chloride channels and transporters, KCNQ potassium channels, and KCl co-transporters. We study their structure-function relationships and their physiological roles, which often become apparent from the pathologies observed upon their disruption. These result in diseases like epilepsy, deafness, kidney stones, osteopetrosis, and neurodegeneration. We have elucidated several human genetic diseases and have generated mouse models for most CLCs and all KCCs. We have identified new beta-subunits for CLC proteins, mutations in which also cause disease. A recent strong interest is in the role of endosomal CLC proteins in endosomal/lysosomal function and of KCCs in the regulation of intracellular chloride. A short, cursory overview over our research activity will be given.

FUNCTION OF CALEB IN REGULATING SYNAPTIC CONNECTIVITY

Jüttner, R.[1], Moré, M.I.[1], Babich, A.[1], Meier, J.[2], Erdmann, B.[1], Grantyn, R.[2], Montag, D.[3], Craveiro, R.B.[1], and Rathjen, F.G.[1]

[1]Max-Delbrueck-Center for Molecular Medicine, Berlin, [2]Johannes Müller Institute of Physiology, Charité, Berlin, [3]Leibniz Institute for Neurobiology, Magdeburg

Proteins, located at the cell surface and modulated by neuronal activity might be promising candidates to transform sensory information into a specific synaptic function including morphological correlates. CALEB, a member of the EGF-family was characterized to be activity-dependent processed on the cell-surface (Jüttner et al., 2005). Developmental regulated expression patterns, with peak levels in periods of synaptogenesis and synapse refinement makes CALEB a promising candidate to be involved in regulation synaptic connectivity.

Analysis of synaptic connectivity in the immature colliculus superior revealed that CALEB regulates the release probability of the neurotransmitter, therefore the absence of this protein results in a reduced activation. While the function of synapses is affected by the absence of CALEB the number and morphological characteristics remained unchanged. In the immature cerebellum CALEB is expressed within in the Purkinje cell layer, while later in development it is primarily found in the molecular layer. The developmental change in the localization in a period of synapse elimination may suggest a specific function. Analysis of the climbing fiber - Purkinje cell synapse revealed an earlier maturation of the adult-like, monosynaptic innervation in the CALEB knockout mouse compared to the wild type. This faster synapse elimination appears not to be induced not by mGluR-mediated signalling by stronger parallel fiber input. However, at least, these changes in the maturation of connectivity lead to deficiencies in the motor coordination of the knockout mouse.

In summary, CALEB is an activity-dependent regulated protein, which plays a role in adjustment of neuronal networks.

Jüttner et al., Neuron 2005

AUTOREACTIVE PHENOMENA INDUCED BY ISCHEMIC BRAIN INJURY

J. Klehmet[1], C. Meisel[2], T. Ziemmssen[3] , K. Prass[1] and A. Meisel[1]

[1] Experimental Neurology, Charité Berlin; [2] Institute of Immunology, Charité, Berlin; [3] Technical University of Dresden

Our previous studies demonstrated that stroke induces an immunodeficiency syndrome (SIDS) leading to severe bacterial infections such as pneumonia and sepsis. This is at least partially due to overactivation of the Sympathetic Nervous System (SNS) causing changes in the immune system such as apoptosis of lymphocytes, dysfunction of lymphocytes (IFNγ deficiency) and deactivation of monocytes. Moreover, it has been widely accepted that ischemic brain jury leads to the breakdown of blood brain barrier leading to an influx of leukocytes into the ischemic territory. There is also substantial evidence that ischemia-induced inflammation plays a critical role in the late stages of cerebral ischemic injury. In addition, clinical data suggest a negative effect of a first ischemic event on the outcome for subsequent ischemic injuries. In the present study we

show that ischemic brain injury leads to induction of autoreactive IFNγ producing CNS-antigens specific T cells. These autoreactive T cells contribute to the neurological outcome. Additionally, we demonstrate in a MOG TCR transgenic mouse model that ischemic brain injury leads to massive infiltration of MOG specific T cells into the ischemic but also the contralateral hemisphere contribute into a worse clinical outcome and higher mortality.

THE BERLIN BRAIN-COMPUTER INTERFACE (BBCI) - SINGLE-TRIAL CLASSIFICATIONS OF PHANTOM-MOVEMENTS OF ARM AMPUTEES

Volker Kunzmann[1], Benjamin Blankertz[2], Guido Dornhege[2], Matthias Krauledat[2], Klaus-Robert Müller[2,3], Gabriel Curio[1]

[1] Neurophysics Group, Campus Benjamin Franklin, Charité - University Medicine Berlin
[2] Fraunhofer FIRST (IDA), Berlin
[3] Dept. of Computer Science, University of Potsdam

Introduction: The Berlin Brain-Computer Interface (BBCI) is based on single-trial classifications of multi-channel pre-movement EEG-signals, discriminating right vs left limb movements with accuracies up to 99 % in healthy subjects. The current study used 128-channel EEG recordings in patients with traumatic amputations of one arm or hand to compare lateralised readiness potentials (LRP) and event related desynchronization (ERD) associated with phantom movements. We analysed the single-trial classification with a BBCI standard EEG-classifier to clarify whether classification rates are in a range suitable for feedback applications like e.g. controlling prostheses.
Methods: We studied eight patients (1 w, 7 m, aged 37-74 years) with amputations between 16 and 54 years ago. A digital metronome played alternatingly two distinct sounds in a steady rhythm (intersound intervals 1 to 1.75 s). Concomitant with the higher sound, the patient had to perform either a finger tap on a keyboard using the healthy hand or a phantom movement with a phantom finger. The deeper sound called for rest. Activity of the stump muscles was controlled by means of surface EMG-recordings.
Results and Discussion: (1) In 7 from 8 patients we found an LRP over the contralateral primary motor cortex associated with the phantom limb movement. (2) While real movements were preceded by standard ERDs, phantom finger/hand movements showed a clearly less distinct ERD. (3) The 'right vs left' single-trial classifications performed with a standard BBCI classifier yielded hit rates between 60-78% (mean ± s.e.m.: 69 ± 7%).
Conclusions: This study demonstrates that patients with traumatic amputations show lateralized RPs associated with phantom limb movements. Classification well above chance level was possible in all 8 subjects. Together, these findings indicate a possibility to exploit lateralized RPs for BCIs in amputees, for example to control a prosthesis.

COMMON MOLECULAR MECHANISMS INVOLVED IN GUIDANCE OF BLOOD VESSELS AND NERVES

Ferdinand Le Noble

Max-Delbrück-Center for Molecular Medicine (Berlin-Buch) MDC

Blood vessels and nerves are complex, branched structures that share a high degree of anatomical similarity. Guidance of vessels and nerves has to be exquisitely regulated to ensure proper wiring of both systems. Although superficially distinct, the mechanisms involved in wiring neural and vascular networks share functional similarities. Axonal growth cones direct the outgrowth of developing axons in response to attractant or repulsive guidance cues. The anatomical equivalent of the axonal growth cone in the vascular system is the endothelial tip cell. This specialized cell leads the growing edge of angiogenic blood vessel sprouts. It sends out numerous filipodia that sense growth factor gradients and guides and positions the angiogenic sprout during early development. We postulate that the molecular mechanisms that regulate tip cell identity and sprout guidance are similar to the developing nervous system. We show that tip cell identiy is controlled by Notch-Delta signaling. An endothelial cell sensing a gradient of the attractant vascular endothelial growth factor (VEGF), transforms in a tip cell, releases the notch ligand delta-like-4 (Dll4), which activates Notch receptors on adjacent endothelial cells resulting in repression of tip cell identify in these cells. The concept of cells repressing differentiation of neighboring cells is called lateral inhibition, an established principle in neuronal development. In addition we show that the repulsive netrin receptor UNC5B expressed in the vascular systems regulates endothelial tip cell behavior and guidance events controlling branching morphogenesis of the vascular system. Our current work focuses on identifying the full repertoire of action of neural guidance genes in the vascular system.

METABOLIC ALTERATIONS IN THE DORSOLATERAL PREFRONTAL CORTEX AFTER TREATMENT WITH HIGH-FREQUENCY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN PATIENTS WITH UNIPOLAR MAJOR DEPRESSION

Alexander Luborzewski

Clinic for Psychiatry, Campus Benjamin Franklin, Charité

Neuroimaging studies suggest a specific role of anterior cingulate cortex (ACC) and left dorsolateral prefrontal cortex (DLPFC) in major depression. Stimulation of the latter by means of repetitive transcranial magnetic stimulation (rTMS) as an antidepressant intervention has increasingly been investigated in the past. The objective of the present study was to examine in vivo neurochemical

alterations in both brain regions in 17 patients with unipolar major depression before and after ten days of high-frequency (20 Hz) rTMS of the left DLPFC using 3-tesla proton magnetic resonance spectroscopy. Six out of 17 patients were treatment responders, defined as a 50% reduction of the Hamilton Depression Rating scale. No neurochemical alterations in the ACC were detected after rTMS. As compared to the non-responders, responders had lower baseline concentrations of DLPFC glutamate which increased after successful rTMS. Correspondingly, besides a correlation between clinical improvement and an increase in glutamate concentration, an interaction between glutamate concentration changes and stimulation intensity was observed. Our results indicate that metabolic, state-dependent changes within the left DLPFC in major depressive disorder involve the glutamate system and can be reversed in a dose-dependent manner by rTMS.

COMBINED INHIBITION OF NA, K-ATPASE AND NO SYNTHASE CAUSE CORTICAL SPREADING ISCHEMIA IN THE RAT CORTEX

Major, S. and Dreier, J.P.

Dept. of Neurology and Experimental Neurology, Charité – Universitätsmedizin Berlin, Germany

Delayed ischemic neurological deficit (DIND) is one of the major complications after subarachnoid hemorrhage (SAH). It occurs in up to 40% of patients who survive the initial bleeding. About 13% of them develop delayed cerebral infarcts on CT.

Based on experiments in rats, it has been proposed that cortical spreading ischemia (CSI) is a mechanism of DIND. CSI is a long-lasting, spreading wave of an ischemic blood flow change leading to widespread cortical infarcts. It represents an inverse hemodynamic response to cortical spreading depression. CSI occurs when the baseline extracellular K^+ concentration ($[K^+]_o$) is increased NO concentration is reduced (e.g. due to nitric oxide synthase (NOS) inhibition by L-NNA) in the subarachnoid space.

In cell culture experiments increased $[K^+]_o$ is associated with a decrease of Na, K-ATPase activity. To test whether this ubiquitous ATPase is involved in the mechanism of CSI, we investigated if CSI occurs after combined brain topical administration of L-NNA and the Na, K-ATPase inhibitor ouabain. A closed cranial window was implanted in rats. Cerebral cortex was superfused with artificial cerebrospinal fluid (ACSF) containing L-NNA (1 mM). Subsequently, increasing concentrations of ouabain (0.5, 5, and 50 μM) were added to the ACSF. The CBF changes were monitored either by Laser-Doppler-Flowmetry or Laser Speckle Contrast Analysis imaging.

Compared to L-NNA or ouabain alone the combination induced CSI in a dose dependent manner (duration of hypoperfusion under L-NNA+ouabain (5 μM): 3:50 (3:00 – 5:26) min and L-NNA+ouabain (50 μM): 6:55 (5:20 – 22:24)min). CBF fell to about 50% of baseline value. Using a digital camera we recorded a propagating progressive constriction of arteries simultaneously with the CBF decrease.

We conclude that combined NOS and Na,K-ATPase inhibition produce CSI in a dose-dependent manner.

ALZHEIMER DISEASE: EARLY MARKERS IN MOUSE AND MAN

Matthias Riepe

Klinik für Psychiatrie, Campus Benjamin Franklin, Charité Berlin

PREDICTING TINNITUS PITCH WITH A COMPUTATIONAL MODEL FOR THE DEVELOPMENT OF NEURONAL HYPERACTIVITY AFTER HEARING LOSS

R. Schaette (1), O. König (2), M. Gross (2) and R. Kempter (1)

(1) Institute for Theoretical Biology, Humboldt-Universität zu Berlin, Germany
(2) Phoniatrics, Charité – University Hospital Berlin, Germany

Tinnitus is often associated with hearing loss, but how hearing loss could lead to the development of tinnitus has remained unclear. In animals, hearing loss through cochlear damage can lead to behavioral signs of tinnitus that are correlated with increased spontaneous firing rates or hyperactivity of neurons in the auditory brainstem.

We have developed a model that shows how such hyperactivity could arise after hearing loss. Our main assumption is that the mean activity of central auditory neurons is stabilized through homeostatic plasticity. Decreased auditory nerve activity after hearing loss is then counteracted through an increase of excitatory and a decrease of inhibitory synaptic strengths. This restores the mean rate, but it can lead to increased spontaneous firing rates depending on the type and degree of cochlear damage. In our model, the amount of hyperactivity along the tonotopic axis therefore depends on the shape of the audiogram. Here we test the model's ability to predict tinnitus pitch from the audiograms of patients with both noise-induced hearing loss and tone-like tinnitus. Given the audiograms, the model is used to determine the spontaneous firing rate along the tonotopic axis. The resulting patterns of hyperactivity exhibit distinct peaks that are associated with steep drops in the audiograms. If such peaks are interpreted as the basis for a tone-like tinnitus sensation, the model predicts tinnitus frequencies that are close to the tinnitus pitch of the patients. The deviations between predicted and observed pitch are within the range of errors typically obtained by psychophysical tinnitus pitch matching. Our model thus constitutes a plausible hypothesis of how hearing loss could lead to tinnitus.

Supported by a grant of the DFG to RK.

NOW YOU FEEL IT – NOW YOU DON´T: ERP CORRELATES OF SOMATOSENSORY AWARENESS

Ruth Schubert[1], Felix Blankenburg[1], Steven Lemm[2,3], Arno Villringer[1], Gabriel Curio[2]

1 Department of Neurology, Charité - University Medicine, Campus Mitte, Berlin, Germany; 2 Neurophysics Group, Charité - University Medicine, Campus Benjamin Franklin, Berlin, Germany; 3 Fraunhofer-Institut FIRST, Kekuléstraße 7, Berlin, Germany

Studies investigating perceptual awareness and its relation to activation of the primary sensory cortex frequently use stimuli at the sensory threshold. Here, we investigated cortical correlates of somatosensory-awareness in the case of supratheshold stimuli using EEG-derived event-related potentials (ERPs) in a masking paradigm: Conscious perception of a weak, but clearly suprathreshold "target" stimulus at one finger was suppressed in a significant number of trials when followed 70 ms later by a higher-intensity "mask" stimulus applied at the contralateral hand. For 12 healthy subjects, somatosensory ERPs were compared for trials with perceived target stimuli versus trials with unperceived target stimuli. Early ERPs, such as the P60 and N80 which are generated in the contralateral S1, were found independent of stimulus perception. In contrast, for trials with consciously perceived target stimuli, significant amplitude enhancements were observed for the parietal P100 and the frontal N140 components. Thus, early activation of S1, even by clearly suprathreshold stimuli, is not sufficient to warrant conscious stimulus perception. Conscious stimulus processing differs significantly from unconscious processing starting around 100 ms after stimulus presentation when the signal is processed in parietal and frontal cortices, brain regions crucial for stimulus access into conscious perception.

FUNCTIONAL ANALYSIS OF CALEB/NGC IN MOUSE BRAIN DEVELOPMENT BY IN UTERO ELECTROPORATION

S. Schumacher[1], M.-R. Rašin[2], J. Vogt[1], S. Khrulev[1], N. Brandt[1], N. Šestan[2], and R. Nitsch[1]

[1]Institute of Cell Biology and Neurobiology, Center for Anatomy, Charité University Hospital, Berlin [2]Department of Neurobiology and Kavli Institute for Neuroscience, Yale University School of Medicine, New Haven, CT 06510

The classical approach to study the function of a protein of interest in vivo is the analysis of knockout mice. However, this approach has some limitations. First, the insertion of foreign DNA into a genome can have unexpected effects on other genes leading to compensation and absence of a phenotype or possibly to a phenotype unrelated to the gene of interest. Second, deleting a gene throughout the entire life span of an organism can also give different results than altering gene function during a certain critical time period. Third, for several functional aspects it may be necessary to target only a subgroup of cells and not all cells in a specific tissue. To circumvent these limitations we took advantage from the mouse in utero electroporation technique. With this technique it is possible to reduce expression levels of specific genes via RNAi, to misexpress genes, to functionally inactivate gene products, or to force expression of specific genes in a subset of cells during a certain critical time period of development. We give a description of this experimental approach, and present data about the functional in vivo analysis of the neural transmembrane EGF family member CALEB/NGC (Chicken Acidic Leucine-rich EGF-like domain containing Brain protein/Neuro-glycan C) in nerve cell differentiation.

Supported by a grant of the Deutsche Forschungsgemeinschaft to StS and RN.

Poster Session I

1 EXPRESSION PATTERN OF OPA1 PROTEIN ISOFORMS IN MOUSE BRAIN

V.R. Akepati, A. Otto *, E.C. Mûller *, and C. Alexander

*Department of Neurodegeneration, * Department of Neuroproteomics, Max-Delbrück Center for Molecular Medicine, Berlin, Germany*

Mutations in the OPA1 gene encoding a dynamin-related mitochondrial protein underlie autosomal dominant optic atrophy (adOA) and may perturb the biogenesis and maintenance of mitochondria. The OPA1 protein is localized to the mitochondrial intermembrane space, where it is tightly bound to the outer leaflet of the inner membrane. Alternative splicing of exons 4, 4b and 5b result in eight isoforms of OPA1. In this study we investigated various mouse tissues for specific expression of different OPA1 protein isoforms and their involvement in protein complex formation.

We raised monoclonal antibodies against OPA1 isoform 1, bacterially expressed as a GST fusion protein. Western blot analysis of mitochondrial lysates with anti-OPA1 monoclonal antibody identified five bands of OPA1 in heart, liver, kidney and brain migrating around 100kDa. Certain OPA1 isoforms presented with higher abundance then others within one given tissue. In addition, comparison of the band patterns of the used lyastes revealed tissue specific expression levels of various isoforms. Immunoprecipitation of OPA1 from mouse brain mitochondrial lysate, followed by tandem MS/MS mass spectrometry analysis, identified isoform 1 and 7 to be predominantly expressed in brain. We applied glycerol density-gradient ultracentrifugation to investigate protein complex formation by these different isoforms. The results indicate that all isoforms of OPA1 are present in molecular weight complexes of 300 -400kDa in size.

2 ANTICONVULSANT EFFECTS OF BILATERAL INJECTION OF N^6-CYCLOHEXYLADENOSINE INTO THE CA1 REGION OF THE HIPPOCAMPUS IN AMYGDALOID KINDLED RATS

Alasvand, M [1]., Mirnajafi-Zadeh, J[2]., Fathollahi, Y[2].

Department of Physiology, Medical School Kurdestan University[1] - Tarbiat Modarres University[2] , Tehran, Iran

Adenosine is a neuromodulator, which has anticonvulsant effects in different animal models of epilepsy including kindling, but it precise site of action has not been recognized.

In this study the role of adenosine A_1 receptors of CA1 region of the hippocampus on amygdala kindled seizures was investigated. All animals were implanted with a tripolar (stimulating and recording) electrode in the amygdala and two guide cannulae in the CA1 region of the hippocampus and were stimulated daily to kindled. Results obtained showed that in kindled animals, bilateral injection of N^6-cyclohexyladenosine (CHA) at doses of 0.1, 1 and 10 μM into the CA1 region of the hippocampus reduced the afterdischarge duration and stage 5 seizure duration significantly, but there were no changes in seizure stage. Also, bilateral injection of 1,3-dimethyl-8-cyclopenthylxathine (CPT) at doses of 0.5 and 1 μM into the CA1 region of the hippocampus couldn't produce any changes in the seizure parameters. Intrahippocampal pretreatment of CPT (1 μM) before CHA (0.1 and 1 μM), reduced the effects of CHA on seizure parameters significantly. Thus, it may be suggested that CA1 region of the hippocampus plays an important role in spreading seizure spikes from the amygdala to other brain regions and activation of adenosine A_1 receptors in this region, participates in anticonvulsant effects of adenosine agonists.

3 A PROTEOMICAL APPROACH OF THE EFFECT OF BRAIN TRAUMA ON BBB

Aspeslagh, S.; Haseloff, R.; Lohrberg, D.; Mikotheit, K.; Blasig, I.

Leibniz-Institut für Molekulare Pharmakologie (FMP), Robert-Rössle-Str. 10, 13125 Berlin, Germany

Total brain trauma (TBI) is a dramatic pathological status characterized by primary and secondary damage pathways. Especially secondary pathways which involve several inflammatory mediators could be an important target for novel pharmacological approaches. Beside counteracting this cytokine release, another therapeutical approach is stem cell transplantation. Despite interesting results, this technique remains to be further analysed because the results regarding whether or not these stem cells really enter the brain parenchyma of traumatized rats are conflicting. It has therefore been hypothezised that stem cells could exert their beneficial action through their release of neurotrophins which could be initiated by the cytokines released by brain endothelial cells constituting the blood-brain barrier (BBB).

Although many experiments have been focused on dying neurons and gliosis forming astrocytes, the BBB is vitally affected as witnesses the life-threatening brain edema, which occurs often after severe TBI. We therefore analysed the influence of acute traumatic brain conditions on the proteome of BBB cells. We assume that this knowledge will help us to elucidate detrimental signalling pathways that cause secondary brain damage after TBI.

Several brain endothelial cell lines were grown with an extract of the brain of traumatized rats for 24h (the homogenate extract was prepared 1h after brain trauma and thus was called acute brain trauma condition). As control condition, we used a respective extract but from non-traumatized rats. The brain capillary endothelial cells (BCEC) were fractionated in 3 parts which correspond to nuclear proteins, membrane proteins and cytosolic proteins. These 3 parts were analysed with 1D-gel electrophoresis and Q-TOF mass spectrometry resulted in a comparative proteome study.
These results are important in the search for targets for neuroprotective and brain edema preventing strategies that could be applied in the future to brain trauma patients.

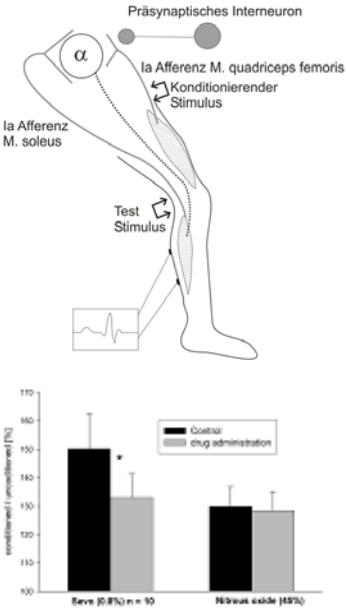
4 SEVOFLURANE BUT NOT NITROUS OXIDE ENHANCES GABAERGIC PRESYNAPTIC IA-INHIBITION IN HUMANS

J.H. Baars, M. Benzke, F. von Dincklage, J. Reiche, B. Rehberg

Department of Anaesthesiology Charité Campus Mitte, Berlin, Germany

Introduction: *In vitro* studies performed on isolated rat spinal cord indicate that presynaptic inhibitory effects of volatile anesthetics play an important role in the suppression of movement responses to noxious stumuli during anesthesia. Specific presynaptic effects have not yet been shown in humans. Here we used heteronymous Ia facilitation of the soleus H-reflex from the femoral nerve [1] as a specific pathway involving GABAergic presynaptic inhibiton to demonstrate presynaptic and probably GABAergic effects of the volatile anesthetic sevoflurane in humans.
Method: The study was carried out on 10 volunteers aged 23-32. The subjects inhaled 0.8 Vol% sevoflurane via a facemask connected to a circuit of an anesthesia work station. This caused a sedative state in which the subjects did not respond to loud verbal commands. The soleus H-reflex was evoked every 6s in the popliteal fossa and was recorded with disc electrodes placed over the soleus muscle. The soleus H-reflex was conditioned (increased in size) by an additional stimulation of the femoral nerve, which was stimulated through a monopolar ball electrode in the femoral triangle (1.15 x motor threshold). The conditioning stimulus was applied within a time window that assures a facilitation of the H-reflex caused by a pure monosynaptic EPSP. Conditioned and unconditioned reflexes were tested in random order. Measurements of the amplitude of the reflex response were performed under 3 conditions: a) prior to sevoflurane administration (1st control) b) during steady-state propofol administration (propofol) c) 35min after sevoflurane administration was stopped (2nd control). A series of 100 unconditioned and 100 conditioned H-reflexes was recorded in each condition.
The amount of facilitation is expressed as percent of the mean unconditioned value. Data from both control measurements was pooled and compared with the sevoflurane measurement (t-test $p<0.05$). To support hypothesis, that the decrease of H-reflex facilitation is due to GABAergic effects the same protocol was carried out in 6 subjects, which inhaled 50% nitrous oxide, which does not interact with GABA-receptors.
Results: In eight subjects soleus H-reflex facilitation was reduced significantly by sevoflurane (t-test, $p<0.01$). Nitrous oxide did not affect H-reflex facilitation, thought the H-reflex itself is even stronger suppressed than the during sevoflurane administration at the chosen concentrations. The average facilitation under sevoflurane and nitrous oxide administration is shown in fig. 2.
Conclusion: The results show that sevoflurane but not nitrous oxide reduces heteronymous Ia facilitation of the soleus H-reflex from the femoral nerve. Our data are the first confirmation in humans that sevoflurane acts a) via a presynaptic effect and b) that this effect is mediated by $GABA_A$ receptors, as previously suggested by in-vitro experiments.[2]

1. Hultborn H, Meunier S, Morin C, Pierrot-Deseilligny E: Assessing changes in presynaptic inhibition of I a fibres: a study in man and the cat. J.Physiol 1987; 389: 729-56
2. Grasshoff C, Antkowiak B: Propofol and sevoflurane depress spinal neurons in vitro via different molecular targets. Anesthesiology 2004; 101: 1167-76



5 A PSYCHOPHYSIOLOGICAL MODEL OF ELEMENTARY COLOR SENSATIONS IN MAN

Werner G. K. Backhaus

Theoretical and Experimental Biology, Bioinformatics, Free University Berlin and University for Technology Berlin, Germany

A psychophysiological model of the elementary color sensations red, green, blue, yellow, black, and white that constitute our color sensations has been developed. The model takes measured spectral sensitivity functions of human cones from the literature into account. The well approved neuronal color opponent coding (COC) model, originally developed for insect vision, is extended and adapted to light discrimination judgments in humans [1]. As was shown to be the case in the bee, the COC neurons are in the case of human color vision assumed to span the subjective light-discrimination space and 2) to steer the amounts of the elementary color sensations piece by piece linearly. 3) A hypothesized normalization-mechanism of the elementary colors keeps the total amounts at 100%. An advantage of the presented model is that all parameters have fixed values, i.e. have no rotational degrees of freedom [2]. Classical psychophysical measurements of the amounts of the elementary color sensations stimulated by monochromatic light were simulated with the model. Best fits of predicted data to data measured in two individual observers allowed to determine the parameters uniquely. The model precisely describes the general characteristics and also the measured individual differences of both observes by respective deviations of the physiological parameters.

[1] Backhaus, W., 2004. A physiological model of human color discrimination. In: Proceedings of the 4th Forum of European Neuroscience (FENS), July 10–14, 2004, Lisbon, Portugal, Abstracts, Vol. 2, A, p. 194.5. FENS, Lisbon.

[2] Backhaus, W., 2006. Psychophysiological simulations of spatial color vision. In: Tagungsband zum V. Symposium "Licht und Gesundheit", 23.-24.2.2006, TU Berlin, Hauptvorträge, pp. 8-21, Hrg.H. Kaase & F. Serick. Kistmacher, Berlin.

6 EFFECT OF NOISE EXPOSURE ON HIGHER AUDITORY STRUCTURES

Dietmar Basta[1], Barbara Tzschentke[2] and Arne Ernst[1]

[1]Dept. of Otolaryngology at UKB, Free University of Berlin
[2]Dept. of Biology, Humboldt-Universität zu Berlin

The peripheral damage within the inner ear cannot fully explain the audiological symptoms in noise-induced hearing loss (NIHL), e.g. tinnitus, recruitment, reduced speech intelligibility, hyperacusis. Effects on central auditory structures seems to play an important role in NIHL. It has been shown that noise leads to eminent neurophysiological and structural changes within the lower auditory pathway. Higher auditory structures (e.g. inferior colliculus (IC), medial geniculate body (MGB), auditory cortex (AC)) are characterized by metabolic changes after noise exposure. However, little is known about electrophysiological or microstructural changes within these structures. The present paper was therefore aimed at investigating the spontaneous neuronal activity as well as the cell density within the higher auditory pathway before and after noise exposure.

Normal hearing mice were exposed to noise (10 kHz center frequency at 115 dB SPL for 3 h) at the age of 21 days under anesthesia.

Following these procedure cell density was significantly reduced in all subdivisions of the MGB and in layer IV-VI of AC. In contrast to this findings cell density remained unchanged in layer I-III of the AC and in the non-auditory control area (Gyrus dentatus). The spontaneous activity of IC-neurons in noise-exposed animals was significantly lower compared to controls. In both groups, the firing rate of approximately 80 % of IC neurons was increased significantly during the application of the $GABA_A$ receptor antagonist bicuculline (10 μM).

The present findings demonstrate a significant noise-induced change of the neuronal cytoarchitecture and spontaneous activity in central key areas of the higher auditory pathway. These changes could contribute to the complex psychoacoustic symptoms of NIHL.

7 INVOLVEMENT OF $GABA_A$-MEDIATED TRANSMISSION IN STIMULUS-INDUCED SHARP WAVE-RIPPLE COMPLEXES IN HIPPOCAMPAL AREA CA3 *IN VITRO*

C. J. Behrens, L. P. van den Boom, J. P. Richter and U. Heinemann

Institute for Neurophysiology, Charité - Universitätsmedizin Berlin, 10117 Berlin, Germany

Generation of sharp wave-ripple complexes (SPW-R) within hippocampal area CA3 was induced by repeated stimulation of orthodromic as well as antidromic pathways of adult rat hippocampal brain slices. SPW-R originated in CA3 and propagated throughout the hippocampus. Intracellular recordings showed that their induction involves time-dependent changes in interactions between clusters of neurons in the CA3 associational network. In about 50 percent of recorded CA3 pyramidal cells synaptic input during SPW-R caused an EPSP generation followed by 1-4 action potentials whereas the remaining cells responded with a compound IPSP. Blocking $GABA_A$-mediated inhibition by Bicuculline or SR-95531 during SPW-R activity led to a gradual transition of SPW-R into prolonged hypersynchronous bursts within area CA3. In comparison to stimulus-induced SPW-R the SR-95531-mediated bursts showed a significantly higher amplitude, duration and frequency content. Extracellular potassium increase following a single burst was >10 fold higher than that followed by a

single SPW-R. Intracellular recordings of all recorded cells during $GABA_A$ receptor blockade showed that the bursts were characterized by a large, prolonged depolarization envelop giving rise to 20-40 action potentials. Application of the gap junction blocker mefloquine during hypersynchronous network activity largely reduced fast ripple oscillations (~300 Hz) without blocking recurrent bursts.
The results show that the generation of SPW-R depends on both excitatory and inhibitory synaptic inputs while a disinhibition of the network converts SPW-R to interictal-like discharges.

8 POSTSYNAPTIC 5-HT_{1A} RECEPTOR FUNCTIONS REVEALED IN TRANSGENIC MICE

B. Bert, A. Rex, J.-P. Voigt, H. Fink

Institute of Pharmacology and Toxicology, School of Veterinary Medicine, Freie Universität Berlin

Serotonin 1A (5-HT_{1A}) receptors are involved in a wide range of physiological functions such as thermoregulation, circadian rhythm, learning, feeding and sexual behaviour, but are also associated with the pathophysiology of anxiety disorders and depression. The somatodendritical and postsynaptic appearance of the 5-HT_{1A} receptor aggravates, however, the assignment to specific mechanisms. Here, we present transgenic mice overexpressing the 5-HT_{1A} receptor postsynaptically in the dentate gyrus and outer cortical layers. A primary behavioural analysis revealed no differences in anxiety-related behaviour and cognitive abilities, only motor activity and body temperature were slightly decreased. Receptor activation by 5-HT_{1A} receptor agonist 8-OH-DPAT led in transgenic mice to an exaggerated response concerning body temperature and motor activity: In transgenic mice the hypothermic effect of 8-OH-DPAT was already apparent in much lower dose. Moreover, in the open field and elevated plus maze test motor activity was highly reduced in consequence of 8-OH-DPAT treatment. In the Porsolt swim test, an animal model used for assessing the effects of antidepressants, transgenic mice showed antidepressant-like behaviour. The treatment with 8-OH-DPAT resulted in a reversion, so that transgenic mice displayed a similar depression-related behaviour to wild-type mice. Taken together, our results indicate that the overexpression of 5-HT_{1A} receptors in the dentate gyrus and outer cortical layers is associated to a broad spectrum of behavioural changes, hence, these mice can serve as a model to elucidate the role of postsynaptic 5-HT_{1A} receptor functions.

9 RESONANCE PROPERTIES OF RAT HIPPOCAMPAL INTERNEURONS IN STRATUM ORIENS *IN VITRO*

A. Boehlen[1,3], A.V.M. Herz[2,3] and U. Heinemann[1,3]

[1]*Cellular Neuro- and Pathophysiology Group, Institute of Neurophysiology, Johannes-Mueller-Center of Physiology, Charité, 10117 Berlin, Germany*

[2]*Department of Biology, Institute of Theoretical Biology, Humboldt University Berlin, 10115 Berlin, Germany*

[3]*Bernstein Center for Computational Neuroscience Berlin, 10115 Berlin, Germany*

Oscillatory neuronal activity is a phenomenon widely found in the central nervous system. In the hippocampus a particularly prominent discharge pattern with slow oscillations in the theta-frequency band (4-10 Hz) has been reported. The mechanisms underlying the generation of the theta rhythm have been extensively studied. Theories propose theta oscillations as being relevant for specific cognitive functions, e.g., pattern recognition, memory formation/consolidation/retrieval, sequence learning and navigation.
Intrinsic oscillations also play a major role for the frequency-dependent information flow in the hippocampal formation. These subthreshold membrane potential oscillations are closely related to resonance, which depends on an interaction between the passive membrane properties and time-dependent ionic conductance. Such resonance phenomena were described in the entorhinal cortex and CA1 pyramidal cells. They may give rise to membrane potential oscillations and may thereby control the temporal precision of action potential discharges.
To investigate whether resonance phenomena indeed exist in hippocampal interneurons, whole-cell patch-clamp experiments were performed in the current-clamp configuration from interneurons in stratum oriens in slices.
The cellular membrane potential response to sinusoidal current injection was used to characterise the neuronal impedance as a function of the stimulation frequency. Preliminary analysis indicates that at physiological temperatures a considerable variability of the frequency-impedance relationship exists between different interneurons.

10 NEURONAL CALCIUM SENSOR (NCS) PROTEIN VILIP-1 MODULATES CGMP SIGNALLING BY REGULATING RECEPTOR GUANYLYL CYCLASE B CELL SURFACE EXPRESSION AND ACTIVITY IN NEURAL CELLS AND HIPPOCAMPAL NEURONS

M. Brackmann[1], N. Buck[2], R. Anand[3], J. Behr[2], and K.-H. Braunewell[1]

[1]*Signaltransduction Research Group,* [2]*Neuroscience Research Center, Charité, Berlin, Germany,* [3]*Neuroscience Center of Excellence, Louisiana State University, New Orleans, Louisiana, USA*

The family of neuronal calcium sensor (NCS) proteins, including NCS-1, VILIP-1 and Hippocalcin, have multiple key roles in controlling neuronal function. The dynamic regulation of membrane signalling via NCS proteins has recently started to be elucidated by examining their activity-dependent membrane association via the mechanism of the

"calcium-myristoyl switch". In hippocampal neurons VILIP-1 shows a fast, stimulus-dependent and reversible translocation to Golgi and cell surface membranes and some dendritic specializations. The calcium-myristoyl switch of VILIP-1 may provide a fast signalling mechanism to shuttle cellular signals to cellular compartments and/or to influence membrane-associated signalling effectors. In line with this notion, VILIP-1 has been implicated in a variety of calcium-dependent signal transduction processes. We have observed effects on membrane-localized signalling systems including nicotinic acetylcholine receptors and receptor guanylyl cyclases. Previously, interaction with these receptors were shown by yeast two hybrid interaction and surface resonance plasmon (SRP) studies, respectively. The functional influence of VILIP-1 on acetylcholine and guanylyl cyclase receptor signalling have been examined in transfected cell lines and oocytes. Here we report for the first time the effect of VILIP-1 on guanylyl cyclase activity in hippocampal neurons, where the proteins co-localize as shown by immunofluorescence microscopy. The overexpression of VILIP-1 in hippocampal neurons increases the cGMP accumulation following stimulation of GC-B with the agonist C-type natriuretic peptide (CNP). In order to investigate the underlying molecular mechanisms, we examined the influence of VILIP-1 on receptor phosphorylation and cell surface expression, which are known mechanisms for receptor regulation. VILIP-1 modulates phosphorylation of the receptor in neural cells and hippocampal neurons following stimulation of GC-B. In addition, in ligand binding assays VILIP-1 influences the surface expression of GC-B in neural cells and hippocampal neurons.
In summary, the NCS protein VILIP-1 is a calcium-dependent modulator of important membrane-localized neuronal signalling cascades in hippocampal neurons. Therefore, the protein is likely to play a novel physiological and pathological role in hippocampal function.

11 CLINICAL PREDICTORS OF EARLY RESPONSE TO ECT AND RTMS

Eva-Lotta Brakemeier, Arnim Quante, Alexander Luborzewski, Stefan Röpke, Malek Bajbouj

Department of Psychiatry, Charité – University Medicine Berlin, Benjamin Franklin Campus, Eschenallee 3, 14050 Berlin, Germany

Background: Several variables have been suggested to predict the response to antidepressant stimulation techniques like electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS) in depressive patients. However, the results of studies concerning different predictors of therapeutic response are not consistent. Object of this study was to identify and compare predictors for antidepressive early response to ECT and to rTMS in a large sample of depressive patients.
Methods: In a retrospective chart review in 100 patients suffering from major depressive disorder and bipolar disorder according to DSM-IV criteria treated with ECT or rTMS, predictors for early response were explored. Information was gathered for a broad variety of clinical, biographical, and technical predictors. Antidepressant treatment response was defined as a 50% reduction of the initial Hamilton score (21-item Hamilton Rating Scale) after two weeks of treatment.
Results: 30% of the ECT patients and 21% of the rTMS patients showed an antidepressant early response after two weeks of treatment. For both treatments, a low score of ATHF (treatment resistance) and a short duration of episode were general positive predictors for early response. In the ECT model, a low level of anxiety and a high level of retardation were significant clinical positive predictors. Concerning rTMS, a high level of sleep disturbances and a low level of agitation were specific clinical predictors for early response.
Conclusion: Assessment of baseline clinical parameters may be a valuable tool to predict early response to antidepressant stimulation techniques.

12 TWO PHOTON IMAGING OF INTERACTIONS BETWEEN IMMUNE CELLS AND NEURAL CELLS IN MODELS OF MULTIPLE SCLEROSIS

A. U. Brandt[1], H. Radbruch[1], A. Hahner[1], V. Siffrin[1], N. Asselborn[1], E. Pohl[2], C. Infante-Duarte[1], O. Aktas[1], F. Zipp[1]

[1]Institute of Neuroimmunology, Charité University Hospital Berlin, Germany, [2]Institute of Cell Biology and Neurobiology, Charité University Hospital Berlin, Germany

Multiple Sclerosis is a chronic inflammatory disease of the Central Nervous System (CNS) that predominantly affects young adults. As the main pathologic correlate an immune reaction against myelin producing oligodendrocytes is postulated. Recently an early occurrence of neuronal and axonal damage in Multiple Sclerosis could be shown. The specific mechanism of neuronal loss still remains unclear, though.
In adopted Experimental Autoimmune Encephalitis (EAE), a murine model of Multiple Sclerosis, the disease can be caused by direct transfer of activated CD4+ T cells, that are specific for PLP, a peptide found within the myelin sheath. However, the exact role of CD4+ T cells and other immune cells on site of disease is not well defined.
We established a two photon imaging system that allows us to directly record interactions between immune cells and neural cells in acute human slices and in acute murine slices by using the model of adopted EAE or direct stimulation of extracted immune cells. Furthermore by using transgenic mice strains, that express Enhanced Green Fluorescent Protein (EGFP) in neural cells of different lineages, we are able to elucidate interactions between immune cells with target cells in chronic neuroinflammationof the CNS directly in living mice.

13 CALEB/NGC REGULATES DENDRITIC TREE COMPLEXITY

N. Brandt, R. Nitsch, S. Schumacher

Institute of Cell Biology and Neurobiology, Center for Anatomy, Charité University Hospital, Philippstraße 12, D-10115 Berlin, Germany.

The development of dendritic arbors is essential for neuronal information processing, but the underlying mechanisms are currently not well understood. The importance of transmembrane proteins for connecting extrinsic cues, which regulate dendrite formation, to intracellular mediators of cytoskeletal rearrangement has been highlighted during the last years. Here we show the neural transmembrane EGF family member CALEB/NGC (Chicken Acidic Leucine-rich EGF-like domain containing Brain protein/Neuroglycan C) to be involved in the process of dendritic tree elaboration. CALEB/NGC is highly expressed in brain, and the expression of this protein is up-regulated during times of dendrite differentiation. It is expressed in hippocampal neurons in tissue and in culture and localizes at dendrites. Increasing expression of CALEB/NGC in primary hippocampal neurons enhances dendritic arbor complexity due to enhanced dendritic branching, whereas reducing the endogenous expression level of CALEB/NGC via RNA interference impairs dendritic tree elaboration. Functional analysis also revealed that a specific region of the cytoplasmic part of CALEB/NGC is necessary for inducing dendritic arbor complexity. These results suggest that CALEB/NGC is a critical mediator for generating dendritic tree complexity.

14 THE OPTIMAL VIEWING POSITION EFFECT NEW EVIDENCE FROM EYETRACKING RESEARCH.

M. Braun[1], F. Hutzler[2], M. Võ[1], V. Engl[1], A. M. Jacobs[1]

[1] Freie Universität Berlin, Habelschwerdter Allee 45, 14195 Berlin, [2]University of Vienna, Liebiggasse 5, 1010 Vienna

During reading, the optimal viewing position (OVP) effect describes the fact that word identification performance declines with increasing distance of the initial fixation from the centre of a word (O'Regan, 1981). In contrast, first fixation durations show an inverse pattern: First fixation durations are longest near the centre of the word but decrease with increasing distance from the centre. In three experiments, eye movements were recorded during OVP tasks to systematically explore the inverse OVP effect. Implications of results on the strategy-tactics- and the cognitive control account are discussed.

15 GENETIC ANALYSIS OF THE ZINC FINGER TRANSCRIPTION FACTOR BCL11B IN THE POSTNATAL HIPPOCAMPUS

Heike Brylka[1], Kevin R Jones[2], Neal Copeland[3], Carmen Birchmeier[1] and Stefan Britsch[1]

[1]Max Delbrück Center for Molecular Medicine - MDC, Robert Rössle-Str. 10, D-13122 Berlin, Germany
[2]Department of Molecular, Cellular, and Developmental Biology, University of Colorado, Boulder, Colorado , USA
[3]Mouse Cancer Genetics Program, Center for Cancer Research, National Cancer Institute, Frederick, Maryland, USA

In the adult brain of mammals the dentate gyrus is one of the two locations with continuing neurogenesis and the primary gateway for inputs into the hippocampus, a cortical structure that is required for learning and memory. During development of the dentate gyrus, the final step of differentiation from a precursor cell into a postmitotic functional neuron is a complex process involving a network of regulatory transcription factors. The zinc finger transcription factor Bcl11b was found to be expressed in the developing and adult hippocampus. Mice with a null-mutation of the Bcl11b gene die after birth, and show defects in lymphocyte development. In order to determine the role of Bcl11b in the developing and adult hippocampus we have employed conditional mutagenesis using the Cre/loxP system. Mice with a forebrain-specific conditional mutation of the Bcl11b gene survive postnatally, but start to die approx. 4 weeks after birth. Mutant animals are consistantly smaller and show striking hyperexcitability. Morphological and immunohistological analyses of the dentate gyrus of mutant animals further indicate critical functions of Bcl11b during neuronal differentiation of dentate gyrus granule cells.

16 THE CONTRIBUTION OF COLD-SENSITIVE TRP CHANNELS TO COLD ALLODYNIA AND NEUROPATHIC PAIN

Ombretta Caspani, Paul Heppenstall

Klinik für Anaesthesiologie, Charité , CBF, Berlin

Cold allodynia is a common feature of neuropathic pain. However the underlying mechanisms of this enhanced sensitivity to cold are not known. Recently, the cloning of several temperature sensitive ion channels belonging to the TRP family has led to the identification of proteins probably involved in cold sensing at the molecular level. Of particular interest are the TRPM8 and TRPA1 channels, which are expressed by peripheral sensory ganglia and respond to cooling temperatures. We are investigating the role of these ion channels in cold allodynia by examining their expression and function following nerve injury.
We used a chronic constriction injury of the sciatic nerve to model neuropathic pain in mice. We dissected lumbar DRG at different time points after

surgery and used real-time RT-PCR, in situ hybridization, immunohistochemistry and calcium microfluorimetry to examine the expression and function of TRPM8 and TPRA1 after nerve injury. We found no gross change in the expression levels of these ion channels in the DRG. However preliminary data indicates that the expression profile of TRPM8 shifted, such that more peptidergic nociceptors expressed TRPM8 after injury. We also examined functional properties of cold transduction using calcium imaging. We found that the number of cold responsive neurons in the DRG more than doubled after nerve injury. In agreement with our expression data, this increase was not due to a change in the number of TRPM8 or TRPA1 positive neurons, rather a novel mechanism of cold sensing became predominant post injury. Our data indicates that cold allodynia does not result from changes in expression of TRPM8 or TRPA1, but might occur via an as yet unknown mechanism of cold sensation that is prevalent after injury.

17 RESPONSE OF MICROGLIA TO GABAERGIC STIMULATION IN EARLY POSTNATAL CORPUS CALLOSUM

Giselle Cheung, Katrin Färber, Helmut Kettenmann

Cellular Neuroscience, Max-Delbrück-Center for Molecular Medicine, Robert-Rössle-Straße 10, 13125 Berlin, Germany

Microglial cells are believed to be originated from the monocytic lineage, invade the brain during early postnatal development and transform from ameboid cell to a ramified form, the resting microglia. We recently found that microglial cells can express a variety of receptors for neurotransmitters including those for the major inhibitory transmitter in the CNS, gamma-aminobutyric acid (GABA). Microglia in culture and ramified microglia in acute brain slices express $GABA_B$ receptors. In the present study, we focused on ameboid microglia which invade the brain in early postnatal development. These cells accumulate on the surface of acute brain slices, particularly in the corpus callosum, from 6-8 days old NMRI mice. Whole-cell patch clamp revealed that ameboid microglia responded to muscimol, a $GABA_A$ receptor agonist, by triggering an increase in the inwardly rectifying K^+ current. The response was completely abolished by SR 95531, a competitive $GABA_A$ receptor antagonist, but was not mimicked by baclofen, a selective $GABA_B$ receptor agonist. Muscimol also increased $[Ca^{2+}]_i$ in 93% of ameboid microglia. We have, however, evidence that the response is rather indirect: The response to muscimol became smaller when the microglial cells were lifted off from the slice surface and disappeared completely at some distance. Moreover, cultured microglial cells never responded to muscimol. We also observed that macroglial cells within the corpus callosum responded to muscimol with Ca^{2+} increase. Our results indicate that ameboid microglial cells in early postnatal brain, although they lack functional $GABA_A$ receptors, can indirectly sense GABAergic activity.

18 DEVELOPMENTALLY REGULATED EXPRESSION PATTERN OF CALEB, AN EGF-LIKE PROTEIN RESTRICTED TO THE CENTRAL NERVOUS SYSTEM

Craveiro, R.B., Jüttner, R., Babich, A. and Rathjen, F.G.

Developmental Neurobiology, Max-Delbrueck-Center for Molecular Medicine, Berlin

CALEB (chicken acidic leucine-rich EGF-like domain containing brain protein) is a transmembrane cell surface protein containing a characteristic EGF-like domain close to its plasma membrane spanning segment indicating that it is a member of the EGF family of growth and differentiation factors. CALEB is converted by neuronal activity and is involved in regulating neuronal connectivity early in development (Jüttner et al., 2005).

To evaluate the function of CALEB further, we analysed the pattern of expression of CALEB during neuronal development and characterised the conversion to a truncated, membrane associated protein.

Immunoblotting revealed that CALEB is restricted to the central nervous system and showed a peak expression in various brain regions between postnatal day 10 and 20, a period of synaptogenesis and synapse refinement. Primarily a chondroitin sulfate proteoglycan containing form of CALEB was observed in immature stages, which was reduced in adult stages. Conversion of CALEB, studied in acute brain slices, is realized by serine/cysteine proteases, as shown by complete inhibition of conversion in the presence of leupeptin. Furthermore, the conversion was shown to be Ca^{2+}-dependent and is mediated by activation of NMDA receptors. The subcellular localization of CALEB was analysed in PSD preparations as well as by immunocytochemistry in primary neuronal cell cultures.

In summary, the developmentally regulated expression pattern of CALEB supported our physiological studies and suggests that CALEB is implicated in the formation of neuronal circuits.

Jüttner et al., 2005

19 FROM BURST ENCODING TO TIME-WARP INVARIANCE

Felix Creutzig[1], Sandra Wohlgemuth[2], Jan Benda[1], Andreas Stumpner[3], Bernhard Ronacher[2], Andreas V.M. Herz[1]

[1] Institute for Theoretical Biology, Humboldt University Berlin, Germany; [2] Institute for Biology, Behavioural Physiology, Humboldt University Berlin, Germany; [3] Johann-Friedrich-Blumenbach-Institute for Zoology and Anthropology, Georg-August-University Göttingen, Germany

Female grasshoppers of the species Chorthippus biguttulus respond to male mating songs that consist of species specific syllable-pause patterns.

Behavioural experiments with artificial stimuli show that the female reaction is not determined by the absolute syllable length but by the ratio between syllable and pause length (time warp invariance) [1]. A small set of auditory ascending neurons is known to be involved in pattern recognition [2], constituting a bottleneck of behaviourally relevant information. We studied the role of a single auditory ascending neuron (AN12) in processing natural and artificial mating songs. The spike count within bursts encodes the length of relative quietness before a syllable. A simple integrate & fire neuron model with two input channels, one instant excitatory and one inhibitory with exponential kernel (ô = 40ms), can explain this behaviour. The integration of subsequent bursts in response to songs over a fixed time effectively multiplies average pause length and syllable frequency and, hence, provides a time-warp invariant presentation of the song pattern.

[1] O. von Helversen and D. von Helversen. Forces driving coevolution of song and song recognition in grasshoppers. Fortschritte der Zoologie, 39:253-284, 1994.

[2] A. Stumpner, B. Ronacher, and O. von Helversen. Auditory interneurons in the metathoracic ganglion of the grasshopper chorthippus biguttulus. II. Processing of temporal patterns of the song of the male. J. Exp. Biol., 158:411-430, 1991.

20 EFFICIENT ESTIMATION OF HIDDEN STATE DYNAMICS FROM SPIKE TRAINS

Márton G. Danóczy[1], Richard H. R. Hahnloser[2]

[1]Institute for Theoretical Biology, Humboldt-Universität zu Berlin, Invalidenstr. 43, 10115 Berlin, Germany
[2]UNIZH / ETHZ, Institute for Neuroinformatics, Winterthurerstrasse 190, 8057 Zürich, Switzerland

Neurons can have rapidly changing spike train statistics dictated by the underlying network excitability or behavioural state of an animal. To estimate the time course of such state dynamics from single- or multiple neuron recordings, we have developed an algorithm that maximizes the likelihood of observed spike trains by optimizing the state lifetimes and the state-conditional interspike-interval (ISI) distributions. Our non-parametric algorithm is free of time-binning and spike-counting problems and has the computational complexity of a Mixed-state Markov Model operating on a state sequence of length equal to the total number of recorded spikes. As an example, we fit a two-state model to paired recordings of premotor neurons in the sleeping songbird. We find that the two state-conditional ISI functions are highly similar to the ones measured during waking and singing, respectively.

21 LAMOTRIGINE EFFECTS ON HUMAN NEOCORTICAL NEURONES IN SLICES FROM EPILEPSY SURGERY TISSUE

Deisz R. A.[1], Lehmann T.-N.[2], Meencke H.-J.[3], and Nitsch R.[1]

[1]Charité University Medicine Berlin, Center for Anatomy, Institute of Cell- and Neurobiology
[2]Charité University Medicine Berlin, Department of Neurosurgery
[3]Epilepsy Centre Berlin-Brandenburg

The anticonvulsant lamotrigine exerts a diversity of cellular effects, including decrease of glutamate release, use dependent block of sodium channels and increase of H-currents. Each of these effects may reduce neuronal hyperexcitability in epileptogenic areas. However, some patients do not become seizure-free with lamotrigine. The cellular effects of lamotrigine in human neocortical neurones are unknown.

We therefore investigated the effects of lamotrigine on human neocortical neurones in slices from epilepsy surgery using sharp microelectrode recordings. The methods for slicing and recording have been described previously (Deisz, 1999). Neuronal and synaptic properties were investigated in layer 2/3 neurones before, during and after bath application of lamotrigine (100μM). Lamotrigine had no significant effect on resting membrane potential, neuronal input resistance and amplitudes of the first action potential. Subsequent action potentials were slightly reduced in number and amplitude by the presence of lamotrigine. Synaptic responses, elicited with incrementing stimulus intensities (2-20V, 100μsec), were depressed by lamotrigine, about 30 % at intermediate stimulus intensities (10V). At higher stimulus intensities the effect was smaller and insignificant. The conductances of $GABA_A$ and $GABA_B$ receptor-mediated synaptic responses were reversibly reduced by 35 and 60%, respectively ($P<0.05$, $n=16$).

The slight reduction of action potentials corresponds to established data. The presence of this effect, also in slices from patients receiving lamotrigine, suggests that it is insufficient for seizure suppression. The apparently paradoxical reduction of $GABA_A$ inhibition might be useful, because we had previously demonstrated excitatory $GABA_A$ responses in human focal tissue. However, this mechanism would reduce also normal $GABA_A$ inhibition, resulting in little net effect.

22 EVIDENCE FOR A VASCULAR CORRELATE OF THE BEREITSCHAFTPOTENTIAL USING NEAR-INFRARED SPECTROSCOPY

J. C. W. Drenckhahn [1,2,3,4], H. Obrig [2,4], J. Steinbrink [2,4], J. Duemmler [1,2], M. Kohl-Bareis [4,5], A. Villringer [2,3,4], J. P. Dreier [1,2,4]

Department of [1]Experimental Neurology and [2]Neurology,

CCM, [3]Department of Neurology, CBF, Charité, [4] Berlin Neuroimaging Center, Berlin, [5] RheinAhrCampus, University of Applied Sciences Koblenz, Remagen

Using near-infrared spectroscopy (NIRS) in human healthy subjects we investigated alterations of deoxy-hemoglobin (Hb_{deoxy}) concentrations in the primary motor cortex (M1) and the supplementary motor area (SMA). M1 and SMA were measured simultaneously in order to identify a correlate of the Bereitschaftspotential following voluntary movement. Seven female, strongly right-handed volunteers underwent different finger tapping tasks which are known to be associated with increase in cerebral blood flow in M1 and SMA. The tasks were designed as blocks with repetitive finger tapping or single finger tapping either self-paced or externally triggered.
8 light sources and 7 detectors were positioned over the left M1 and the SMA covering 12.5x7.5cm. Time course and amplitude were analysed for the concentration of Hb_{deoxy}. For spatial analysis, the recording points with significant decrease in Hb_{deoxy} were determined.
We detected a circumscribed decrease in Hb_{deoxy} at two different locations corresponding to SMA and M1 during motor activation. Decrease of Hb_{deoxy} in the SMA started 1.2s prior to that in M1 demonstrating a vascular correlate of the Bereitsschaftspotential. The most prominent changes in Hb_{deoxy} were located within an area of $\sim$10cm^2 in projection on M1 and $\sim$15cm^2 in projection on SMA, respectively.
We established a non-invasive bedside method to measure changes of Hb_{deoxy} reflecting changes of cerebral blood flow in primary and secondary motor areas during functional activation. Simultaneous investigation of M1 and SMA indicated a change of Hb_{deoxy} in SMA related to the Bereitschaftspotential.

23 FOLATE DEFICIENCY, HYPERHOMOCYSTEINEMIA AND BASE EXCISION REPAIR: ARE THE NEUROPATHOLOGICAL AND BEHAVIORAL CONSEQUENCES RELATED TO ALTERED NEUROTROPHIN LEVELS?

S. Eckart[1], G. Kronenberg[1,2,3], M. Endres[2], H. Hörtnagl[4], R. Hellweg[1]

[1] Department of Psychiatry, Charité-University Medicine Berlin, Campus Benjamin Franklin, Germany, [2] Department of Neurology, Charité-University Medcine Berlin, Campus Mitte, Germany, [3] Neuronal Stem Cells, Max Delbrueck Center for Molecular Medicine, Berlin-Buch, Germany, [4] Institute of Pharmacology and Toxicology, Charité-University Medicine Berlin, Germany

Uracil-DNA glycosylase (UNG) is involved in base excision repair of aberrant uracil residues in nuclear and mitochondrial DNA. These frequently occurring uracil residues result from the spontaneous or chemically induced hydrolytic deamination of cytosine and by misincorporation of deoxyuridine triphosphate opposite adenine.
We used UNG knockout mice (KO) generated by gene targeting, which are fertile and phenotypically normal. Folate deficiency (FD) leads to hyperhomocyteinemia and a decrease of S-adenosylmethionine (SAM). It is known that when lacking SAM, the occurrence of uracil residues in DNA is fostered, thus FD was a further interesting "stressor" to characterize the phenotype of UNG-KO mice.
The neurohistological analysis showed a decrease of neurons in the CA3 region of the hippocampus (HC) in UNG KO mice; under FD these effects were even bigger. In behavioral tests, these mice reveal learning problems and an anxious, depressive phenotype. In the HC BDNF and NGF protein levels were significantly increased in UNG-KO mice with normal diet and wt FD mice, while significantly decreased in UNG-KO FD mice compared to the control group. An explanation could be that UNG KO mice being phenotypically normal are protected by increased hippocampal NGF and BDNF within a physiological range. In combination with FD leading to decreased cerebral NGF and BDNF content, this hypothesized endogenous protection might be exhausted with the consequence of increased vulnerability to cell death and mitochondrial dysfunction, as has also been reported recently for an animal model of Alzheimer's disease (Hellweg et al., 2003).
Supported by DFG GK429
References: Hellweg, R., von Arnim, C.A.F., Büchner, M., Huber, R., Riepe, M.W.: Neuroprotection and neuronal dysfunction upon repetitive inhibition of oxidative phosphorylation. Experimental Neurology 183: 346-354, 2003

24 THE ECTONUCLEOTIDASE *CD39*/ ENTPDASE1 MODULATES PURINERGIC-MEDIATED MICROGLIAL MIGRATION AND MICROGLIAL RESPONSES TO CEREBRAL ISCHEMIA

Katrin Färber[1], Sören Markworth[1], Ulrike Pannasch[1], Vincent Prinz[2], Golo Kronenberg[2, 4], Matthias Endres[2], Keiichi Enjyoji[3] Simon C. Robson[3], Helmut Kettenmann[1]

[1]Cellular Neuroscience, Max-Delbrück-Center for Molecular Medicine, Robert-Rössle-Straße 10, 13125 Berlin, Germany
[2]Klinik und Poliklinik für Neurologie, Charité-Universitätsmedizin Berlin, Campus Mitte, Schumannstr. 20/ 21, 10117 Berlin, Germany
[3]Research North, Transplantation Center, BIDMC, 99 Brookline Ave, Room 359, Boston, MA 02215
[4]Department of Psychiatry, Charité, Campus Benjamin Franklin, Eschenallee 3, 14050 Berlin

Microglial cells express a variety of purinergic receptors and *cd39*/NTPDase1, an ectonucleotidase that is chiefly responsible for catalysis of nucleotide mediators to nucleosides. Wild type microglial cells are known to migrate in response to ATP and ADP. Here, we demonstrate that inhibition of adenosine receptors impairs ATP triggered microglial migration.

Moreover, ATP fails to stimulate migration of *cd39* null microglia. The effects of ATP on *cd39* null cell migration can be restored by reconstitution with apyrase (a soluble ectonucleotidase), or by co-stimulation with adenosine (or serotonin). These data suggest that the co-stimulation of P2 and adenosine (or serotonin) receptors is a requirement for microglial migration. Using patch-clamp techniques, we detect functional P2Y and P2X purinergic receptors in *cd39* null microglial cells, indicating differential P2-reactivity in mutant cells. Moreover, we studied the response of microglia after transient occlusion of the middle cerebral artery in vivo. The *cd39* null mice exhibited larger ischemic brain lesions and the density of microglial cells in the prenumbra was decreased when compared to controls. We conclude that microglial expression of *cd39* regulates microglial migration by the co-ordinated phosphohydrolysis of extracellular nucleotides and thereby influences evolution of ischemic brain lesions.

25 MECHANISM OF INTRACELLULAR CA^{2+} OSCILLATIONS

M. Falcke, A. Skupin

Department Theory, Hahn Meitner Institute, Glienicker Str. 100, 14109 Berlin

Many cells – including astrocytes – exhibit oscillations of cytosolic Ca^{2+} driven by the dynamics of uptake and release by the endoplasmic reticulum. Despite the vast knowledge on molecular properties of the IP_3R and features of oscillations on cell level, the link between molecular behavior and oscillatory cellular dynamics is not clarified yet. Does each channel cluster together with local concentration dynamics represent an oscillator or are higher levels of complexity required to generate oscillations? We provide experimental and theoretical insights into the oscillation mechanism.

26 LONG-TERM DEPRESSION IN BURST AND REGULAR FIRING NEURONS OF THE SUBICULUM

P. Fidzinski, J. Behr

Department of Psychiatry and Psychotherapy, Institute of Neurophysiology, Charité Berlin, Germany

The subiculum is regarded as the main output structure of the hippocampus and was shown to play a pivotal role in learning and memory. Although synaptic plasticity is considered as the cellular basis for learning processes, the exact mechanisms governing synaptic plasticity in subicular neurons remain unknown. A recent study (Wozny et al., submitted) described the correlation of pre- and postsynaptic forms of LTP with the intrinsic properties of subicular neurons. Here we report that also LTD is differentially induced in burst and regular spiking cells of the subiculum.
In acute brain slices of juvenile Wistar rats, EPSPs of single subicular neurons were recorded with sharp microelectrodes upon stimulation of CA1 efferents. For LTD induction, paired pulse stimulations (50 ms intervals) of 15 min duration with 4 different frequencies (0.5; 1.0; 3.0 and 5.0 Hz) were tested. In burst firing cells, stable LTD (>30 min) was induced upon the entire range of frequencies tested, whereas in regular firing cells only 1 Hz stimulation was successful in LTD induction (n = 8 per frequency/cell type). No difference in LTD strength was observed between burst (67.7±7.9% of baseline at 1 Hz) and regular firing cells (65.1±6.7%). In addition, the paired pulse index (PPI) increased in burst firing cells (115±7% and 112±3% of baseline PPI at 1 Hz and 3 Hz, respectively), but not in regular firing cells (84±4% and 94±4%), indicating different expression sites of LTD in each cell type.
Overall, our data supports the idea of different mechanisms of LTD in subicular neurons depending on their intrinsic properties. However, further studies are necessary to uncover the exact induction/expression mechanisms involved.

27 LOSS OF OPA1 (OPTIC ATROPHY 1) LEADS TO EARLY DEATH DURING GASTRULATION IN THE MOUSE

M. Fiket,[1] M. Seeliger,[2] C. Alexander[1]

[1]Neurodegeneration, Max-Delbrueck-Center for Molecular Medicine, Berlin-Buch, Germany, [2]Retinal Electrodiagnostics Research Group, Dept. of Pathophysiology of Vision and Neuroophthalmology, University Eye Hospital, Tuebingen, Germany

OPA1 is a nuclear gene encoding a large mitochondrial dynamin-related GTPase implicated in mitochondrial dynamics. Mutations affecting the coding region of *OPA1* result in the clinical phenotype of autosomal dominant optic atrophy (adOA). Patients suffer from visual loss due to degeneration of the optic nerve.
We generated OPA1-deficient mice by disrupting exon 2 of the *mOPA1* gene. A neomycin cassette was inserted at the exon/intron border of exon2/intron2. Our targeting strategy completely abolished functional gene expression from this *mOPA1* allele. Our OPA1(-/-) mouse is the first animal model showing a loss-of-function effect of OPA1 in-vivo. Homozygous mutant mice are embryonic lethal and die during gastrulation. The OPA1(-/-) embryos are much smaller than wildtype embryos, and the mitochondrial network is altered. Histological analysis of retinae and optic nerves in heterozygous mice was done at different stages of postnatal development (P0-P90), but did not reveal any changes compared to wildtype animals. Electrical recordings from the retina (ERG) and scanning laser ophthalmoscopy (SLO) did not show pathological signs.
We conclude that a proper mitochondrial network is necessary for survival during gastrulation and that OPA1 is required to maintain such network properties. Optic nerves of heterozygous mice are currently examined by electron microscopy.

28 REGULATION OF NOCICEPTOR HEAT SENSITIVITY BY THE C-KIT/ STEM CELL FACTOR SIGNALLING SYSTEM

Christina Frahm[1], Nivena Milenkovic[1], Max Gassmann[2], Carmen Birchmeier[1], Gary R. Lewin[1] and Alistair N. Garratt[1]

[1]Max-Delbrueck-Center for Molecular Medicine, Robert-Roessle-Str. 10, 13092 Berlin; [2]Veterinary School, University of Zürich, Winterthurerstr. 260, CH-8057 Zürich

Painful stimuli are detected by cutaneous free nerve endings of small diameter sensory neurons (C-fibre afferents) whose cell bodies are located in the dorsal root ganglia. The sensitivity of nociceptive circuits to specific stimuli can be regulated by engagement of cell surface receptors located in the sensory fibre terminals, leading to alterations in the pain threshold. One molecule expressed by subsets of pain-sensing afferent neurons is c-Kit, a type III receptor tyrosine kinase which binds the ligand, Stem Cell Factor. Genetic analyses have shown that the c-Kit/SCF signalling system is essential for the development of several cell lineages, including primordial germ cells, mast cells, and melanocytes. We characterised c-Kit expression in dorsal root ganglia by immunohistochemistry and in situ hybridisation. C-Kit is expressed by subsets of peptidergic (CGRP+ or SP+) and non-peptidergic (IB4+) nociceptors, and is co-expressed in a proportion of neurons expressing the TRP channel VR1, which is required for inflammatory thermal hyperalgesia. We found that mice homozygous for a loss of function allele of *c-Kit* (W/W) displayed thermal hypoalgesia. In the converse experiment, administration of SCF ligand (i.p.) resulted in acute thermal hyperalgesia in wild-type mice. Electrophysiological analysis using the skin-nerve preparation revealed a marked reduction in the sensitivity of polymodal heat-sensitive C_{MH} nociceptors in *c-Kit* mutants (e.g. the median temperature at which C_{MH} nociceptors start to repond to noxious heat was shifted by ~5°C to higher temperatures). We are currently determining whether SCF can influence heat-activated currents in isolated DRG neurons and are performing biochemical analyses to establish the molecular mechanism downstream of c-Kit which regulates heat sensitivity of nociceptors.

29 SLOWNESS LEADS TO PLACE CELLS

M. Franzius, H. Sprekeler, L. Wiskott

HU-Berlin, Institute for Theoretical Biology (ITB), Berlin

We present a model for the self-organized formation of hippocampal place cells based on unsupervised learning on natural visual stimuli. Our model consists of a hierarchy of Slow Feature Analysis (SFA) modules, which were recently shown to be a good model for the early visual system (Berkes & Wiskott, Journal of Vision 5(6):579). The system extracts a distributed representation of position, which is transcoded into a place field representation by sparse coding (ICA). We introduce a mathematical framework for determining the solutions of SFA, which accurately predicts the distributed representation of computer simulations.

30 SMOKING AND STRUCTURAL BRAIN DEFICITS: A 3 TESLA VOLUMETRIC MR INVESTIGATION

Gallinat J, Staedtgen M, Kalus P, Heinz A

Clinic for Psychiatry and Psychotherapy, Charité University Medicine, Campus Mitte, Berlin, Germany

Introduction: Growing evidence from animal studies indicates brain damaging properties of nicotine exposure. Investigations in humans found a wide range of functional cerebral effects of nicotine and cigarette smoking, but studies focusing on brain damage are sparse. Methods: In 17 smokers and 23 nonsmokers possible differences of the cerebral structures were investigated using magnetic resonance imaging and voxel-based morphometry. Results: Significantly smaller gray matter volume and lower gray matter density were observed in the frontal regions (anterior cingulate, prefrontal, and precentral cortex) and the occipital lobe in smokers compared to nonsmokers. Group differences of one or the other parameter were also found in the thalamus, cerebellum and temporal cortex, among other regions. Smokers did not show greater volumes than nonsmokers in any cerebral region. Magnitude of lifetime exposure to tobacco smoke (pack years) was inversely correlated with volume of frontal and temporal lobes and cerebellum. Conclusion: The data indicate structural deficits of several cortical and subcortical regions in smokers relative to nonsmokers. The topographic profile of the group differences matches brain networks known to mediate drug reinforcement, attention and working memory processing. The present findings may explain in part the frequently reported cognitive dysfunctions in chronic cigarette consumers.

31 BACE1 CLEAVAGE AND RELEASE OF NEUREGULIN-1 DETERMINES THE ENSHEATHMENT FATE OF AXONS

A.N. Garratt[1], M. Willem[2], L. Rabe[2], B. Novak[2], A. Rittger[3], P. Saftig[3], C. Dorner-Ciosek[4], B. De Strooper[5], C. Birchmeier[1] and C. Haass[2]

[1]Max-Delbrueck-Center for Molecular Medicine, Berlin; [2]Department for Alzheimer's Research, Ludwig-Maximilians-University of Munich, Munich; [3] Institute of Biochemistry, Christian Albrecht University Kiel, Kiel; [4] Boehringer Ingelheim Pharma GmbH und Co KG, Biberach/Riss; [5] Center for Human Genetics, VIB4 and KULeuven, Leuven, Belgium

BACE1 (beta-site APP cleaving enzyme), an aspartyl protease, plays a critical role in the production of amyloid Abeta peptides; insoluble plaques containing Abeta constitute the molecular basis of pathogenesis

in Alzheimer's disease. Abeta is generated by sequential proteolytic cleavage of amyloid precursor protein (APP) by beta- and gamma-secretases. BACE1 appears to be the major beta-secretase in the brain: Abeta-cleavage is abrogated in BACE1 KO mice and can be reduced by BACE1 inhibitors *in vivo*. Several proteins, e.g. APLP1, APLP2, and LRP, have been identified as BACE1 substrates, but the functional consequences of their processing by BACE1 remains elusive. Recently, it was shown that the EGF-like ligand Neuregulin-1 (NRG1), and its receptors, members of the ErbB receptor tyrosine kinase family are substrates for regulated intramembrane proteolysis mediated by gamma-secretase. Genetic analysis in mice has previously demonstrated the essential role of axonally-derived NRG1 in Schwann cell development and myelination of the peripheral nervous system. We show here that NRG-1 is a novel BACE1 substrate and demonstrate that BACE1 is required *in vivo* for peripheral nerve myelination. We propose that BACE1-dependent cleavage of Type III NRG1 is a critical switch regulating myelination in the peripheral nervous system. Our results also prompt the consideration of downstream effects of BACE1 inhibitors, currently being tested for treatment of Alzheimer's disease, on NRG-1/ErbB signalling *in vivo*.

32 PROMOTER ANALYSIS OF THE PLASTICITY RELATED GENE-1

Beate Geist, Thorsten Trimbuch, Olaf Ninnemann & Robert Nitsch

Charité - University Hospital Berlin, Center of Anatomy, Institute of Cell- and Neurobiology, Berlin

We performed a differential screen for gene products upregulated during development and after hippocampal lesion; we identified a novel candidate, named plasticity related gene-1(PRG-1). PRG-1 is a membrane associated protein specifically expressed in neurons. It is only expressed during late developmental stages (from E18 in the rat). Our results so far show that PRGs are neuron-specific components of the LPA signal transduction pathway. The interesting temporal and spatial expression pattern of PRG-1 raises the question of it's specific regulation. In silico analysis indicates a GC-rich TATA-Box less promoter sequence.

For the investigation of transcriptional activity of different PRG-1 promoter fragments Dual-Luziferase-Reporter-Assays were performed, showing a ca. 500 bp fragment upstream the transcriptional start site with maximal activity. Transfection of primary neuron- or primary astrocyte- cultures documents a significant higher activity of this fragment in primary neurons, indicating the presence of CNS specific regulatory elements upstream the transcription start site.

Via 5´-RACE several transcription start points of the murine gene were mapped. Prior treatment with tobacco acid pyrophosphatase strongly favoured the detection of CAPed full length transcripts.

Further analysis of this promoter includes electro-mobility shift assays to identify candidate transcription factor binding sites.

In order to analyze *in vivo* expression pattern of PRG-1, we also generate mouse models using the BAC (bacterial artificial chromosome) transgenic technology according to N. Heintz (Rockefeller Institute). In these transgenic mouse lines the reporter proteins ECFP/EYFP are expressed in the same way as the endogenous PRG-1, allowing the analysis of PRG-1 regulation during development and in cultured organotypic slice preparations of the transgenic animals.

33 PRIMARY MICROCEPHALY WITH A SEVERE CHROMOSOME CONDENSATION PHENOTYPE CAUSED BY A NOVEL MISSENSE MUTATION, W75R, IN THE BRCT DOMAIN OF MICROCEPHALIN

Ghani Kakhki M, Morlot S, Neitzel H

Institute of Human Genetics, Berlin

Autosomal recessive primary microcephaly type 1 (MCPH1) is a neurodevelopmental disorder characterized by congenital microcephaly and mental retardation, in absence of other neurological problems. The underlying gene encodes an 835 amino acid protein, *microcephalin,* which contains three *BRCT* domains. RNA interference studies suggest that *microcephalin* might be involved in the regulation of *BRCA1* and *CHK1*. Furthermore, *microcephalin* forms irradiation-induced nuclear foci and colocalizes with *H2AX*.

The hallmark of mutations in the *MCPH1* gene is a cellular phenotype detectable in routine cytogenetic preparations in which a high proportion (~10%) of cells have prophase-like chromosomes (PLCs) due to premature chromosome condensation in the early G2 phase of the cell cycle and delayed decondensation postmitosis.

In an *MCPH1* patient from consanguineous parents, chromosome analysis showed a very high frequency of prophase-like cells(>15%). Sequencing genomic DNA revealed a homozygous missense mutation 223T>C in exon 3 of the *MCPH1* gene resulting in the change of tryptophan to arginine residue at codon75 (Trp75Arg). The mutation was heterozygous in both parents and absent from 200 Caucasian control alleles. Trp75Arg lies in the N-terminal *BRCT* domain, a position which is highly conserved from human to zebrafish.

So far, only one missense mutation in the *MCPH1* gene with an extremely mild clinical and cellular phenotype has been described (80C>G; Thr27Arg). In contrast, the missense mutation Trp75Arg seems to have more profound effects on the protein function as judged by the high number of cells with aberrant chromosome condensation.

To study the transcriptional level of *BRCA1* and *CHK1* in patient cells with mild and severe cellular phenotype,

we applied quantitative real-time RT-PCR. Furthermore, immunofluorescence studies have been used for the quantitative analysis of nuclear DNA repair foci after ionizing irradiation in the MCPH1 patient cell lines with the different mutations.

34 SPIKE PRECISION AND RELIABILITY IN AUDITORY RECEPTOR NEURONS OF THE LOCUST

S. Glauser, A. V. M. Herz, J. Benda

Institute for Theoretical Biology, Computational Neuroscience Group, Humboldt-Universität zu Berlin, Germany

The spike response of neurons to injections of sinusoidal currents is most reliable if the frequency of the stimulus matches the mean firing rate of the response or half (subharmonic) or twice (first harmonic) of it. Both theoretical as well as experimental findings support this resonance property of single neurons.

We investigate this phenomenon in auditory receptor cells of the locust *Locusta migratoria* by comparing their response to sinusoidal and rectangular amplitude modulation stimuli as well as white noise amplitude modulation stimuli with variable (cut-off) frequencies. For the sinusoidal stimuli we find that the reliability and precision of the spike response is indeed highest when the stimulus frequency matches the firing rate. However, for higher stimulus frequencies the reliability monotonically decreases without showing any peak at the first harmonic and an increased reliability at the subharmonic has only been observed in a few cases. For rectangular stimuli the spike precision depends on the duty-cycle (width of the rectangles relative to the period). For low duty-cycles the reliability decreases quickly to values near zero whereas for high duty cycles the reliability is almost independent of the stimulus frequency.

In summary our findings suggest that the precision-resonance phenomenon strongly depends on the type of stimulus used, probably reflecting the non-linear nature of neurons.

Supported by the Deutsche Forschungsgemeinschaft (SFB 618)

35 IDENTIFICATION AND CHARACTERIZATION OF TWO NOVEL TUBULIN-BINDING MOTIFS LOCATED WITHIN THE C-TERMINUS OF TRPV1

[1, 2]Chandan Goswami, [1]Tim Hucho, and [2]Ferdinand Hucho

1. Freie Universität Berlin, Institut für Chemie/Biochemie, Thielallee 63, 14195 Berlin, Germany; 2. Max Planck Institute for Molecular Genetics, Ihnestraße 73, 14195, Berlin, Germany

The capsaicin receptor, TRPV1, was reported to interact with the soluble $\alpha\beta$ -tubulin dimmer and with polymerised microtubules (Goswami et al. 2004, 2006). A tubulin-binding site within the C-terminal cytoplasmic domain of TRPV1 is unknown. In the absence of a crystal structure of the C-terminus of TRPV1 and with no characterized tubulin binding motifs therein available, we used a systematic deletion approach to identify the tubulin-binding site and characterized the TRPV1 region interacting with tubulin. We found that the TRPV1 C-terminus preferably interacts with β-tubulin. We identified two short - basic amino acid stretches located within the TRPV1 C-terminus, which are sufficient for the tubulin interaction. One of these two stretches is highly conserved in all mammalian TRPV1 orthologues and partially conserved in some of the TRPV1 homologues. This indicates that TRPV1 interacts with tubulin and microtubules through novel and unique tubulin-binding motifs.

36 MAPPING COMPLEX OLFACTORY LEARNING TASKS WITHIN THE HONEYBEE BRAIN BY PROCAINE INJECTIONS

B. Grünewald[1], S. Seifert[1], A. Blunk[1], J. Podufall[1], T. Papouin[2], M. Giurfa[2], J.-M. Devaud[2]

[1] Institut für Biologie - Neurobiologie, Freie Universität Berlin, Germany; [2] CRCA, CNRS, Toulouse, France

The honeybee is a valuable model organism to study neural mechanisms of olfactory learning. We used two training situations to study the role of the mushroom bodies (MBs) during memory formation: 1. Reversal learning. Bees learn to reverse their responses to two odorants, one rewarded (A+) and one unrewarded (B-), if their contingencies are changed (A- B+). 2. Positive patterning. Bees learn to discriminate two unrewarded odorants from their rewarded mixture (A- B- AB+). We injected the local anesthetic, procaine, to impair neural activity in the mushroom bodies and analyzed behavioral consequences. In parallel we tested the potency of procaine to block ionic currents of honeybee neurons.

Using patch clamp techniques we recorded action potentials and voltage-sensitive currents from cultured adult mushroom body neurons. Procaine (2-10%) completely blocks spiking. Procaine blocks voltage-gated Na+ and K+ currents (complete block of INa at 10mM). The effects are completely reversible within a few minutes of wash.

Injecting procaine either into both MB alpha lobes or unilaterally impaired reversal learning. Procaine left retention of the initial learning (A+ B-) intact. Similarly, during procaine treatment bees could not learn a rule of positive patterning. In contrast, differential tasks involving novel odorants (C+ D-, A- B- CD+) were intact under procaine.

Our experiments thus show that local injections of procaine can be used to map learning tasks onto specific regions of the insect brain. We conclude that intact mushroom body activity is required for the acquisition of reversal learning and positive patterning, but not for simple differential learning tasks. Bilateral

processing seems to be necessary for reversal learning.

37 KNOCKDOWN OF *FOXP2* IN ZEBRA FINCH AREA X IMPAIRS SONG LEARNING

S. Haesler[1,2]; P. Licznerski[3]; B. Georgi[1], P. Osten[3], C. Scharff[1,2]

[1]Max Planck Institute for Molecular Genetics, Berlin, Germany; [2]Freie Universität Berlin, Dept. of Behavioral Biology, Berlin, Germany; [3]Max-Planck-Institute for Medical Research, Heidelberg, Germany

Most vertebrate species communicate acoustically, but few, including humans and three orders of birds, learn this trait. FOXP2 is the first gene linked to human speech, as it is mutated in individuals with a severe speech and language deficit. Since the way songbirds learn their song parallels early stages of language development in humans in many aspects, we asked what was the role *FoxP2* for vocal learning in this model system. In songbirds, like in humans, FoxP2 is predominantly expressed in the cerebellum and the striatum, a basal ganglia brain region affected in patients with FoxP2 mutations. Strikingly, in zebra finches, the striatal nucleus Area X, that is essential for vocal learning, expressed more FoxP2 than the surrounding tissue at the time when vocal learning occurs. Moreover, in adult canaries, FoxP2 expression in Area X differed seasonally; increased *FoxP2* expression was associated with times of song plasticity. To investigate whether there is a causal relationship between *FoxP2* expression and song learning, we injected a lentivirus targeting FoxP2 by RNAi stereotactically into Area X at the beginning of the song learning period of young zebra finches. Subsequently, injected animals were tutored by adult male animals. When animals reached adulthood, they were sacrificed to verify correct targeting of the virus in Area X. Song analysis of adult song revealed that copying of the tutor song was incomplete in zebra finches with FoxP2 knockdown in Area X. In contrast, animals that received injections with control virus constructs learned the entire tutor song successfully. Knockdown birds also copied individual song elements less accurately than control animals. Finally the variability in singing the song motif was greater from rendition to rendition in knockdown than in control animals. Taken together, this suggests, that FoxP2 is required for vocal learning in songbirds.
Supported by SFB665 "Developmental disturbances of the nervous system"

38 THE ROLE OF CX_3CR1-EXPRESSING NK CELLS IN MULTIPLE SCLEROSIS

I. Hamann, T. Prozorovski, F. Zipp and C. Infante-Duarte

Institute of Neuroimmunology, Charité Universitätsmedizin Berlin, Germany

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS) with an unknown etiopathogenesis. Combining large-scale gene expression and flow cytometric analyses, we previously demonstrated a significantly lower expression of the chemokine receptor CX_3CR1 in MS patients compared to healthy individuals. Patients' NK cells represented the unique cell population responsible for this reduced CX_3CR1 expression. Furthermore, we demonstrated that CX_3CR1 expression on NK cells correlates with cytotoxic activity, and found an association between disease activity and frequency of CX_3CR1-positive NK cells in relapsing-remitting (RR) MS patients.
To better elucidate the possible role of CX_3CR1-expressing NK cells in MS pathology, we have further investigated the phenotype and effector function of CX_3CR1^+ vs. CX_3CR1^- NK cells. Here we show that while IFN-gamma expression was comparable in both NK cell subsets, the CX_3CR1^- NK cells expressed higher amounts of TNF-alpha and GM-CSF as well as elevated levels of anti-inflammatory and Th2-like cytokines such as IL-10, IL-13 and IL-5. Regarding the possible regulatory function of one of these NK cell subpopulations, we have as yet been unable to demonstrate any direct effect of NK cells on syngenic T cell immune response. Thus, the expression of CX_3CR1 on NK cells discriminates two cell populations which show distinct cytotoxic activity and express different patterns of effector cytokines.
This study was supported by a grant from the Charité (Rahel-Hirsch Stipend) to C. Infante-Duarte.

39 DOES THE FREQUENCY OF THE ANTECEDENT NOUN AFFECT THE RESOLUTION OF PRONOMINAL ANAPHORS? AN EEG STUDY.

Angela Heine, Sascha Tamm, Markus Hofmann, Florian Hutzler and Arthur M. Jacobs

Dept. of Psychology – Cognitive Neuropsychology, Freie Universität Berlin, Germany

Behavioral studies investigating the influence of the relative word frequency of antecedent nouns on the processing of anaphoric pronouns have yielded contradictory results. While some researchers found no effect of an antecedent's frequency of occurrence on coreference resolution [26], others report shorter reading times for pronouns referring to low compared to high frequency nouns [9]. Using event-related potentials, our study aimed to further investigate the issue.
Participants were presented with sentence pairs, of which the first contained either a high frequency, a middle frequency or a low frequency noun. The second sentence contained a pronoun which referred back to the noun in the first sentence. ERP waves were determined, time-locked to both the nouns and the anaphoric pronouns. We observed a graded N400 effect for antecedents of the three frequency classes with amplitudes reversely related to the word's

lexical frequency. Coreferential pronouns elicited aP300, with amplitudes dependent on the noun's relative frequency of occurrence, i.e. the lower the antecedent's word frequency, the higher was the amplitude of the P300. This amplitude effect at the pronoun is interpreted in terms of the allocation of attentional resources to salient discourse entities. In order to identify the exact cognitive processes which form the basis of these effects in detail, more sensitive EEG measures such as time-frequency analysis were employed.

40 CHRONIC ETHANOL EXPOSURE OF SH-SY5Y CELLS IMPAIRS RETINOIC ACID-INDUCED NEURONAL DIFFERENTIATION INVOLVING ERK-1/2 RESPONSIVENESS TO BDNF AND RAF KINASE INHIBITOR PROTEIN

Hellmann J, Wernicke C, Rommelspacher H

Section Clinical Neurobiology, Dept. of Psychiatry and Psychotherapy, Charité-University Medicine Berlin, CBF

Chronic ethanol exposure has striking effects on growth, survival and differentiation of neurons, involving discrete changes in the synthesis and downstream signaling of retinoids and members of the neurotrophin family such as NGF and BDNF, however, the effects are distinct and depend on the model system, stimulation- and treatment paradigm. In these signalling events affected by ethanol, the protein kinases ERK-1/2 and PKC are involved, modulating synaptic plasticity, neuronal growth and differentiation. Of particular relevance to the regulation of these signaling cascades is Raf-1 kinase inhibitor protein (RKIP). In plants, RKIP regulates flowering, a process somewhat similar to differentiation in mammalian cells, where PKC has been shown to functionally interact with RKIP, suggesting a role for RKIP in mediating cross-talk between these two signaling pathways. Interestingly, ethanol has been shown to affect both, ERK- and PKC-mediated signal transduction in neurons. To study the effects of long-term ethanol treatment and ethanol withdrawal on the process of neuronal differentiation, we investigated basal ERK activity, BDNF-mediated ERK-responsiveness and the expression of RKIP, MEK-1, ERK-1 and SNAP-25. As an established model system, we chose SH-SY5Y cells, which differentiate in the presence of 10 μM retinoic acid. We show that neuronal differentiation induced by retinoic acid (RA) correlates with specific changes in the mRNA transcription / protein expression profile for Raf-1, MEK, Erk, and RKIP. Furthermore, we show that Erk responsiveness to BDNF is impaired in long-term ethanol exposure and that ethanol-induced morphological changes correlate with RKIP expression, supporting our hypothesis, that RKIP is involved, possibly required for neuronal differentiation.

Supported by DFG GK429.

41 DISENTANGLING NEURAL PROCESSES ON A MICRO-SECOND TIME SCALE DESPITE MILLI-SECOND SPIKE-TIME VARIABILITY

Andreas V.M. Herz

Bernstein Center for Computational Neuroscience Berlin and Institute for Theoretical Biology, Humboldt-University

Every sensation begins with the conversion of a sensory stimulus into the response of a receptor neuron. Typically, this involves a sequence of multiple biophysical processes that cannot all be monitored directly. In this work, we present an approach that is based on analyzing different stimuli that cause the same final output, here defined as the probability of the receptor neuron to fire a single action potential. Comparing such iso-response stimuli within the framework of nonlinear cascade models allows us to extract the characteristics of individual signal-processing steps with a temporal resolution much finer than the trial-to-trial variability of the measured output spike times. Applied to insect auditory receptor cells, the technique reveals the sub-millisecond dynamics of the eardrum vibration and of the electrical potential and yields a quantitative four-step cascade model. The model accounts for the tuning properties of this class of neurons and explains their high temporal resolution under natural stimulation. Owing to its simplicity and generality, the presented method is readily applicable to other nonlinear cascades and a large variety of signal-processing systems.
This contribution is based on the article: "Disentangling sub-millisecond processes within an auditory transduction chain" by Tim Gollisch and Andreas V.M. Herz [PLoS Biology, vol 3, e8, 2005]

42 MECHANOSENSITIVE CHANNELS IN THE NEURITES OF CULTURED SENSORY NEURONS

Jing Hu and Gary R. Lewin

Growth Factors and Regeneration Group, Max-Delbrück Center for Molecular Medicine and Charité Universitäts-medizin Berlin, Robert-Rössle-Str. 10, Berlin-Buch D-13125 Germany.

Almost all sensory neurons in the dorsal root ganglia have a mechanosensory function. The transduction of mechanical stimuli in vivo takes place exclusively at the sensory ending. For cutaneous sensory receptors it has so far proved impossible to directly record the mechanically gated receptor potential due to the small size and inaccessibility of the sensory ending. Here we asked whether mechanosensitive channels are present in the neurites of freshly isolated adult mouse sensory neurons in culture. Virtually all sensory neuron neurites possess ion channels gated by sub-micron displacement stimuli (>90%). Three types of mechanically activated conductances were characterized based on different inactivation kinetics. A rapidly adapting conductance was found preferentially in larger sensory neurons with narrow

action potentials characteristic of mechanoreceptors. Slowly and intermediate adapting conductances were found exclusively in putative nociceptive neurons. Mechanically activated currents with the same kinetics were found after mechanically stimulation of the cell soma. However, somal currents differed in two important respects form the neurite current: they were only observed in around 60% of cells tested and the displacement threshold for the current was several fold larger than for the neurite. The apparent reversal potential of the rapidly adapting current differed from that of the slowly adapting current possibly indicating distinct ion channel entities underlying these two currents. In summary, our data suggest that the high sensitivity and robustness of mechanically gated channels in the sensory neurite make this a useful in vitro model for the mechanosensitive sensory endings in vivo.

43 EFFECTS OF MITOCHONDRIAL COMPLEX I INHIBITION DURING BRAIN DEVELOPMENT

C. Huchzermeyer[1], M. Schuelke[2] and O. Kann[1]

[1]Institute for Neurophysiology and [2]Department of Neuropediatrics, Charité - Medical University of Berlin, Germany

Patients with Leigh syndrome suffer from severe generalized epilepsy, muscle weakness and deafness and develop necrosis in basal ganglia and areas of brain stem and hippocampus later in life. In many patients, defects in complex I and IV of the mitochondrial respiratory chain have been described and it is proposed that mitochondria play a crucial role in programmed neuronal death during brain development.

We hypothesize that mitochondrial complex I (and IV) defects are involved in premature apoptosis during neuronal path finding and layer formation, which might explain epilepsy and malformations. Mitochondrial dysfunction might lead to alterations in energy metabolism, calcium homeostasis and free radical production, which might explain neuronal degeneration.

Here we report that rotenone, a selective mitochondrial complex I inhibitor, can mimic pathological effects on the cellular level in acute and chronic experimental models.

Bath application of rotenone (1μM) leads to a decrease in electron transport chain activity as revealed by NAD(P)H and FAD fluorescence recordings in acute hippocampal slices and organotypic hippocampal slice cultures. The effects of rotenone application are weaker in area CA3 as compared to areas CA1 and dentate gyrus. Moreover, rotenone disrupts mitochondrial membrane potential as indicated by cationic dyes, JC-1 and Rhodamine-123. Chronic application of rotenone in slice cultures leads to neuronal degeneration in a concentration-dependent manner (10nM, 20nM, 50nM) as determined by Fluorojade-B staining.

The results demonstrate that mitochondrial complex I activity is crucial for mitochondrial functioning and cellular integrity of neurons. The combination of rotenone and fluorescence imaging techniques provides a powerful tool to investigate the interaction of mitochondrial (dys)function and neuronal cell death in specific brain regions and developmental stages.

Supported by Deutsche Forschungsgemeinschaft (SFB665).

44 ELECTROPHYSIOLOGICAL ANALYSIS OF NEURONAL PROPERTIES IN DIFFERENT LAYERS OF THE MOUSE AUDITORY CORTEX

S. Huggenberger[1], R. A. Deisz[2], M. Vater[1]

[1]University of Potsdam, Institute for Biochemistry and Biology, 14476 Golm, Germany; [2]Charité University Medicine Berlin, Center for Anatomy, Institute of Cell and Neurobiology, 10098 Berlin, Germany

Cortical information processing depends not only upon summation of excitatory and inhibitory input but also on intrinsic neuronal properties modulating this synaptic input. These mechanisms are poorly understood in the auditory cortex. We therefore investigated neuronal properties in slices of the auditory cortex of NMRI mice using whole-cell-patch-clamp recordings and compared responses to current injections and voltage activation of pyramidal neurons in layers 2/3, 4 and 5/6.

A total of 212 pyramidal neurons, selected by IR-image microscopy, were included in the analysis. Based on firing pattern to depolarizing current injections, two basic response pyramidal cell types were distinguishable: bursting neurons (BN) and regular firing neurons (RN). Layer 2/3 was characterized by a low percentage of BNs (7.5%) compared to layer 4 (24.5%) and layer 5/6 (31%; $p<0.001$). Furthermore, RNs of layer 2/3 have the highest threshold for AP generation ($p<0.001$) and largest amplitudes of inward-rectifying and hyperpolarization-activated currents (Kir and Ih; $p<0.001$). The large Ih in layer 2/3 may effectively prevent temporal summation, which, together with the higher activation threshold, would provide improved temporal resolution and preferential transfer of high threshold input. These properties may serve as time-dependent filters in layer 2/3, while the lower activation threshold in neurons of layer 5/6 might favor cortical (e.g. commissural) and corticofugal spread of processed and filtered signals.

45 ADEQUATE ANTIPSYCHOTIC TREATMENT NORMALIZES NERVE GROWTH FACTOR SERUM CONCENTRATIONS IN SCHIZOPHRENIA WITH AND WITHOUT CANNABIS OR ADDITIONAL SUBSTANCE ABUSE

Maria C Jockers-Scherübl, Johannes Rentzsch, Nicole Radzei, Heidi Danker-Hopfe, Falk Schürer, Sharif Bahri, Rainer Hellweg

Department of Psychiatry and Psychotherapy, Charité-University Medicine Berlin, Campus Benjamin Franklin, Eschenallee 3, 14050 Berlin, Germany

Neurotrophins such as nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) are important for the development and maintenance of function of neurons. Neurodevelopment is thought impaired in schizophrenia, and vulnerable schizophrenic brains may be more sensitive to toxic influences. Thus, cannabis as a neurotoxin (and other substances) may be more harmful to schizophrenic brains than to non-schizophrenic brains when used chronically. In a previous study we could demonstrate earlier disease onset and significantly raised NGF-serum concentrations in drug-naïve schizophrenic patients with previous long-term cannabis abuse in comparison to schizophrenics without cannabis abuse and cannabis abusers without schizophrenia. Therefore we investigated whether this difference is still observed with treatment. NGF was measured in the serum of 114 treated schizophrenic patients (schizophrenia alone n=66; schizophrenia plus cannabis abuse n=42; schizophrenia plus multiple substance abuse n=6) and no significant differences among those groups and the control groups (healthy controls n=51; cannabis controls n=24; multiple substance controls n=6) was found any longer with respect to serum levels. In an additional prospective study with 28 patients suffering from schizophrenia (S) and from schizophrenia with cannabis abuse (SC), we could confirm those results. Formerly raised NGF-serum levels (S: 83.44±265.25 pg/ml; SC: 246.89±310.24 pg/ml) declined to 10.72±14.13 pg/ml (S) and 34.19±38.96 pg/ml (SC) respectively after sufficient antipsychotic treatment. We thus conclude that antipsychotic treatment leads to recovery of neural integrity showing in renormalized NGF-values.

46 THE NOVEL PROSPERO-RELATED HOMEODOMAIN TRANSCRIPTION FACTOR PROX2 IDENTIFIES A SUBPOPULATION OF PLACODE-DERIVED VISCEROSENSORY NEURONS

Anita John[1], Tatiana V. Petrova[2], Kari Alitalo[2], Carmen Birchmeier[1] and Stefan Britsch[1]

[1]Max Delbrück Center for Molecular Medicine - MDC, Robert-Rössle-Str. 10, 13122 Berlin, Germany; [2]Molecular/ Cancer Biology Laboratory and Ludwig Institute for Cancer Research, University of Helsinki, Finland

In vertebrates, peripheral sensory neurons derive either from placodal or from neural crest cells. Placodes are focal regions of thickened ectoderm in the vertebrate head, which give rise to both neuronal and non-neuronal cells. Cranial placodes include a series of three epibranchial placodes, which generate viscerosensory neurons of the distal geniculate, petrosal and nodose ganglia, associated with the VIIth (facial), IXth (glossopharyngeal) and the Xth (vagal) cranial nerves, respectively. The molecular mechanisms that control induction and differentiation of sensory neurons from placodal cells are still incompletely understood.

Here we describe the novel murine Prospero-related homeodomain transcription factor Prox2 to be specifically expressed in placode-derived viscerosensory ganglia. By in situ hybridization we demonstrate that Prox2 is expressed in the primordia of the distal geniculate, petrosal and nodose ganglia, soon after the cells have detached from the ectoderm. In order further to characterize Prox2 expressing cells, we have generated Prox2-specific antibodies. Immunohistology reveals that Prox2 positive cells co-express the neuronal markers Phox2a and Phox2b, but exclude expression of the glial marker Sox10. Only part of the Phox2a/b expressing cell population shares Prox2 expression, indicating that Prox2 identifies a specific subpopulation of cranial viscerosensory neurons.

We have generated mice with a targeted deletion of the Prox2 gene to analyse further the functions of Prox2 during peripheral nervous system development.

47 BLOCK OF DRUG TRANSPORTER ACTIVITY AND EFFICACY OF ANTIEPILEPTIC DRUGS IN HUMAN EPILEPTIC HIPPOCAMPUS

S. Kim[1], L. Leite Antonio[2], R. Kovács[1], D. Päsler[1], C. Raue[1], U. Heinemann[1], S. Gabriel[1], and T.-N. Lehmann[1*]

[1]Institute of Neurophysiology and [1]Department of Neurosurgery, Charité-University Medicine Berlin, Germany; [2]Neurologia Experimental, Universidade Federal de Sao Paulo-Escola Paulista de Medicina, Sao Paulo, Brazil

Ectopic expression of multidrug transporter proteins (Pgp, MRP1, MRP2) in astrocytes or neurons has been observed in resected hippocampal tissue of patients operated on mesial temporal lobe epilepsy. To find out whether Pgp and MRPs contribute to hippocampal drug resistance we test whether inhibition of transporter activity by probenecid (400 μM) and / or verapamil (40 μM) affects self-sustaining ictaform activity induced in the dentate gyrus of slices from resected hippocampal tissue and maintained despite application of the antiepileptic drugs carbamazepine (CBZ, 50 μM) or valproate (VPA, 1 mM).

Here we report that block of drug transporter activity rarely reverses CBZ- or VPA –resistant activity in slices from sclerotic hippocampi (2 out of 18 slices in 1 out of 7 patients) but effectively suppresses such activity in slices from non-sclerotic specimens (6 out of 9 slices in 3 out of 4 patients; $p<0.01$, $p<0.05$, respectively). Our preliminary data about localization (see poster of C. Raue) and activity of drug transporters show that drug transporter expression and –activity are detectable in different subregions of hippocampal slices except for the dentate gyrus from sclerotic as

well as non-sclerotic hippocampus. Further experiments are necessary to explain the different effects of drug transporter inhibition in sclerotic and nonsclerotic tissue.
Supported by a grant of the DFG SFB T3 to TNL and UH and by CAPES Brazil to LLA.

48 CONTRIBUTION OF NITRIC OXIDE TO INITIATION OF SEIZURE-LIKE EVENTS IN THE LOW [MG^{2+}] MODEL OF EPILEPSY

R. Kovács[1,2], A. Rabanus[1], J. Otahal[1,3].; U. Heinemann[1], O. Kann[1]

[1]Institute for Neurophysiology, Charité - Medical University of Berlin, Germany; [2]Institute of Biomolecular Chemistry, Budapest, Hungary; [3]Institute of Physiology, Czech Academy of Sciences, Prague, Czech Republic

The free radical, nitric oxide (NO) is considered to be a Janus faced molecule in terms of its pro and anti-epileptic effects, depending on the model of epilepsy. NMDA-receptor activation in the hippocampus increases NO formation, which in turn might interfere with synaptic transmission by influencing various receptors, neurotransmitter release and the rate of mitochondrial respiration.
Here we studied the contribution of NO to expression of epileptiform activity as induced by low [Mg^{2+}] ACSF, which removes the Mg^{2+}-block of NMDA receptors. The study was performed in organotypic hippocampal slice cultures from rat and acute entorhinal-hippocampal cortex slices from mice. NO formation was monitored by the rate of fluorescence increase of the NO sensitive probe, DAF-fm. The onset of epileptiform activity was associated with an increase in NO formation in both, slice cultures and acute slices. The combined application of the NO-synthase (NOS) inhibitors and NO-scavengers prevented development of seizure-like events (SLEs), whereas interictal activity was still present. This effect was NO specific, since an external NO donor was able to re-initiate SLEs. Application of different NOS inhibitors revealed a role for neuronal NOS in acute slices, whereas both neuronal and inducible NOS might be involved in SLE initiation in slice cultures. Whole cell patch clamp recordings in CA3 pyramidal cells revealed that the frequency of both IPSCs and EPSCs was decreased under NO depletion. We conclude that regulation of synaptic release by NO contributes to the transition from interictal activity to SLEs.

49 MODULATION OF PREFRONTAL CORTEX ACTIVATION BY EMOTIONAL WORDS IN RECOGNITION MEMORY

Lars Kuchinke[a], Arthur M. Jacobs[a], Melissa L.-H. Võ[a], Markus Conrad[a], Claudia Grubich[b] and Manfred Herrmann[c,d]

[a]Department of Psychology, Freie Universität Berlin, Germany; [b]Department of Psychiatry and Psychotherapy, Königin Eliszabeth Krankenhaus Herzberge , Berlin, Germany; [c]Institute for Cognitive Neuroscience, Department of Neuropsychology and Behavioral Neurobiology, and [d]Center for Advanced Imaging, Bremen University, Germany

We employed event-related functional magnetic resonance imaging (fMRI) to examine the modulation of verbal recognition memory by emotional valence. Using a yes/no recognition task we focussed on prefrontal cortex (PFC) responses to positive, negative and neutral words. Behavioral data confirmed enhanced processing of emotional items and functional imaging revealed different subregions in prefrontal cortex supporting retrieval of emotional words. Correct retrieval for negative words was observed in right mid-ventrolateral PFC, while right ventromedial and orbitofrontal PFC showed enhanced responses to positive words. Additionally, differences between old and new items mainly affected bilateral orbitofrontal regions when processing positive words. The results are discussed in terms of higher monitoring demands due to familiarity based recognition bias for emotional words, extended to specific orbitofrontal PFC recruitment in processing positive items.
LK was supported by the DFG and the research group ''Neuroscience of Emotion'' at the Hanse Institute for Advanced Study, Delmenhorst/ Bremen, Germany.

50 MODELING THE ACTIVITY OF THE AUDITORY NERVE AFTER HEARING LOSS

P. T. Kuokkanen, R. Schaette, and R. Kempter

[1] Institute for Theoretical Biology, Humboldt University, Berlin, Germany

Hearing loss can be caused by a variety of factors, for example damage to the middle ear, damage to or loss of the hair cells in the cochlea, or even by damage to the auditory nerve. The resulting changes in the auditory nerve activity after hearing loss can only be measured to a very limited extent and length. In a model ear, however, the desired stimuli can be presented as long as needed, and different types of hearing loss can be induced and studied extensively. To quantify the impact of hearing loss on auditory nerve activity, we use the Auditory Modeling System (AMS), which has been developed in the group of Ray Meddis in Essex, UK (see e.g. Meddis et al. 2001, JASA). The model is based on a phenomenological description of the ear, from the pinna to the cochlea, cochlear hair cells, and synapses to the auditory nerve. AMS therefore is able to reproduce several key features of basilar membrane and auditory nerve response in healthy ears.
Here we implemented various types of hearing loss in AMS by changing the relevant, biophysically plausible parameters. We focus on hearing loss due to cochlear disfunctions that are caused by

malfunctioning or loss of hair cells. Cochlear hair cells are often affected by acoustic trauma, aging and ototoxic drugs like cisplatin, which is used in cancer treatments.
We describe and analyze the statistics of typical changes in auditory nerve activity caused by damage to outer hair cells or the stereocilia of inner and/or outer hair cells. Our results show that the changes in the auditory nerve activity strongly depend on the type of the hearing loss, which might help in developing more specific hearing aids. Results based on this study may also give detailed input for studies of the auditory nervous system such as modeling studies on tinnitus.

51 RECORDING OF PATHOPHYSIOLOGICALLY RELEVANT PARAMETERS NON-INVASIVELY USING SIMULTANEOUS MAGNETOENCEPHALOGRAPHY AND NEARINFRARED SPECTROSCOPY

Leistner, S [1], Sander, T [2], Liebert, A [2], Wabnitz, H [2], Burghoff, M [2], Macdonald, R [2], Curio, G [1], Trahms, L [2] and Mackert, BM [1]

[1] Department of Neurology, Campus Benjamin Franklin, Charité - Universitätsmedizin Berlin; [2] Physikalisch-Technische Bundesanstalt, Institute Berlin; Germany

Important pathophysiological stroke concepts include anoxic depolarisation, periinfarct-depolarisation and spreading depression. In this regard highly relevant parameters are DC-currents as well as oxy- and deoxy-hemoglobin. For recordings of slow neuronal activity (<0.1 Hz) DC-magnetoencephalography provides advantages in comparison to DC-electroencephalography (DC-EEG) which is susceptible for drift artifacts generated mainly at the electrode-skin interface. In animal models magnetic field changes resulting from spreading depression and concomitant changes of oxy- and deoxy-hemoglobin have been recorded invasively.
Here, in a physiological test condition, i.e. during a prolonged simple finger motor task, we proved, that using simultaneously DC-MEG and time resolved near infrared spectroscopy (trNIRS) cortical DC-fields as well as oxy- and deoxy-hemoglobin changes can be recorded non-invasively in healthy subjects and in patients suffering from stroke.
We recorded DC-MEG and trNIRS simultaneously over the left primary motor cortex hand area in healthy subjects and stroke patients during prolonged finger movement periods of the right hand (alternating 30 sec. movement/30 sec. rest; n=30). DC-fields and trNIRS parameters followed closely the motor task cycles revealing statistically significant differences between periods of finger movements and rest. In subjects with sufficient signal-to-noise ratio the analysis of variance of photon time of flight demonstrated hemodynamic changes originating from a deeper layer, i.e., the cortex. Notably, while onset and relaxation started simultaneously trNIRS signals reached 50% of the maximum level 1-4 sec later than MEG-signals.
The feasibility to non-invasively monitor cortical low amplitude DC-fields, deoxy- and oxy-Hb simultaneously in humans and also in stroke patients might allow to scrutinise pathophysiological stroke concepts, e.g. anoxic depolarisation, periinfarct-depolarisation and spreading depression.

52 FAIR-MRI BLOOD FLOW IMAGING IN A MOUSE MODEL OF STROKE: COMPARISON WITH 14C-IODOANTIPYRINE AUTORADIOGRAPHY

Leithner, C; Gertz, K; Villringer, A; Dirngal, U; Lindauer U; Endres, M; Royl, G.

Experimentelle Neurologie, Charité Universitätsmedizin, Berlin

Background and Purpose: Blood flow imaging is an important tool in stroke research. Mice are of special interest because of the potential to generate knock out variants. MRI provides three dimensional non invasive quantitative methods of CBF (cerebral blood flow) imaging, but MRI techniques of CBF determination have not yet been validated for mice. We compared CBF imaging using FAIR-MRI and 14C-iodoantipyrine autoradiography in a mouse model of acute stroke.
Materials and Methods: 29 mice were studied 30 minutes after left sided MCAO (middle cerebral artery occlusion) using two different anesthetic protocols, etomidate and isoflurane. CBF imaging was performed using 14C-iodoantipyrine autoradiography in 14 and using FAIR-MRI in 15 mice.
Results: Using 14C-IAP autoradiography the average CBF was 160.23 ± 27.45 (isoflurane, n=5) and 59.97±22.48 ml/(100mg*min) (etomidate, n=7) in the intact hemisphere and 42.78 ± 9.8 (isoflurane, n=5) and 35.59 ±12.43 ml/(100mg*min) (etomidate, n=7) in the MCAO hemisphere. Using FAIR-MRI the corresponding average CBFs were 219.61± 65.24 (isoflurane, intact hemisphere, n=7), 84.90 ± 9.93 (etomidate, intact hemisphere, n=7), 75.75 ± 25.74 (isoflurane, MCAO hemisphere, n=7) and 48.21±14.59ml/(100mg*min) (etomidate, MCAO hemisphere, n=7). FAIR-MRI overestimated CBF by around 40%. Relative reduction of CBF in the ischemic hemisphere compared to the nonischemic hemisphere was 39.5 ± 4.2 % for 14C-IAP and 41.8 ± 21.4 % for FAIR in the etomidate groups and 72.5 ± 8.4% for 14C-IAP and 63.5% ± 13.4% for FAIR in the isoflurane groups.
Conclusion: When averaging over hemispheres and taking into account a 40% overestimation FAIR-MRI can provide repetitive quantitative measurements of CBF in a mouse model of stroke.

53 INFLAMMATORY PAIN INSENSITIVITY IN THE AFRICAN NAKED MOLE RAT (*HETEROCEPHALUS GLABOR*)

Gary R. Lewin[2], Ying Lu[3], Jing Hu[2], Antje Brand[1], Gireesh Anirudhan[2], Paul A. Heppenstall[4], Nevena Milenkovic[2], Bettina Erdmann[5], Christiane Wetzel[2], Charles E. Laurito[3], Stephen P. Wilson[6], Thomas J. Park[1]

[1]Laboratory of Integrative Neuroscience, Department of Biological Sciences, University of Illinois at Chicago, Chicago, Illinois, USA. [2]Growth Factors and Regeneration Group, Max-Delbrück Center for Molecular Medicine, Robert-Rössle-Str. 10, Berlin-Buch D-13092 Germany and Charité-Universitätsmedizin, Berlin. [3]Department of Anesthesiology, University of Illinois at Chicago, Chicago, Illinois, USA. [4]Klinik für Anaesthesiologie und Operative Intensivmedizin, Charité Universitätsmedizin Berlin, Campus Benjamin Franklin, Hindenburgdamm 30, D-12200 Berlin, Germany. [5]Electron microscopy, Max-Delbrück Center for Molecular Medicine, Robert-Rössle-Str. 10, Berlin-Buch D-13092 Germany. [6]Department of Pharmacology, Physiology and Neuroscience, University of South Carolina School of Medicine, Columbia, SC 20208, USA

In all mammals tissue inflammation leads to pain and behavioral sensitization to thermal and mechanical stimuli called hyperalgesia1. Here we studied pain mechanisms in the African naked mole rat, an unusual rodent species that lacks pain-related neuropeptides (eg. Substance P) in cutaneous sensory fibers2. These animals show a unique and remarkable lack of pain behaviour, including insensitivity to acidic solutions and the algogen capsaicin. Furthermore, when exposed to inflammatory insults or known mediators, naked mole rats never display thermal hyperalgesia. Using electrophysiology we show that primary afferent nociceptors in naked mole rats are insensitive to acid stimuli, consistent with their lack of acid induced pain behaviour. In contrast, nociceptors do respond vigorously to capsaicin and we also show that sensory neurons express a TRP-V1 ion channel that is capsaicin sensitive. However activation of capsaicin sensitive sensory neurons in naked mole rats does not produce pain behaviour. We find that spinal administration of the neuropeptide Substance P could rescue capsaicin-induced hyperalgesia and pain in these animals, suggesting that capsaicin sensitive afferents can be functionally reconnected with central pain circuits. The pain biology of the naked mole is unique amongst mammals so why is this species so insensitive to acid and other algogens? We suggest that extreme selection pressure generated by very high ambient pCO2 concentrations in the environment of a naked mole rat ancestor shut down molecular mechanisms enabling thermal hyperalgesia and acid induced pain. Studying pain mechanisms in this unusual species can provide significant insights relevant for the study of pain and its prevention in man.

54 LONG LASTING DETERIORATION OF SPATIAL NAVIGATION ON REPETITIVE INHIBITION OF ENERGY METABOLISM - AGE MATTERS

Lohmann, P.; Riepe, M.W.

Charité University, Department of Psychiatry, Berlin

Age dependent differences in spatial navigation has been observed in many experimental studies. Toxicological effects on spatial behavior have also been shown in rodents. In our study we examined young and middle aged CD-1 mice in a complex maze after repetitive administration of 3-nitropropionic acid (3-NPA). Furthermore we tested old mice long time after preconditioned with 3-NPA in a complex maze and a non spatial version of an 8-arm radial maze. Whereas young mice are not impaired in performing the complex maze, middle aged animals are strongly impaired by 3-NPA. They did not improve performance over the whole experimental period. In old mice, the hippocampus-dependent spatial task of the complex maze could not be solved significant better over the whole experimental period both by control and pre-treated animals. In contrast both groups improved significantly the non spatial task of the radial maze. However a significant better performance in both mazes is observed in sham-treated animals. This means that repetitive administration of 3-NPA in young mice has no immediate effect but impairs sustainable performance of old animals in a hippocampus-dependent spatial version of a complex maze.

55 A NEW TECHNIQUE FOR ENRICHMENT OF CLAUDINS AND CLAUDIN ASSOCIATED PROTEINS

Lohrberg, D., Winkler, L., Piontek, J., Haseloff, R. F., Krause, E., Schümann, M. and Blasig, I. E.

Leibniz-Institut für Molekulare Pharmakologie (FMP), Robert-Rössle-Str. 10, 13125 Berlin, Germany

The blood-brain barrier (BBB) is a diffusion barrier, which protects the microenvironment of the brain by limiting the transport of potentially harmful substances from blood to brain. It is composed of specialized endothelial cells which express functional and regulatory proteins that form a sophisticated complex of tight junctions (TJ). The TJs selectively seal the paracellular space between the endothelial cells and thereby form the structural basis of the BBB. TJs are composed of numerous proteins whose interaction and contribution to the integrity of the BBB have not been fully understood yet. The present study is aimed at analysing the composition of the TJ complex and to disclose proteins binding to TJ proteins which may influence the barrier function. Special emphasis was placed on claudins which are a major constituent of the tight junction strands and play an important role in the maintenance of the BBB. Initially,

fractionation and enrichment techniques were applied to cell lysates to reduce the sample complexity and to increase the concentration of low abundant proteins. Two different strategies have been followed for the enrichment of TJ proteins: binding of the second extracellular loop of claudin-3 to the C-terminal region of *Clostridium perfringens* enterotoxin was utilised to create a modified pull-down assay. Claudins and claudin-associated proteins were eluted, separated by SDS-PAGE and identified by mass spectrometry (MS). In a second enrichment approach immunoprecipitation using antibodies directed against BBB-relevant claudins was combined with subsequent gel electrophoresis and MS identification. The detailed analysis of the protein identities is in progress. It is expected that the results obtained by this novel proteomic approach will contribute to a better understanding of the protein-protein interactions at the BBB.

56 HIGH TONIC Cl^- CONDUCTANCE IN DEVELOPING HIPPOCAMPAL NEURONS OVEREXPRESSING A HIGH-AFFINITY GLYCINE RECEPTOR RESULTS IN ALTERED DENDRITE MORPHOLOGY DUE TO CHANGES IN THE E/I RATIO OF SYNAPTIC INPUT

J.C. Meier, S. Kirischuk and R. Grantyn

Developmental Physiology, Johannes Müller Centrum, Charité, Berlin

Nonsynaptic actions of ambient GABA and glycine influence the survival, growth and connectivity of developing neurons. Drug-induced enhancement of Cl^- conductances in the immature brain is known to have deleterious effects on cognitive abilities at older age. By inducing overexpression of a high affinity GlyR a3 in cultured hippocampal neurons we aimed at clarifying the effects of enhanced nonsynaptic tonic Cl^- conductances on dendrite morphology and synapse development. To this end, hippocampal neurons were transfected with a GlyR a3 isoform (a3P185L) that has previously been demonstrated in neonatal and adult brain as a result of RNA editing (Nat. Neurosci. 8:736). In mature neurons a3P185L produces tonic inhibition. Here we report that expression of a3P185L resulted in reduced dendritic length, enhanced dendritic branching and a higher ratio of excitatory/inhibitory (E/I) synaptic terminal numbers, if compared with controls expressing the non-edited receptor isoform. As hippocampal neurons display an inverse relationship between the number of glutamatergic contacts and dendritic length (J. Neurosci. in press) we investigated the possibility that suppression of dendrite elongation was due to enhancement of glutamatergic synaptic input in neurons overexpressing a3P185L. Indeed, chronic treatment with GluR antagonists abolished the suppression of dendrite growth although the number of glutamatergic contacts was even higher than in untreated controls. These results suggest that persistent increase of nonsynaptic Cl^- conductance in developing hippocampal neurons alters the E/I ratio of synaptic input and this imbalance may lead to pathological dendrite morphology. Other possible consequences of persistent high Cl^- conductance need to be analyzed to fully understand the nonsynaptic effects of inhibitory neurotransmitters in the developing brain.

57 A NOVEL APPROACH TO STUDY NEUROPROTECTIVE GENES

Mergenthaler, P.; Freyer, D.; Muselmann, C.; Dirnagl, U.; Meisel, A.

Experimental Neurology, Charité Universitätsmedizin Berlin

Gene transfer into primary neurons is often ineffective or toxic. Although electroporation (EP) is a common, versatile and easy to use, only a few reports on successful neuronal EP were published. Based on the Amaxa technology we established an improved protocol to direct plasmid DNA into rat primary cortical neurons. Compared to other methods for gene delivery into primary neuronal cultures, EP is efficient, easy to use and highly reproducible. Using a fluorescent protein (DsRed2) encoding plasmid and neuron specific antibody we demonstrated an exclusive transfection of neurons. 24h after EP, transfection efficiency reaches 40-60% and declines to 15-20% ten days later. Using two different fluorescent protein plasmids we demonstrated a co-transfection rate of more than 90%. Our novel approach to study protective genes is based on co-cultivating two independently transfected neuronal populations. To differentiate both populations we use two different fluorescent proteins encoding plasmids (eGFP, DsRedE), one for each population. We hypothesized that co-transfection with a neuroprotective gene in one population will improve survival of these neurons under stress conditions compared to the other neuronal population. To stress neurons, we applied an in vitro model of cerebral ischemia (oxygen-glucose-deprivation) 10 days after EP. In order to establish our method we used the well known anti-apoptotic gene Bcl-XL. We co-transfected Bcl-XL and eGFP (green fluorescent neurons) encoding plasmids into one population and compared their survival to the other (control) population, solely transfected with a fluorescent gene (DsRed2, red fluorescent neurons) containing plasmid. Comparing the numbers of green (Bcl-XL) and red (controls) neurons immediately before and 24h after OGD, we found an increased ratio of green vs. red fluorescent neurons following OGD. Using Bcl-XL for proof of principle we confirmed our hypothesis. Thereby we demonstrated that this approach allows a powerful analysis of (putative) neuroprotective genes in primary cortical neurons.

58 VAGUS NERVE STIMULATION IMPROVES RESTLESS LEGS SYNDROME ASSOCIATED WITH MAJOR DEPRESSION: A CASE REPORT

Angela Merkl, Eva-Lotta Brakemeier, Heidi Danker-Hopfe, Malek Bajbouj

Department of Psychiatry, Charité – University Medicine Berlin, Benjamin Franklin Campus, Eschenallee 3, 14050 Berlin, Germany

Vagus nerve stimulation (VNS) has shown beneficial effects in treating epilepsy and major depression (MDE). In RLS possible treatment options are agents that enhance inhibitory mechanisms like benzodiazepines or anticonvulsive drugs. We report on the case of a woman with RLS and MDE whose restless legs resolved after VNS.

A 69-year-old woman with MDE and RLS received VNS treatment over 10 weeks. VNS was applied with an intensity of 1.0 mA, a pulse width of 250 μs, a frequency of 40 Hz and device on-time of 30 sec (off-time: 600 sec). Continuous treatment with duloxetine (60mg) was administered 4 weeks prior to two consecutive polysomnographic evaluations. Clinical efficacy was assessed using the 21-item Hamilton Depression Rating Scale (HDRS), the Montgomery Asberg Depression Rating Scale (MADRS), and the International Restless Legs Syndrome Scale (IRLS).

RLS severity improved from 19 points to 8 points on IRLS after VNS. Comparison of the polysomnographies showed a reduction in number of myoclonia with arousal (124 to 109) and periodic leg movements per time (19.7/hour to 16.9/hour). Total sleep time was identical (378 min to 385 min) and sleep efficiency was unaltered (78.7% to 79%). Scores in HDRS (29 points) and MADRS (26 points) stayed unchanged.

To our knowledge, this is the first report to show that VNS may be an effective alternative for treating RLS. New anticonvulsive drugs working via potentiation of GABA transmission have shown promising results the treatment of RLS. Thus, the beneficial effects of VNS might be due to its anticonvulsive properties.

59 SCREENING FOR NOCICEPTOR SPECIFIC GENES

Nevena Milenkovic and Gary R. Lewin

Growth Factors and Regeneration Group, Max-Delbrück Center for Molecular Medicine, Berlin-Buch, Germany

Sensory neurons in the dorsal root ganglion (DRG) transduce diverse sensory sensations like touch, heat and pain. Among them one can differentiate slowly and rapidly adapting Aβ fibers, Aδ and C fibers. C fibers present about 60% of DRG cell population, most of them are polymodal responding both to noxious thermal and mechanical stimuli.

Neurotrophins are required for the survival of DRG neurons and they influence their phenotypic fate. Nerve Growth Factor (NGF) has strong effect on development of C-fibers, in the early postnatal development it is required for expression of the appropriate nociceptor phenotype.

We suppressed the effect of NGF in early postnatal days of mice by injecting antibody for NGF first two weeks postnatal. This treatment leads to changes of the proportion of Aδ fibers and the proportion of C fibers of different modalities, CM and CMH. Using in-vitro skin nerve preparation we showed that heat threshold is altered after the treatment, 50% of fibers start to fire at 40C while the heat threshold is 35C in control mice.

We used DRGs for gene chip expression analysis; 35% transcripts scored as present, 141 genes is upregulated and 119 genes downregulated. Screening the data bases we organized them by their potential function. They should correspond to genes of AM, D-hair, C-MH or C-M fibers. Regulated genes might play a role in setting mechanosensitivity of nociceptors or may play a role in noxious heat transduction. Expression pattern analysis is done using high throughput in-situ. The functional characterization for some of the genes that are expressed in small cells, C-kit and RGS4, is already done and they fit with the predictions of this screening.

60 SPECIFICATION AND DIFFERENTIATION OF DORSAL SPINAL CORD INTERNEURONS

Thomas Müller[1], Hendrik Wildner[1], Domenique Bröhl[1], Mathias Treier[2], and Carmen Birchmeier[1]

[1]Max-Delbrück-Center for Molecular Medicine, Berlin, Germany; [2]EMBL, Heidelberg, Germany

The dorsal horn of the spinal cord receives sensory information from the periphery, processes this information and relays it to higher brain centers and to motor neurons in the ventral spinal cord. Interneurons of the dorsal horn are organized in laminae, which receive sensory input of characteristic modalities. For instance, nociceptive sensory fibers synapse in superficial laminae, whereas proprioceptive sensory fibers project into the deep dorsal horn. Interneurons in the dorsal horn have diverse physiological characteristics. Their molecular characteristics are only now beginning to be understood. We have focused on the analysis of molecular mechanisms that are responsible for the specification of different neuron types of the dorsal horn. During development, two classes of dorsal spinal cord interneurons can be distinguished. Class A neurons are born dorsally in a roof plate-dependent manner and give rise to deep dorsal horn interneurons. Class B neurons are born more ventrally in a roof plate-independent manner and give rise to interneurons in superficial layers of the dorsal horn. Olig3 is a bHLH factor that is expressed in progenitor cells of all class A neuron types, and is required for the specification of class A neurons. In *Olig3* mutant mice, the majority of class A neurons are lacking and ectopic class B neurons arise instead. The homeobox factor Lbx1 is expressed in class B

neurons, and in *Lbx1* mutant mice these neurons assume class A character. In electroporated chick embryos, Olig3 represses *Lbx1* expression and induces the formation of ectopic class A neurons. In contrast, Lbx1 imposes a class B fate on dorsal neurons in the chick spinal cord. Olig3 and Lbx1 are therefore important determinants in the development of class A and B dorsal spinal cord neurons.

Poster Session II

61 TOWARDS MODELLING THE FUNCTION OF TOP-DOWN VISUO-SPATIAL ATTENTION

Aki Naito, Antje Kraft, Stephan Brandt, Laurenz Wiskott

Department of Neurology, Humboldt University Berlin, Bernstein Center for Computational Neuroscience Berlin

We aim to investigate the function that underlies the effect of top- down covert attention in the visuo-spatial domain. The goal of this study is twofold: (1) to build a theoretical neural network model that is able to learn invariant representations of the visual objects, (2) to incorporate the function of visual attention into the developed model and compare the outcomes by referring to the experimental study on humans over sustained (endogenous) attention. The theoretical model is built upon the slowness principle, i.e., a learning principle that allows the extraction of slowly varying properties from fast varying input signals. The slow feature analysis (SFA) algorithm employed here has been shown to reproduce a rich representation of the V1 complex cell properties when trained on natural image sequences. The model consists of multiple layers with increasing receptive field size, each performing SFA. The comparison to the psychophysical and physiological data are primarily done against the experimental study on the spatial characteristics of human visual attention by Kraft et. al. (2005)

Reference:
Wiskott, L. and Sejnowski, T.J. (2002).
Slow Feature Analysis: Unsupervised Learning of Invariances. Neural Computation, 14(4):715-770.
Berkes, P. and Wiskott, L. (2005).
Slow feature analysis yields a rich repertoire of complex cell properties. Journal of Vision, 5(6):579-602
Kraft et. al. (2005).
Interactions between task difficulty and hemispheric distribution of attended locations: implications for the splitting attention debate. Brain Res Cogn Brain Res. 24(1):19-32.

62 TWO METHODS FOR TIME-RESOLVED INTER-SPIKE INTERVAL ANALYSIS

Martin Nawrot [1,2] and Jan Benda [1,3]

[1] Bernstein Center for Computational Neuroscience (BCCN) Berlin, Germany; [2] Neuroinformatics, Institute of Biology – Neurobiology, Free University Berlin, Germany; [3] Fachinstitut für Theoretische Biologie, Humboldt University Berlin, Germany

Neurons observed in a living organism typically exhibit temporal changes in their spike train statistics in response to sensory input. Most obvious are changes in firing rate, while changes of other properties, like for example the variability of inter-spike intervals (ISIs), are more difficult to detect. We suggest two complementary approaches for a time-resolved analysis of the statistics of inter-spike intervals. The first method uses a sliding window of fixed width and collects ISIs within this window. The temporal resolution of this method is limited by a bias due to the neglecting of ISIs that do not completely fall within the observation interval. The second method considers ISIs that contain a particular point in time, i.e. exactly one ISI per trial. Thus, its temporal resolution is much higher and only limited by the width of the ISI distribution. However, this method requires more trials to achieve similar accuracy. With respect to trial-by-trial variability of firing rate, the first method yields a better estimate of interval variability. For equilibrium and ordinary renewal processes we quantified the bias of estimation for mean interval, interval variance and the coefficient of variation (CV) of intervals analytically. We confirmed our results with numerical simulations of a gamma process. Finally, we applied both methods to the same sets of experimental data.

Supported by the German Federal Ministry of Education and Research (BMBF) to BCCN Berlin (grant 01GQ0413) and by the DFG through SFB 618.

63 SELECTIVE ANTERIOR CINGULATE CORTEX DEFICIT DURING CONFLICT SOLUTION IN SCHIZOPHRENIA: AN EVENT-RELATED POTENTIAL STUDY

Andres H. Neuhaus, Simone Koehler, Carolin Opgen-Rhein, Carsten Urbanek, Eric Hahn, Michael Dettling

Department of Psychiatry and Psychotherapy, Charité University Medicine, Campus Benjamin Franklin, Berlin, Germany

Background: Schizophrenia research has gained a new focus on identification and further characterization of neurocognitive deficits in the search for behavioural endophenotypes of this disorder. The objective of this study was to explore differential cortical processing during executive control in schizophrenia as assessed with the Attention Network Test (ANT). Methods: 16 schizophrenic patients and 16 healthy controls matched for gender, age, education, and nicotine consumption were tested with the ANT while recording 29-channel-electroencephalogram (EEG). Visual event-related potentials (ERP) N200 and P300 were topographically analyzed and cortical mapping using low resolution brain electromagnetic tomography (LORETA) was applied to localize neuroelectric generators of ERP. Results: Behaviourally, significant differences between schizophrenic patients and controls were found only for the conflict condition ($p < .05$) and for conflict adjusted by mean reaction time ($p < .01$). Examining ERP of control subjects, N200 failed to show robust flanker congruency effects. P300 amplitude was reduced at Pz ($p < .05$) and P300 latency was increased at Cz ($p < .005$) for the conflict condition. Schizophrenic patients differed significantly in P300 latency at Cz during late conflict processing ($p < .005$). Source analysis revealed a deficit in anterior cingulate cortex ($p < .05$). Conclusion: Our results are in line with previous reports about dysfunctional ACC activation in schizophrenia and argue in favour of a selective deficit of cortical conflict resolution. It is further proposed that dysfunctional ACC activation during executive processing may be a neurophysiologic endophenotype candidate of schizophrenia.

64 MOLECULAR INTERACTIONS OF THE COXSACKIEVIRUS AND ADENOVIRUS RECEPTOR (CAR), A NEURAL CELL-ADHESION PROTEIN

C. Patzke[1], A. Dorner[1], J. Behlke[1], M. Henning[1], E. C. Müller[1], A. Otto[1], H. Schmidt[1], S. Kröger[2] and F. G. Rathjen[1]

[1]Max-Delbrueck-Center for Molecular Medicine, Cellular Neuroscience, Berlin, Germany; [2]University of Mainz

Specification of neuronal connections during the develolment of the nervous system requires neuronal activity. In order to characterize the molecular components influencing the development of synapses, cell surface proteins were searched which are regulated in an activity-dependent manner. We identified the Coxsackievirus and Adenovirus Receptor (CAR), which - in contrast to CALEB - appears to be up-regulated following neuronal activity (Jüttner et al., 2005).

CAR has a strong expression in the developing nervous system, in the heart and colocalizes with the acetylcholine receptor subunits on myotubes. Mice deficient for CAR die during embryonic stages because of defects in cardial development (Dorner et al., 2005), however, the precise physiological function of CAR remains to be determined.

Here, we show that antibodies against CAR block attachment of CAR-expressing cells on extracellular matrix glycoproteins (ECM) such as fibronectin and laminin, and interfere with neurite extension on basal laminae preparations or in eye organ cultures. Interestingly, this antibody effect can be neutralized by fibulin-1, also an ECM glycoprotein. Additionally, we show that antibodies against CAR are able to disturb the Agrin induced aggregation of the acetylcholine receptor on myotubes.

Equilibrium sedimentation analysis revealed that the extracellular part of CAR is interacting with ECM glycoproteins mentioned above.

Taken together our data suggest that CAR might be implicated in the regulation of cell-matrix contacts, such as basal laminae, or other extracellular matrices.

Jüttner R, More MI, Das D, Babich A, Meier J, Henning M, Erdmann B, Müller EC, Otto A, Grantyn R, Rathjen FG.: Impaired synapse function during postnatal development in the absence of CALEB, an EGF-like protein processed by neuronal activity, Neuron. 46 (2): 233-245, 2005

Dorner, A.A., Wegmann, F., Butz, S., Wolburg-Buchholz, K., Wolburg, H., Mack, A., Nasdala, I., August, B., Westermann, J., Rathjen, F.G. and Vestweber, D. Coxsackievirus-Adenovirus Receptor (CAR) is essential for early embryonic cardiac development. Journal of Cell Science 118: 3509-3521, 2005

65 ALZHEIMER-DISEASE-LIKE PATHOLOGY ALTERS ASTROCYTE PROPERTIES IN SITU

Peters O., Phillips A., Haas B., Pannasch U. , Wang L.-P., Schipke C. G., Kettenmann H.

Department of Psychiatry, Charité – CBF, Berlin

Here we studied the gap-junction coupling and electrophysiological properties of astrocytes in an Alzheimer's disease (AD) mouse model. Crossbreeding of APP-overexpressing mice ($PDAPP^+$), which develop numerous extracellular Aß-deposits while aging, and GFAP-EGFP transgenic mice, allowed to identify astrocytes from single-($PDAPP^-/EGFP^+$) and double- ($PDAPP^+/EGFP^+$) transgenic mice (15-25 months old) in situ (slice preparation,150 ì m thick). Cells in the hippocampus (HC) and in the neocortex (NC) were assigned as

astrocytes by their EGFP-fluorescence, randomly selected, studied with the patch-clamp technique and filled via the patch-pipette with biocytin. Gap-junction coupling was visualized by staining of biocytin using the diaminobenzidine method. In analogy to earlier findings the highest plaque-load in the PDAPP$^+$ model was found in HC. In HC the proportion of astrocytes with a complex membrane current pattern was higher in PDAPP$^+$/EGFP$^+$ double-transgenic animals (74%, n=60 cells investigated), compared to PDAPP$^+$/EGFP$^+$ mice (53%, n=51), while in NC the population of cells with passive and complex currents were similar in single (12%, n=60) and double transgenic mice (20%, n=20). While in wild-type animals only few, and uncoupled cells responded to both kainate and aspartate, about half of the astrocytes in PDAPP$^+$ animals reacted, indicating that these cells express both kainate/AMPA receptors and glutamate transporters. The extent of astrocyte coupling was assessed by the number of biocytin-labelled cells. Networks in PDAPP$^+$/EGFP$^+$ animals were found to be smaller than those in PDAPP$^-$/EGFP$^+$ controls. These smaller networks were more prominent in NC (46,6±7,2 cells; n=14 slices, vs. 67,9±14; n=8) compared to HC (34,2±6,6; n=18 vs. 39,5±10; n=16) and most prominent in NC close to an amyloid plaque (<250ì m distance; 32,7±11,5; n=9). We conclude that chronic exposition to AD-like pathology leads to a modified gap-junction coupling and altered membrane properties in astrocytes.

66 FUNCTIONAL INVESTIGATION OF THE SECOND EXTRACELLULAR LOOP OF CLAUDIN-5 IN TIGHT JUNCTION FORMATION

C. Piehl, L. Winkler, J. Piontek, I.E. Blasig

[1]Forschungsinstitut für Molekulare Pharmakologie, 13125 Berlin, Germany

Claudin-5 is present in many endothelial tight junctions (TJ) including those of the blood-brain barrier (BBB). Here it is responsible for preventing the paracellular flux of molecules < 800 Da. Unfortunately by this barrier drugs are prevented to reach brain tissue. A deeper understanding of TJ formation in BBB could help to develop new strategies for affecting barrier properties.

Transfection and expression of claudins in HEK293 cells that are normally unable to build TJ leads to intramembranous fibril formation (*side-by-side* interaction) and kissing points between membranes of two apposing cells (*head-to-head* interaction).

In previous works we demonstrated the homophilic interaction of claudin-5 by immunocytochemistry together with confocal microscopy and fluorescence resonance energy transfer (FRET) between coexpressed claudin-5-CFP and claudin-5-YFP.

By side directed mutagenesis we introduced amino acid substitutions in the second extracellular loop of claudin-5. Using this approach we could identify amino acids that are specifically necessary for homophilic head to head but not for side by side interaction. One example is the substitution of tyrosine 148 to alanine To investigate whether this block of interaction results in a functional difference in the barrier activity of claudin-5, we generated stablely transfected MDCKII cell lines that express either wild type or mutant claudin-5. We are currently establishing an assay based on the culture of these cell lines in Millipore CM filter inserts and measurements of the transepithelial electrical resistance (TEER). Only wild type claudin-5 but not mutants that are affected in head to head interaction sould facilitate an increase in TEER and decrease in paracellular flux. In addition a Ca2+-switch assay is applied to investigate whether the mutations affect the TJ-incooparation of claudin-5 during TJ assembly.

Using the same system of transfected HEK293 cells we also analyse the possible interaction between claudin-5 and the other major integral membrane component of the mammalian tight junction named occludin.

67 DRUG TRANSPORTERS AND PHARMACORESISTANCE IN EPILEPSY: REGIONAL AND CELLULAR DISTRIBUTION OF MRP1, MRP2 AND PGP IN HUMAN HIPPOCAMPUS

C. Raue[1], L. Leite Antonio[2], D. Päsler[1], U. Heinemann[1], S. Gabriel[1] and T.-N. Lehmann[1*]

[1]Institute for Neurophysiology and [1] Department of Neurosurgery, Charité-University Medicine, Berlin, Germany; [2]Neurologia Experimental, Universidade Federal de Sao Paulo-Escola Paulista de Medicina, Sao Paulo, Brazil*

Drug transporter expression is upregulated in resected human epileptic tissue of pharmacoresistant patients, but little is known about the cellular and regional distribution of those proteins.

We investigate cryosections of hippocampal slices obtained from patients undergoing neurosurgical treatment by immunohistochemistry following standard protocols using well described monoclonal antibodies, ABC-Peroxidase-System and diaminobenzidine as chromogen. Cell counting is done in 10 fields for each region and 3 sections per case and protein. In order to consider cell loss we determine the ratio of immunoreactive cells to total number of cells.

We found neuronal expression of MRP2 (26%), MRP1 (23%) and Pgp (18%). Fraction of labeled glial cells was highest for MRP2 (18%) followed by Pgp (12%) and MRP1 (7%). Neuronal and astrocytic expression did not differ between the proteins and hippocampal subregions with one exception: granule cells and astrocytes of dentate gyrus (DG) did not display labeling.

Our preliminary results (n=7 patients) indicate that neither neurons nor astrocytes in DG express drug transporters. This may also explain that epileptiform activity induced in DG is resistant to application of Carbamazepine (CBZ) alone or in combination with transporter inhibitors (see abstract by S. Kim).

Whether there are differences in drug transporter expression associated to the sclerotic grade of the tissue needs to be determined by further investigation.
Supported by a grant of the DFG SFB TR3 to UH and TNL.

68 ANTICONVULSANT ACTIVITY OF DELPHINIUM DENUDATUM ON EPILEPTIFORM ACTIVITY INDUCED BY COMBINED APPLICATION OF BICUCULLINE AND 4 AMINOPYRIDINE IN RAT HIPPOCAMPAL ENTORHINAL CORTEX SLICES

Raza, M.[1]; Shaheen, F.[2]; Choudhary, M.I.[2]; Gabriel, S.[3]; Heinemann, U.[3]

[1]Department of Physiology, School of Medical Sciences, Tarbiat Modares University, Tehran Iran. [2]HEJ Research Institute of Chemistry, University of Karachi, Karachi, Pakistan. [3]Johannes Muller Institute for Physiology, Humboldt University, Berlin, Germany.

Pharmacoresistant epilepsies pose a major challenge to present day physicians. *Delphinium denudatum,* is a medicinal plant used for the treatment of epilepsy in South Asia. We have previously reported anticonvulsant activities in FS-1 fraction of *D. denudatum* on sustained repetitive firing of pyramidal neurons as well as inhibition of 4 aminopyridine (4 AP) -induced seizure like events in rat hippocampal-entorhinal cortex (HEC) slices. In this report we investigated effect of FS-1 fraction of *D. denudatum* on seizure like events induced by combined application of 4 AP and Bicuculline (BIC) in HEC slices, which represents an in vitro model of resistant epilepsy. Transverse HEC slices (400 microns thick) were prepared from Wistar rats (150-200 g). Slices (n=8) were then perfused with pre-warmed (36°C) carbogenated Artificial Cerebrospinal Fluid (ACSF) 1.5 ml/min. Slices were kept in interface chamber for 2 hours before electrophysiological recording was carried out using extracellular ion-sensitive electrodes in CA1 region and entorhinal cortex (EC). Introduction of 4 AP (100 μM) and BIC (100 μM) in ACSF resulted in regular seizure like events (duration 20-35 sec, amplitude 2-3 mV) with corresponding rise in extracellular K^+ concentration. Addition of Fraction FS-1 (5, 7.5 and 10 μL/ml) to ACSF resulted in a dose-dependent reduction in the duration, frequency and amplitude and finally complete blockade of seizure-like events and corresponding rise of K^+ in 8-12 minutes. Complete suppression of seizure like events was observed in CA1 region while isolated spikes were observed in entorhinal cortex. The seizure like activity returned with the removal of fraction FS-1 from ACSF. Results suggest presence of potent anticonvulsant compounds in fraction FS-1 that can be candidates for drugs for pharmacoresistant epilepsies in humans. We conclude that further studies on isolation and anticonvulsant activities of fraction FS-1 may lead to discovery of new class of naturally occurring potent anticonvulsant drugs.
Supported by research grants from HEJ Research Institute and Johannes Muller Institute for Physiology.

69 PREATTENTIVE INFORMATION PROCESSING IN SCHIZOPHRENIA WITH CANNABIS ABUSE: AN ERP STUDY

J. Rentzsch, A. Penzhorn, T. Wolf, M. Jockers-Scherübl

Department of Psychiatry and Psychotherapy, Charité University Medicine, Campus Benjamin Franklin, Berlin, Germany

Introduction: Cannabis abuse is discussed as an independent risk factor for schizophrenia and it can worsen the course of the illness. Little is known about the influence of cannabis on the disrupted information processing in schizophrenia. In a double stimulus paradigm the auditory evoked P50 potential is reduced with the second stimulus, which is known as intact preattentive gating. This is disrupted in schizophrenia (Bramon et al. 2004) and in abstinent chronic cannabis users (Patrick et al. 2000). It is so far unknown what the influence of cannabis use is on the sensory gating in schizophrenia.
Methods: Clinically stable, medicated schizophrenic patients with (N=25) and without (N=25) significant cannabis abuse, controls with former cannabis use (N=21) and healthy controls (N=26), all without other DSM-IV diagnosis, were examined in an auditory paired stimulus paradigm (80 paired clicks, 90dB SPL, ISI=0,5s, IPI=8s, eyes closed). The evoked response was measured at Cz linked to both earlobes (ground-electrode at forehead, sampling rate 500Hz, bandpass filter P50: 10Hz - 90Hz, notch filter 50Hz). The sensory gating index was measured with peak to peak amplitudes as follows: amplitude stimuli-2/ amplitude stimuli-1x100. Significant cannabis use was defined as an average consumption of at least 1g cannabis per day for one year with the last consumption longer than 28 days prior to the present investigation. Positive urine drug screening led to exclusion from the study. There were no differences in the PANSS scores between the schizophrenic user and non-user group (PANSS for all patients: positive=13,69; negative=17,67). All patients were on atypical antipsychotics including clozapine, 14 patients received an additional SSRI for treatment of negative symptoms and 6 patients carbamazepine.
Results: The evoked potentials are shown in figure 1. There was no significant thc-use*diagnosis interaction with respect to the gating of the P50 ($F(3)=1.06$, $p=.37$). While the P50 amplitudes seem to be larger for S1 and S2 in the schizophrenic cannabis users (figure 1), the thc-use*diagnosis interaction shows only a trend for the P50 S2 amplitude. However, the thc-use*diagnosis interaction was significant for the P50-S2 latency. In the post-hoc t-test the schizophrenic cannabis users showed a trend for a lower amplitude of P50-S2 ($T=1.88$, $df=45$, $p=.067$) and a significant later latency

(T=-4.78, df=45, p=.001) compared to the schizophrenic patients without cannabis use.
Discussion: We found no significant differences in the P50 sensory gating ratio among the four groups. While the patients with former cannabis abuse show a better P50 gating compared to the patients without abuse, this difference was not significant. The normal gating ratio in the patient group is mainly due to the atypical medication, which is known to improve P50 sensory gating deficits. The absence of a abnormal P50 sensory gating ratio in the control-user-group is in contrast to Patrick et al (2000). It must be pointed out, that the P50-gating-ratio has only a low retest-reliability, whereas the reliability of the amplitudes and latencies are some better (Boutros et al. 1991). However, there was a different influence of cannabis-use on the latencies and amplitudes of the P50 after the second stimulus in schizophrenics and controls. While cannabis in schizophrenics seems to delay and reduce the second P50, no such influence was seen in healthy controls. Thus, cannabis may affect the preattentive information processing in controls and schizophrenics in a different manner. Cannabis use in schizophrenics seems to delay the preattentive information processing to the second stimulus. Possibly, this compensates for the sensory gating deficit of the disease, resulting in a normal gating ratio. Further studies are needed.
Boutros NN, Overall J, Zouridakis G. Test-retest reliability of the P50 mid-latency auditory evoked response. Psychiatry Res. 1991 Nov;39(2):181-92.
Bramon E, Rabe-Hesketh S, Sham P, Murray RM, Frangou S. Meta-analysis of the P300 and P50 waveforms in schizophrenia. Schizophr Res. 2004 Oct1; 70(2-3):315-29
Patrick G, Struve FA., Reduction of auditory P50 gating response in marihuana users: further supporting data. Clin Electroencephalogr. 2000 Apr;31(2):88-93.

70 EFFECTS OF 8-OH-DPAT ON HIPPOCAMPAL NADH FLUORESCENCE *IN VIVO* IN ANAESTHETISED RATS

A. Rex, H. Fink

Institute of Pharmacology and Toxicology, School of Veterinary Medicine, Freie Universität Berlin, Koserstr. 20, 14195 Berlin, Germany

Systemic administration of the 5-HT_{1A} receptor agonist 8-OH-DPAT modifies 5-HT neuronal transmission via stimulation of presynaptic and postsynaptic receptors. Compared to the effects of presynaptic receptor stimulation, there are less data on the effects of postsynaptic 5-HT_{1A} receptors and the net effects of a stimulation of both, pre- and postsynaptic, 5-HT_{1A} receptors available. We measured the neuronal activity in the rat hippocampus following systemic treatment with 8-OH-DPAT in doses (30 – 300 μg/kg) known to reduce 5-HT release and anxiety-like behaviour in rodents. Neuronal activity was assessed by laser-induced fluorescence spectroscopy determining changes in nicotinamide adenine dinucleotide (NADH) fluorescence in the ventral hippocampus of anaesthetised rats *in vivo*. NADH, a co-substrate for energy transfer in the respiratory chain, mirrors mitochondrial activity. Increased NADH fluorescence signals lower consumption of NADH caused by neuronal inhibition.
8-OH-DPAT in a dose of 300 μg/kg, but not 100 μg/kg and 30 μg/kg, increased NADH fluorescence by maximal +27±3.5%, suggesting a decreased neuronal activity in the ventral hippocampus. The selective 5-HT_{1A} antagonist WAY-100635 (3mg/kg) prevented the increased NADH fluorescence following 8-OH-DPAT, but had no own effect.
The results show that systemic administration of the 5-HT_{1A} agonist 8-OH-DPAT dose-dependently affects neuronal activity in the ventral hippocampus. The dose of 300 μg/kg seemingly activates presynaptic and postsynaptic receptors with dominating inhibitory postsynaptic effects.

71 APOPTOSIS ONSET AND BAX PROTEIN DISTRIBUTION IN SPINAL MOTONEURONS OF NEWBORN RATS FOLLOWING SCIATIC NERVE AXOTOMY

Rezaie, M.J. ; Tirihi, T.

Departments of Anatomical Sciences and Pathology, Medical Sciences, of Kurdestan University, Tehran, Iran

Extensive apoptosis in spinal cord motoneuron was reported to occur in the newborn following sciatic nerve axotomy. The purpose of this study was to evaluate the onset of cell death at early stages of axotomy, and the changes in Bax protein distribution pattern in the apoptotic cell. Newborn rats were divided into seven groups, axotomized at day 5 postnatal and sacrificed at the following time points: 1, 3, 6, 12, 24, 48, and 72 h after surgery. The left sciatic nerve was transected while the right side was kept as a control. Three experiments were made for morphometric, immunohistochemical, and ultrastructural studies. Morphometric study showed sustained reduction in the number of neurons in the ventral horn. Neuronal losses onset occurred at the first hour after axotomy and the highest loss occurred in the 72-h group (33.7%). The percentage of survived motoneuron (PSM) was calculated. The test of linearity showed that neuron reduction pattern was nonlinear. A nonlinear curve fitting of PSM against time showed an exponential decline in the number of neurons. Immunohistochemistry results showed three Bax protein patterns; early stage increase in Bax gene expression; Bax protein punctation; and dense Bax protein immunoreactivity (DBI). The last two can either be early or late patterns. Bax gene expression increased as early as the first hour post-axotomy and the number of Bax-positive motoneurons continued to increase throughout the time course. Ultrastructural study of the cytoplasm showed an early vacuolation

in Golgi apparatus and endoplasmic reticulum that was associated by mitochondrial and nuclear changes.

72 ROLE OF THE MOUSE TEASHIRT HOMOLOGUES IN DEVELOPMENT AND FUNCTION OF THE NERVOUS SYSTEM

Rocca, E.; Frahm, C.; Griffel, C.; Birchmeier, C.; Garratt, A.N.

The three mouse homologues of the *Drosophila* gene *teashirt (tsh)* were identified amongst more than one hundred genes with enriched expression in the dorsal spinal cord of the postnatal mouse, using Affymetrix microarray hybridization. This screen was undertaken in order to identify genes with potential function in the development/maturation of the dorsal spinal cord, some of which will be further selected for functional analysis in the mouse through gene targeting. The murine homologues, *Mtsh1, Mtsh2* and *Mtsh3*, encode proteins with three Teashirt-like zinc-fingers (consensus: CX2CX6LX2L/MX2HMX4H), also present in the *Drosophila* Tiptop protein, and in the proteins encoded by the vertebrate and *Drosophila schnurri* genes, which function as transcriptional modulators downstream of Bmp signals. Studies with the *Drosophila tsh* gene have shown that *tsh* has a homeotic function in defining trunk identity. Tsh also plays an important role in transmission of Wingless/Wnt signals: it forms a transcriptional repressor complex with the proteins Brinker and CtBP, and interacts with the Wingless target, armadillo (β-catenin in vertebrates). Interestingly, the mouse homologues also contain a homeobox sequence not found in the *Drosophila* Teashirt protein. We are characterising the expression patterns of the mouse *teashirt* homologues during embryonic and postnatal development, and are generating *floxed* alleles of all three genes in the mouse germline, using BAC-"recombineering" techniques. We have knocked-out all three *teashirt* genes in the mouse, and will also generate conditional mouse models. *Mtsh1*, *Mtsh2* and *Mtsh3* are expressed in several tissues of the developing embryo, including the central and peripheral nervous system, and are potentially interesting targets for functional analysis in the mouse.

73 HOW TO SWITCH FROM AN INTEGRATOR TO A RESONATOR IN GENERAL NEURONAL MODELS

Roehner, U.; Benda, J.

ITB, HU Berlin Germany

They are two types of neurons, known as integrators and resonators. They are distinguished by the bifurcation type they undergo when excited. Integrators show a Saddle-node bifurcation while resonators a Hopf bifurcation, resulting in a negative or positive derivative of the steady-state Current(I)-voltage(V)-curve dI/dV, respectively.

We investigate general conductance-based neuron models. For each parameter we determine its possible influence on the transition from integrators to resonators, by looking at the derivative dI/dV. Our results show that the capacities and the time constants have no influence. When considering passive currents we find that only their conductance, g, has an influence, while their reversal, E, potential does not. For currents equipped with gating variables we show analytically under which conditions g and E have an influence. We treat the parameters within the gating variables numerically and show that the midpoint potential has an essential influence. To be more exactly, for two gating variables within one current we show that the overlap of both is crucial for the transition from integrators to resonators or vice versa.

74 ANALYZING THE TOXIC EFFECTS CYCLOHEXIMIDE HAS ON CELL CULTURES

T. Roland

International Graduate Program Medical Neurosciences, Charité, Berlin, Germany

Tumor necrosis factor-á (TNF-á) is a cytokine that when introduced to cells can lead to apoptosis and mitochondrial dysfunction. TNF-á induced apoptosis or mitochondrial dysfunction can be measured by performing specific assays like an MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay. The MTT assay measures the ability of viable cells to metabolize yellow MTT (tetrazolium) into an oxidized purple formazan product. Cells are treated with different concentrations of a toxic agent and mitochondria in viable cells have dehydrogenase enzymes that convert tetrazolium into formazan. Cells treated with a toxic agent are compared to control cells.

A TNF-á assay was performed which normally involves stimulation of cells with different concentrations of lipopolysaccharide (LPS) and inhibition with dexamethasone. For this experiment cycloheximide instead of dexamethasone was used and this led to substantial apoptosis. It appeared that this concentration of cycloheximide was too toxic for the cells.

As a result an experiment was designed to determine which concentration of cycloheximide was optimal a TNF-assay by performing MTT assays with cycloheximide concentrations ranging from 120μg/μl to 0.004μg/μl. Concentrations of less than 1μg/μl appeared to be optimal to determine cell viability by not causing massive apoptosis. Very low concentrations between 0.016μg/μl to 0.004μg/μl stimulated cell proliferation instead of causing apoptosis.

75 IMPROVED REPERFUSION AND NEUROPROTECTION BY CREATINE IN A MOUSE MODEL OF STROKE

G. Royl[1], K. Prass[1], U. Lindauer[1], D. Freyer[1], D. Megow[1], U. Dirnagl[1], G. Stöckler-Ipsiroglu[2], T. Wallimann[3], J. Priller[1,4]

[1]Department of Experimental Neurology, Charité Universitätsmedizin Berlin, D-10117 Berlin, Germany; [2]Department of Neonatology and General Pediatrics, University Hospital of Vienna, 1090 Vienna, Austria; [3]Institute of Cell Biology, ETH-Hönggerberg, 8093 Zurich, Switzerland; [4]Department of Psychiatry and Psychotherapy, Charité Universitätsmedizin Berlin, D-10117 Berlin, Germany

Stroke leads to energy failure and subsequent neuronal cell loss. Creatine and phosphocreatine constitute a cellular energy buffering and transport system, and dietary creatine supplementation was shown to protect neurons in several models of neurodegeneration. Although creatine has recently been found to reduce infarct size after cerebral ischemia in mice, the mechanisms of neuroprotection remained unclear. We provide evidence for augmented cerebral blood flow (CBF) after stroke in creatine-treated mice using an MRI-based technique of CBF measurement (FAIR-MRI). Moreover, improved vasodilatory responses were detected in isolated middle cerebral arteries obtained from creatine-treated animals. After three weeks of dietary creatine supplementation, minor changes in brain creatine, phosphocreatine, ATP, ADP and AMP levels were detected, which did not reach statistical significance. However, we found a 40% reduction in infarct volume after transient focal cerebral ischemia. Our data suggest that creatine-mediated neuroprotection can occur independent of changes in the bioenergetic status of brain tissue, but may involve improved cerebrovascular function.

This work was supported in part by the Deutsche Forschungsgemeinschaft, the Hermann and Lilly Schilling Stiftung and the Swiss Society for Research on Muscle and Neuromuscular Diseases.

76 MICRORNA EXPRESSION AND FUNCTION DURING MOUSE CNS DEVELOPMENT

Rybak, A., Smirnowa, L.; Fuchs, H., Wulczyn, G.; Nitsch, R.

Center for Anatomy, Institute of Cell Biology and Neurobiology, Charité University Hospital Berlin

MicroRNAs (miRNAs) are a class of small (20-24 nt) noncoding RNAs that regulate gene expression by binding to complementary sequences in target mRNAs. Predicted miRNA genes in the mouse number in the thousands, with a particularly rich repertoire expressed in the CNS. As a first step in functional characterization of neural miRNA we have studied the expression of a set of highly expressed neural miRNAs during mouse embryonic development using locked-nucleic acid-modified oligonucleotides probes (LNA). *In situ* hybridization studies of selected spatial and temporal expression patterns will be presented, focusing on members of the paradigm *let-7* miRNA family.

In an accompanying poster, we describe the validation of a mouse NHL family protein, mLin-41, as a *let-7* target gene. During stem cell differentiation, *let-7* and mLin-41 display reciprocal expression patterns. We will present current data detailing mlin-41 expression during mouse development and in particular the early CNS employing whole mount *in situ* hybridization. Ongoing studies characterize mLin-41 protein localization and expression by immunocytochemistry.

77 DC-MAGNETOENCEPHALOGRAPHY TECHNIQUE FOR THE STUDY OF NEURO-VASCULAR COUPLING

T.H. Sander, M. Burghoff, L. Trahms

Physikalisch-Technische Bundesanstalt, Berlin

For the non-invasive study of brain activity several methods are widely used. They can be classified into methods probing directly the electrical activity of neuronal ensembles and methods probing the vascular response, which is an indirect measure. The link between neuronal activity and vascular response is not well understood. As the vascular response has a time constant on a scale of seconds the usual

AC-magnetoencephalography is not well suited to study electrical and vascular responses simultaneously using e.g. near infrared spectroscopy. Therefore modulation based dc- Magneto-encephalography was developed. Here a new system for dc-magnetoencephalography without modulation will be presented consisting of a 304 channel vector magnetometer installed in an extremly well magnetically shielded room. First data suggest that neuro-vascular coupling can be studied using this facility.

78 THE EFFECT OF INTERVENING TASKS ON RESPONSE PREPARATION. AN ERP STUDY

Sangals, Joerg; Sommer, Werner

Institute for Psychology, Humboldt University, Berlin, Germany

The effect of intervening tasks during response preparation was examined in 3 ERP experiments. Participants performed a precued hand choice reaction task. Between precue and response signal presentation, an additional auditory signal required an intervening foot response. Exp. 1 compared interference effects at different times during the foreperiod. The Lateralized Readiness Potential (LRP) indicated that participants wait with response preparation until the intervening task is completed. Late interference evoked additional impairments of response preparation, consistent with central bottleneck accounts. In Exp. 2, the probability of

intervening responses was found not to affect the participant's waiting strategy. Exp. 3 demonstrated that time pressure on the precue task led to an LRP before the intervening task, indicating a less conservative preparation strategy. Furthermore, interference susceptibility was not found to depend on the level of preparation, hinting at other, possibly non-motoric loci of interference. Finally, increased CNV amplitudes long after completion of the intervening task may indicate monitoring processes.
Supported by a grant of the Deutsche Forschungsgemeinschaft to WS.

79 CALEB/NGC MEDIATES DENDRITIC SPINE COMPLEXITY

H. Schadt, N. Brandt, R. Nitsch, S. Schumacher

Institute of Cell Biology and Neurobiology, Center for Anatomy, Charité University Hospital, Philippstraße 12, D-10115 Berlin, Germany

Dendritic spines are small protrusions from many types of neurons, which receive most of the excitatory input to the cell. Spines are thought to have important roles in neural information processing and plasticity, yet we still have a poor understanding of how they emerge during development. We show here that the neural transmembrane EGF family member CALEB/NGC (Chicken Acidic Leucine-rich EGF-like domain containing Brain protein/Neuroglycan C) is expressed on dendritic filopodia and spines and is involved in the regulation of spine morphology during development. We analyzed the effects of CALEB/NGC on spine differentiation in hippocampal neurons in culture either by forcing CALEB/NGC expression of by reducing endogenous CALEB/NGC expression levels via RNA interference. We also examined several pre- and postsynaptic marker proteins to get mechanistic insight into CALEB/NGC function on spine morphology.
The results of theses studies point to the view that CALEB/NGC mediates dendritic spine complexity, partially directly or by regulating the expression levels of other postsynaptic proteins.

80 ASTROCYTIC CALCIUM ACTIVITY IS SUFFICIENT TO INDUCE LONG-TERM SYNAPTIC DEPRESSION OF CA1 SCHAFFER COLLATERAL SYNAPSES

C. G. Schipke, A. Serrano, J.-C. Lacaille and R. Robitaille

Université de Montréal, Département de Physiologie, C.P. 6128, succursale Centre-ville, Montréal (Québec), Canada, H3C 3J7

Glial and neuronal networks are functionally associated during the genesis of heterosynaptic plasticity at mammalian central excitatory synapses, glial cells being a necessary step in the production of heterosynaptic depression in the hippocampus. However, it is not clear whether astrocytic activity alone is sufficient to induce synaptic plasticity. Here, we examined whether selective and specific activation of astrocytes in the CA1 region of the mouse hippocampus can induce synaptic depression of Schaffer collateral synapses. Field potential recordings were performed simultaneously with imaging of the astrocytic Ca^{2+} level while astrocytes were selectively activated using photolysis of caged Ca^{2+} .
Following specific loading of astrocytes with DMNP-EDTA-AM, photolysis with a two-photon laser at 730 nm induced a Ca^{2+} rise in glial cells and subsequent oscillations in the cytosolic Ca^{2+} level that persisted throughout the experiment. This rise in the astrocyte Ca^{2+} level caused a depression of fEPSPs which was persistent throughout the recording time (up to 30 min.). This suggests that Ca^{2+} activation of glial cells is sufficient to induce synaptic depression. The glial-induced depression was blocked by an A_1 receptor antagonist (CPT). However, the effect was not influenced by the $GABA_B$ receptor antagonist CGP55845 although $GABA_B$ receptor activation is necessary for the expression of heterosynaptic depression after tetanic stimulation.
Our work shows that activation of astrocytes in the CA1 region of the hippocampus is not only essential but also sufficient to induce depression of Schaffer collateral synapses. Thus, astrocytes are key players in the cellular network responsible for the induction of synaptic plasticity at mammalian central excitatory synapses.

81 ATYPICAL NEUROLEPTIC (OLANZAPINE) INCREASES EFFICACY OF THE PREFRONTAL CORTEX IN SCHIZOPHRENIA

Florian Schlagenhauf,[1] Jana Wrase,[1] Thorsten Wüstenberg[3], Michael Koslowski[1], Dimitri Filonov[1], Jürgen Gallinat[1], Georg Juckel,[2] Andreas Heinz[1]

[1] Department of Psychiatry, Charité – University Medical Center Berlin, Germany; [2] Department of Psychiatry, Ruhr-University Bochum, Germany; [3] Department of Medical Psychology, Georg August University, Göttingen, Germany

Introduction: Dysfunctional activation of dorsolateral prefrontal cortex (DLPFC) in working memory function has repeatedly been observed in schizophrenic patients. The reduced efficacy may be related to a prefrontal dopamine deficit in schizophrenic patients. Some of the new generation "atypical" neuroleptics such as olanzapine are supposed to increase prefrontal cortex (PFC) dopamine concentrations, whereas no such effect has been observed when traditional, "typical" neuroleptics such as haloperidol were applied.
Methods: We measured activation of DLPFC during a working memory task (2-back vs. 0-back condition) using fMRI in seven schizophrenic patients (age: 33.4+/-10.9 years, one female) first as they received typical neuroleptic medication for at least ten days and second after they were switched to olanzapine for at least two weeks. A matched healthy

control group (age: 33.1+/-10.7 years, one female) was investigated at two corresponding time points.
Results: The schizophrenic patients showed higher activation of the right dorsolateral prefrontal cortex (BA 46) as they received typical neuroleptics compared to olanzapine, although the task performance was similar at both sessions. Healthy controls showed activation of the middle frontal gyrus, the parietal cortex and the cerebellum at both scans and there were no significant differences between first and second session. There was a significant interaction between group and session for the activation in the right DLPFC (BA 46).
Conclusion: Schizophrenic patients displayed an enhanced efficiency of dorsolateral prefrontal activation during a working memory task as they were medicated with olanzapine compared to typical neuroleptics. This may be explained by increased PFC dopamine concentrations caused by olanzapine treatment.
This study was supported by the German Research Foundation (Deutsche Forschungsgemeinschaft; HE 2597/4-2) and by investigator-initiated trails funded by Lilly Germany.

82 DIFFERENTIAL REGULATION OF NEUROTROPHINS AND SEROTONERGIC FUNCTION IN MICE WITH GENETICALLY REDUCED GLUCOCORTICOID RECEPTOR EXPRESSION

Olaf Schulte-Herbrüggen[1], Heide Hörtnagl[2], Sabine Chourbaji[3], Stephanie Ridder[3], Christiane Brandwein[3], Peter Gass[3], and Rainer Hellweg[1]

[1] Department of Psychiatry and Psychotherapy, Charité-University Medicine Berlin, Campus Benjamin Franklin, Berlin, Germany; [2] Institute of Pharmacology and Toxicology, Charité-University Medicine Berlin, Campus Mitte, Berlin, Germany; [3] Central Institute of Mental Health Mannheim (ZI), Mannheim, Germany

Background: The neurotrophin and serotonin (5-HT) hypotheses of depression were studied in a mouse model of reduced glucocorticoid receptor (GR) function ($GR^{+/-}$ mice), which recently has been proven as an excellent murine model of predisposition for depressive behaviour occurring under stressful conditions. In this model we focused on the contribution of changes in neurotrophins and serotonergic function and in their diurnal variations in the predisposition for depressive behaviour.
Methods: Morning and evening levels of brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), 5-HT and its metabolite 5-hydroxyindoleacetic acid (5-HIAA) were analysed in representative brain regions of $GR^{+/-}$ and wildtype mice.
Results: The diurnal variation of hippocampal BDNF with higher levels in the morning occurring in wildtype mice was absent in $GR^{+/-}$ mice. Hypothalamus and parietal cortex displayed enhanced BDNF levels in $GR^{+/-}$ mice. In the frontal cortex, striatum and hypothalamus NGF increased from morning to evening in both genotypes, with an exaggeration in $GR^{+/-}$ mice. The diurnal variation of 5-HT levels and turnover did not differ between $GR^{+/-}$ and wildtype mice.
Conclusion: The present data indicate a contribution of an altered regulation of BDNF and NGF protein to the predisposition for depressive behaviour in the $GR^{+/-}$ mice model of depression, but argue against an eminent role of the serotonergic system.

83 ROLE OF KININ RECEPTOR 1 (B1) IN THE PATHOGENESIS OF EAE

U. Schulze Topphoff[1], A. Smorodchenko[1], M. Mori[2], N. Nowakowski[1], T. Prozorovski[1], H. Radbruch[1], M. Bader[2], F. Zipp[1] and O. Aktas[1]

[1] Institute of Neuroimmunology, Neuroscience Research Center, Humboldt-University, Berlin, Germany, [2] Max-Delbrück-Center for Molecular Medicine, Molecular Biology of Peptide Hormones, Berlin, Germany

MS is a chronic inflammatory disease of the central nervous system (CNS). Its pathogenesis includes the activation of encephalitogenic, i.e. autoimmune myelin-specific T cells outside the CNS, followed by an opening of the blood-brain barrier, T cell and macrophage infiltration, microglial activation, demyelination and irreversible neuronal damage. A great deal is known about the mechanisms responsible for the encephalitogenicity of T cells. However, little is known as yet regarding the body's endogenous control mechanisms for regulating harmful T cell responses to the CNS. Based on previous in vitro observations from MS patients, we hypothesized that the kinin receptor B1, predominantly expressed on immune cells upon activation, may play such a regulatory role. Therefore, we investigated the contribution of B1 to disease pathology in the MS animal model, experimental autoimmune encephalomyelitis (EAE). B1-deficient mice ($B1^{-/-}$) immunized for EAE with myelin oligodendrocyte glycoprotein (MOG) peptide did indeed display enhanced clinical symptoms at disease onset and over a prolonged observation period as compared to corresponding wild type C57BL/6 animals. Histopathology revealed that EAE in $B1^{-/-}$ animals leads to increased axonal damage and microglial infiltration in the spinal cord. Initial ex vivo analyses in $B1^{-/-}$ revealed an enhanced expression of CD80 on CD11b+ splenocytes after EAE manifestation, while the primary T cell response to MOG was apparently less affected. Our data are in line with previous reports which showed that the migration of the T cells of MS patients can be effectively reduced by an B1 agonist in vitro, whereby this effect was reversible using a selective B1 antagonist. Thus, we suggest a critical role for the B1 system in autoimmune neuroinflammation, representing a novel control mechanism responsible for the endogenous limitation of harmful autoimmune responses targeting the CNS.

84 FUNCTION OF THE MOUSE STOMATIN-LIKE PROTEIN-2 (MSLP2) DURING DEVELOPMENT AND IN MATURE SENSORY NEURONS

Alexandra C. Seifert[1], Paul A. Heppenstall[2], Dieter Riethmacher[3], and Gary R. Lewin[1]

[1]Growth Factors and Regeneration Group, Max-Delbrück-Center for Molecular Medicine, Robert-Rössle-Str. 10, D-13092 Berlin, Germany; [2]Klinik für Anaesthesiologie, Charité –Universitätsmedizin Berlin, Campus Benjamin Franklin, Freie Universität Berlin, Hindenburgdamm 30, D-12200 Berlin, Germany; [3]Zentrum für Molekulare Neurobiologie Hamburg, Falkenried 94, D-20251 Hamburg, Germany

In C. *elegans* the stomatin homologue MEC-2 regulates ion channel function and is required for sensory mechanotransduction. Here we have investigated the function of an uncharacterized mammalian stomatin-like protein called mSLP 2 and a novel shorter splice variant, mSLP2s. Expression analysis showed that mSLP-2 is expressed in most tissues with highest expression in the nervous system but mSLP-2s could only be detected in the brain and dorsal root ganglia (DRG). Immunofluorescent experiments indicate that mSLP-2 is predominantly localized to the plasma membrane in sensory neurons. We generated a complete knockout of mSLP2 in the mouse using conventional gene targeting. The mSLP-2 knockout mouse was lethal before embryonic day 9, abnormal homozygote embryos were occasionally found at E8 but placenta development was normal. With in situ hybridizations we now try to analyze the expression of mSLP-2 in embryos before E7.5. We are also generating a Floxed allele of the mSLP-2 gene in order to examine its function in mature sensory neurons. This is the first example of a stomatin domain containing protein that is essential during early embryonic development. We hope to dissect the role of this essential protein in development and maturity using the Cre/loxP genetic system in mice once a Floxed allele has been introduced into mice.

85 AMCREB RESPONSE TO CA^{2+}-STIMULATION OF CULTURED HONEYBEE KENYON CELLS AND TO INDUCTION OF LONG TERM MEMORY *IN VIVO*

Stefanie Seifert*, Anja Froese*, Bernd Grünewald and Dorothea Eisenhardt

*contributed equally

Institut für Neurobiologie, Freie Universität Berlin, Germany

The transcription factor CREB (cAMP response element binding protein) is required for the formation of a stable long term memory. We study the cellular mechanisms of CREB activation in the honeybee, *Apis mellifera*. We first investigated whether learning alters the phosphorylation of the honeybee CREB, AmCREB. Bees were trained to associate an odour with a sucrose reward, such that the animals formed a long term memory. We then quantified the amounts of total and of phosphorylated AmCREB at various intervals after training. *Western blots* with two different antibodies yielded a increase in phosphorylated AmCREB six hours after learning. Furthermore, preliminary evidence indicates a reduction of one AmCREB variant three hours after training.
Secondly, we developed an *in vitro* approach to quantify AmCREB in cultured Kenyon cells from adult honeybee brains. These neurons build up the mushroom bodies, which are essential neuropils for long term memory formation. Using the same *Western blot* technique, we found that stimulations with the Ca^{2+}-Ionophore A23187 (10μM) caused a reduction of the total amount of one of the three AmCREB variants. In addition, elevating the intracellular Ca^{2+} concentration appeared to increase the phosphorylation of at least one AmCREB variant. *In vivo* application of the adenylyl cyclase activator, forskolin, increased slightly but not significantly the phosphorylation of AmCREB.
We conclude that both second messenger pathways, cAMP/PKA and Ca^{2+}, increase AmCREB phosphorylation in honeybee Kenyon cells. Internal Ca^{2+} may also regulate the intracellular concentration of AmCREB proteins. Future experiments will reveal whether the coincident activation of both pathways will lead to stronger CREB activation in the honeybee mushroom body neurons.

86 PHYSIOLOGICAL CHARACTERIZATION OF THE *KV 1.1* $^{-/-}$ MICE

Seo, E.Y.; Milenkovic, N.; Lewin, G. R.

Max-Delbrück Center for Molecular Medicine, Growth Factors and Regeneration Group, Berlin

Somatic sensory mechanoreceptors transducing sensations of cutaneous touch and pain have their somas in the dorsal root ganglia (DRG). A skin is innervated by diverse mechanoreceptor types that vary widely in their response thresholds, dynamic sensitivities and adaptation properties. A D-hair receptor is a type of mechanoreceptor with the lowest mechanical threshold and the highest dynamic sensitivity of all vertebrate mechanoreceptors. We already found out the D-hair receptor was less expressed in the mature neurotrophin 4 knockout mouse (*NT-4* $^{-/-}$; also known as *Ntf5*). Therefore, the *NT-4* $^{-/-}$ was used to screen out for differentially expressed transcripts. Using murine oligonucleotide microarrays together with subtractive cDNA libraries, we identified a down-regulated gene, the shaker-related potassium channel Kv1.1, in the adult *NT-4* $^{-/-}$ DRG. In order to study Kv 1.1 channel's role in mechanoreceptors function, we secured *Kv 1.1* $^{-/-}$ mice then performed phenotype characterization using *in vitro* skin-nerve preparation. We used adult *Kv 1.1* $^{-/-}$ and *Kv 1.1* $^{+/+}$ in these studies and the results will be presented. Approximately 50% of the homozygous mice die between the third and fifth weeks of life, so we assume that genetic background

could maybe influence the mechanoreceptive phenotype in survivors. Therefore we plan to characterize newborn *Kv 1.1* $^{-/-}$ using the *in vitro* skin-nerve preparation as well.

87 STOCHASTIC CHANNEL BEHAVIOUR DRIVES INTRACELLULAR CA^{2+} OSCILLATIONS

A. Skupin, M. Falcke

Department Theory, Hahn Meitner Instiute, Glienicker Str. 100, 14109 Berlin

The ongoing theoretical discussion in mathematical modelling of intracellular Ca^{2+} dynamics pivots around the question whether this system is a deterministic limit cycle oscillator or fluctuations drive oscillations. We provide experimental evidence that oscillations are driven by the random opening and closing of channels, i.e. by thermal fluctuations.

88 REGULATION AND FUNCTION OF *LET–7* MICRORNA DURING NEURAL DIFFERENTIATION

Lena Smirnova[1], Agnieszka Rybak[1], Heiko Fuchs[1], Robert Nitsch[1], Gregory Wulczyn[1]

Institute of Cell- and Neurobiology, Center for Anatomy, Charité University Hospital, Berlin

MicroRNA (miRNA) represent a large class of small (~22nt) RNA molecules. Several miRNA are known to participate in developmental control of gene expression. We have examined the role of miRNA precursor processing in the temporal control and lineage specificity of the paradigm *let-7* miRNA. Levels of both primary *let-7* transcripts and cytoplasmic precursors showed little change during neural differentiation of embryonic and embryocarcinoma stem cells, in contrast to strong induction of the mature miRNAs. Neural differentiation is accompanied by a specific shift in precursor RNA binding profiles. Binding profiles correlate with an increase in *in vitro* processing activity during neural differentiation of stem cells and greater activity in primary neurons than astrocytes. The composition of neuron-specific precursor-binding complexes will be discussed.

Lineage specificity of *let-7* expression is reflected in preferential regulation of *let-7* sensor constructs in neurons compared to astrocytes. Induction of neural differentiation of embryocarcinoma cells also led to downregulation of *let-7* sensor expression. Using this assay we have screened experimentally predicted miRNA target genes. We have identified a mouse lin-41 homolog as a *let-7* target gene in early neural differentiation, and have characterized the role of *let-7* in the regulation of mouse *lin-41*.

89 AXONAL OUTGROWTH IS CONTROLLED BY PLASTICITY-RELATED GENE-1 – RAS-SPECIFIC EXCHANGE FACTOR 2 INTERACTION

Anna Soriguera[1], Jakub M. Swiercz[2], Stefan Offermanns[2], Singh Bhumika[3], Rosemarie Grantyn [3], Robert Nitsch[1], Anja U. Bräuer[1]

[1]PRGs Research Group, Center for Anatomy, Charite-Universitätsmedizin Berlin, Philippstr. 12, D-10115 Berlin, Germany; [2]Institute of Pharmacology, University of Heidelberg, Im Neuenheimer Feld 366, D-69120 Heidelberg, Germany; [3]Sensory and Developmental Physiology, Institute of Neurophysiology, Johannes-Müller-Center of Physiology, Charite-Universitätsmedizin Berlin, Tucholskystr. 2, D-10117 Berlin, Germany.

Plasticity-related gene-1 (PRG-1) is the first identified member of the plasticity-related gene family (PRG-1-5). PRG-1 belongs to the LPP family, which is characterized by its six transmembrane domains, ectoenzymatic activity located on the external surface of the plasma membrane, and its intracellularly located N- and C-terminals. PRG-1 is expressed in brain from postnatal stages until adulthood and *in vivo* data shows an up-regulation after brain lesion.

In order to clarify the pathway involved, a yeast two-hybrid screening was performed and one of the putative interaction partners was Ras-specific exchange factor 2 (Ras-GRF2). Ras-GRF2 belongs to a family of calcium/calmodulin-regulated guanine nucleotide exchange factors that activate Ras proteins. In particular, Ras-GRF2 can activate Ras-GTPases via their Cdc25-like catalytic domains. Signals involved in Ras-GRF2 activation are not fully characterized, but its key role in mediating neuronal functions such as neurite growth is clear.

We could confirm the interaction between PRG-1 and Ras-GRF2 in mammalian cells using co-immunoprecipitation assays. Ras activation assays showed clear inhibition of the N-Ras protein, an interesting finding since N-Ras is known to induce neuronal outgrowth. Because of this result morphology analyses in primary neurons were performed, overexpressing PRG-1 and knocking down PRG-1 using an siRNA technique. First results show PRG-1 overexpression leads to a decrease in axon length.

Further studies will be done to detect the extracellular molecule triggering PRG-1/Ras-GRF2 interaction and therefore N-Ras inhibition and neuronal outgrowth control. We will discuss the findings with an emphasis on the underlying molecular signaling mechanisms.

90 ANALYTICAL DERIVATION OF COMPLEX CELL PROPERTIES FROM THE SLOWNESS PRINCIPLE

Henning Sprekeler[1], Laurenz Wiskott[1,2]

[1] Institut für Theoretische Biologie, Humboldt-Universität Berlin, Berlin, Germany; [2] Bernstein Center for Computational Neuroscience, Berlin, Germany

Ever since the seminal experiments by Hubel and Wiesel, cells in primary visual cortex are conceived as edge or line detectors. Based on the degree of invariance with respect to phase shift of their preferred stimulus, they are categorized as simple and complex cells. Their receptive fields have been shown to be selective for a variety of stimulus properties, e.g. for orientation and spatial frequency.
Recently, Berkes and Wiskott (Journal of Vision, 2005) demonstrated that the unsupervised learning principle of temporal slowness can account for a wide range of complex cell properties, including optimal stimuli, phase shift invariance and orientation and frequency selectivity. The structure of the simulated receptive fields was shown to crucially depend on the transformations present in the image sequences used for training while being largely independent of the statistics
of natural images.
Using this observation as a starting point, we develop a mathematical framework for the simulations, which is based on the Lie group of the transformations in the training data. We show that the optimal receptive fields are the solutions of a partial differential eigenvalue equation, which can in certain cases be solved analytically. The properties of the resulting non-linear receptive fields are in agreement with those of simulated and physiological cells.
The theory demonstrates that the results of the simulations can be largely understood analytically and provides an intuitive explanation why the simulated receptive fields are optimal for temporal slowness learning.

91 ANALYSIS OF AXONAL PATHFINDING ERRORS IN MICE DEFICIENT FOR CGKI SIGNALING BY AN IMPROVED DII TRACING METHOD

A. Stonkute, H. Schmidt, R. Jüttner, F.G. Rathjen

Max Delbrueck Center for Molecular Medicine, Developmental Neurobiology, Berlin, Germany

In vivo studies showed that cGMP signaling via cGMP dependent protein kinase I (cGKI) is important in axonal pathfinding and connectivity of sensory neurons. Phenotypical analysis of cGKI knock-out mice using crude DiI tracing (whole axonal fiber labelling or whole axonal bundle labelling) demonstrated that many sensory axons fail to bifurcate correctly at the dorsal root entry zone (DREZ) of the spinal cord and instead grow directly to the central canal in the absence of cGKI (Schmidt et al., 2002). However, only whole axon bundles but not separate axons had been analysed.
Here, we established a method to visualize single axons in an embryonic spinal cord preparation (embryonic day 12-14). Using a low concentration of the lipophilic tracer DiI allowed us to label single axons and visualize the T-branching in different regions of the spinal cord.
Analysis of axonal pathfinding in the DREZ on the single axon level confirmed the deviations in sensory axon pathfinding in cGKI knock-out mice compared to wild type. While in the wild type mice the majority of axons form a regular T-branch in all levels of the spinal cord, in cGKI knock-out mice most axons turn to the rostral or caudal direction.
In summary, this method for visualization of axonal trajectories at the single axon level can be used to analyse pathfinding errors resulting from gene defects in specific proteins. In the next step we plan to extend our studies on mice lacking VASP, putative downstream target of cGKI in sensory neurons.
Schmidt H., Werner M., Heppenstall P.A., Henning M., More M.I., Kühbander S., Lewin G.R., Hofmann F., Feil R., Rathjen F.G. 2002. J. Cell Biol. 159: 489-498.

92 FIGHTING PANIC: FROM A BETTER UNDERSTANDING OF FEAR CIRCUIT MECHANISMS TO MORE EFFECTIVE PSYCHOLOGICAL TREATMENT

A. Ströhle

Department of Psychiatry and Psychotherapy, Campus Charité Mitte, Charité – Universitätsmedizin Berlin, Germany

The spontaneous panic attack is the key feature of panic disorder, which has a prevalence of 1% to 2%. This anxiety disorder is associated with pervasive social and health consequences similar to or greater than those associated with major depression. Within the BMBF-announcement "Psychotherapieforschung" a network will be supported to study the relevant fear circuit mechanisms in panic disorder for a more effective psychological treatment. Under the coordination of Prof. Dr. V. Arolt (Münster) a network of psychiatrists, psychologists and cognitive neuroscientists with centers in Münster, Dresden, Berlin, Aachen, Würzburg and Greifswald is established. A multi-center treatment study aims to identify the active treatment ingredients of cognitive behavioral therapy (CBT) for panic. Linked to the clinical trial network basic and applied research on the psychological and neurobiological mechanisms of panic disorder are performed. The neural circuitry of the fear network in the brain will be examined. The cerebral findings will be directly related to peripheral readout systems, i.e. recordings of fear and panic by verbal report, physiological, endocrine, and behavioral responses. This multi-system assessment of fear and anxiety networks will be complemented by genetic analyses. These experiments are expected to provide a better understanding of mechanisms of action of the core ingredients of effective CBT in panic disorder patients and the design of better intervention modules.

93 ANALYZING OLFACTORY CODING USING EXTRACELLULAR RECORDINGS FROM MUSHROOM BODY-EXTRINSIC NEURONS IN THE HONEYBEE

Martin Strube, Martin P. Nawrot, Sonja Grün and Randolf Menzel

Neurobiology, Institute of Biology, Free University of Berlin, Germany; Bernstein Center for Computational Neuroscience (BCCN) Berlin, Germany

Mushroom bodies (MBs) within the insect brain are higher-order centers performing integration of olfactory, visual and mechano-sensory information. They are involved in neural plasticity underlying associative olfactory learning.
The aim of our project is to study the interhemispheric information transfer between the two MBs using learning paradigms. To begin with we focused on the activity of extrinsic output neurons that leave the MBs via the alpha-lobe and project partially into the contralateral hemisphere. To evaluate the general response properties of these single extrinsic neurons under learning conditions we studied the variability of their response patterns to an odor, to an odor presented with a reinforcer (CS+) as well as during a possible extinction phase after the CS+ stimulations. Each combination was presented repeatedly. To monitor single-unit activity we inserted three closely-spaced electrodes (insulated copper, 14 microns, 3-7 MOhm) into the alpha-lobe. Signals used for spike detection were measured differentially from all three electrode pair combinations. Applying semi-automatic spike sorting techniques (Spike2) we separated up to 4 individual neurons per recording. Although the rate responses of single alpha-lobe extrinsic neurons to repeated odor presentation may exhibit a decreasing or increasing trend the variability of the responses remains small. Responses to the CS+ are typically enhanced over successive trials. During the subsequent test phase where the odor is presented again alone the response rate again decreases. That could be interpreted as extinction after learning.
Supported by the German Federal Ministry of Education and Research (grant 01GQ0413) and the Stifterverband für die deutsche Wissenschaft.

94 GENERATION OF CONDITIONAL KO-MICE FOR PRG-1 AND PRG-2 USING RED RECOMBINATION TECHNOLOGY

T. Trimbuch, B. Geist, O. Ninnemann, R. Nitsch

Charité – University Hospital Berlin, Center of Anatomy, Institute of Cell- and Neurobiology, Berlin

Resulting from a screen for molecules involved both in the maturation and reorganization of cortical connections, we recently reported on a new class of molecules we named plasticity related genes (PRG), which may play an important role in axonal outgrowth and cortical layer formation. We were able to show that PRG-1 and PRG-2 have distinct expression patterns during development. Studies using antibodies generated against PRG-1 and PRG-2, respectively, revealed that both molecules are exclusively expressed in neurons, not in glial cells, but are absent in other tissues of the body.
Predictions on to the structural features of these molecules indicate the presence of six transmembrane domains with an extracellular motif showing significant homology to the ectophosphatase domain of lipid phosphate phosphatases (LPPs). LPPs are transmembrane proteins capable of dephosphorylation of extracellular phospholipids like lysophosphatic acid (LPA) and thereby influence diverse cellular processes. We could show that both PRGs are able to interfere with LPA-signalling in the extracellular space. There is reason to assume that lack of PRG-1 and PRG-2 results in relevant disturbances of nervous system development as the molecular components of this LPA-signalling pathway are highly conserved in all vertebrates and our cell biological data indicate a distinct function during layer formation and the formation of axonal connections of PRG-2 and PRG-1, respectively.
This poster reviews our knock-out strategy for PRG-1 and PRG-2 and gives an overview of the construction of conditional gene targeting vectors for PRG-1 und PRG-2 by using Red recombination technology. Furthermore we show our latest progress in the generation of the knock-out mice.

95 MISSENSE MUTATIONS IN GAP JUNCTION PROTEIN ALPHA 12 ARE ASSOCIATED WITH SEVERE CNS HYPOMYELINATION IN HUMANS

Birgit Uhlenberg[1], Bernhard Weschke[1], Jutta Gärtner[2], Christoph Hübner[1]

[1]Neuropediatric Department at the Children's Clinic Charité, University Medicine Berlin, and [2]University Göttingen

Leukodystrophies are inborn errors of white matter formation or maintenance. A well known leukodystrophy with hypomyelination is Pelizaeus-Merzbacher disease (OMIM#312080) that is due to mutations, deletions or duplications of the X chromosomal PLP1 (proteolipidprotein) gene, coding for the major protein component of myelin. We mapped a phenotypically identical disease (Pelizaeus-Merzbacher-like disease, OMIM#608804) in a consanguineous Turkish family with three affected patients to chromosome 1q41 and subsequently identified the disease underlying mutation in the gene gap junction protein alpha 12 (GJA12, also known as connexin 46.6 or 47, Cx47). The patients present with connatal nystagmus, developmental delay, progressive spasticity and severe ataxia, the disease is following a resessive trait. MRI scans of the brain demonstrate virtual absence of myelin in the CNS. Moreover we identified other patients with Pelizaeus-Merzbacher-like disease to be affected by missense, nonsense and frameshift mutations in the GJA12

gene. To date the oldest patient is 21 years old.
GJA12 is highly expressed by oligodendrocytes, there are at least 20 other homologous connexins expressed in a wide variety of tissues. Connexins hexamerize into hemichannels that might appose to hemichannels of adjacent cells to form fully functional non-selective intercellular channels. The function of GJA12 in myelination is not clear. Generation of the mouse carrying the mutation of our index patients and transfection of different missense mutants into oligodendrocytes will help to understand the pathophysiology of mutant GJA12 in myelination defects.
Supported by the Rahel-Hirsch-Scholarship of the Charité to BU and the Deutsche Forschungsgemeinschaft (SFB Developmental Disturbances of the Central Nervous system) to BU and HK.

96 LIPID PHOSPHATE PHOSPHATASES PROMOTE NEURITE OUTGROWTH

Velmans T[1,2], Savaskan NE[2], Moolenaar W[2], Nitsch R[1], Bräuer AU[1]

[1]PRGs Research Group, Institute of Cell Biology and Neurobiology, Centrum of Anatomy, University Medical school Charité, Berlin; [2]Division of Cellular Biochemistry, The Netherlands Cancer Institute, Amsterdam, The Netherlands

Lysophosphatidic acid (LPA) is an extracellular lipid mediator that shapes neuronal morphology during development, and acts as a strong neurite retractor and inhibitor of neurite outgrowth. LPA acts specifically through four G-protein-coupled receptors (LPA_{1-4}) and activates RhoA and Rac thereby.
Lipid phosphate phosphatases (LPP) are integral membrane proteins and are believed to act as ectoenzymes able to dephosphorylate extracellular phospholipids such as LPA. Up to now three LPPs are known (LPP1-3) which have three conserved motifs forming a subclass of the LPP-superfamily. Whereas the catalytically active domain can be found on the surface of the cell, both N- and C-terminal tails are localized intracellularly. The tissue- and isoform-specific distribution and function of LPPs in the brain, if any, still remain unknown. *In situ* hybridization and real-time PCR analysis revealed that mRNA of LPP-1 and its splice variant LPP-1a is dynamically expressed in the brain during development. Live-cell-analysis showed that the expression of LPP-1/1a causes enhanced neurite outgrowth in neuronal cells. In time-lapse experiments we could show that LPP-formed neurites are resistant to collapse-inducing substances like LPA. To test the hypothesis that LPPs act extracellularly, we used the nonhydrolysable LPA analogon XY-17. Surprisingly LPP-1/1a-expressing cells were still resistant to the XY-17-induced axon collapse. Thus, these data indicate that LPP-1/1a act intracellularly rather than on the extracellular side.
So far, our data indicate that LPP-1 and its isoform signal downstream of the LPA receptors, thereby interfering with LPA-mediated cytoskeletal reorganization. We will discuss these findings with emphasis on the underlying molecular signaling mechanisms.

97 THE FUNCTIONAL ROLE OF NEUROMODULATORY CELLS IN THE MOTOR SYSTEM OF *MANDUCA SEXTA*

R. Vierk, H.-J. Pflüger

Free University Berlin, Biology/Chemistry/Pharmacy Department, Institute for Neurobiology, Berlin

The nervous system of the hawkmoth *Manduca sexta* undergoes a major reorganisation from larva to imago to accommodate adult behavior. Large efferent octopaminergic unpaired median neurons (DUM/VUM), which innervate bodywall- and leg-muscles in larvae are remodeled during metamorphosis, because they innervate different targets in larvae and adults. It is known that during larval motor behavior all thoracic and abdominal VUM neurons are activated simultaneously. However, work in locusts (such as crawling) has shown that the population of octopaminergic VUM neurons is divided into different functional subsets which serve various different behavioral requirements. One major question is now, whether and how a homogeneous population of neuromodulatory neurons might be divided into different functional subsets during metamorphosis. As a first step towards this question I examine the activation of these neuromodulatory cells during fictive flight in adults by intracellular recording from mesothoracic VUM neurons before and after pharmacologically induced fictive flight. At present we have no indication that VUM neurons are recruited during flight in adult manducas thus revealing a great difference to locusts.
In a second step the postembryonic maturation of the central motor circuitry (flight motor) for flight is studied. The experimental approach contains electrophysiological recordings from agonistic and antagonistic flight muscles in adults and different pupal stages during pharmacologically induced flight. Based on the obtained data motor pattern features like cycle period, phase relationship and precision are evaluated in the light of structural and physiological refinement of participating motoneurons.
Supported by the Deutsche Forschungsgemeinschaft and the States of Berlin and Brandenburg.

98 LUMBAR SPINAL CORD NEURONAL CELL LOSS IN CHRONIC NEUROINFLAMMATION

J. Vogt*, O. Aktas#, K. Müller-Wielsch#*, R. Nitsch*, F. Zipp#

** Institute for Cell- and Neurobiology, Center for Anatomy, Charité; # Institute for Neuroimmunology, Neuroscience Research Center, Charité*

Since its initial description in 1933, experimental

autoimmune encephalomyelitis (EAE) has served as an animal model for studying mechanisms of myelin-specific autoimmunity and for testing therapies in the demyelinating disease multiple sclerosis (MS). Using high-precision design-based stereology in different EAE models, we discovered a significant loss of alpha- and gamma-motoneurons but also of interneurons in the peak phase of the disease. The neuronal cell loss reached around 70% of total neuronal numbers in the passive EAE and around 50% in the active EAE. While in some cases we observed a neuronal cell loss already at the onset of the disease, we found no further neuronal cell loss in the chronic phase of the disease.
Our findings confirm an early and in the course profound neuronal damage, also indicated by magnetic resonance imaging studies in patients. These results, moreover, point to an unexpected spinal cord pathology which we are currently further investigating with the same stereological approach in the human pathology.

99 DYNAMICS OF NEURONAL DEVELOPMENT IN THE ADULT HIPPOCAMPUS

Imke Vollmar[1], Friederike Klempin[1,3], Golo Kronenberg[1,2], Gerd Kempermann[1,3]

[1]Max Delbrück Center for Molecular Medicine (MDC) Berlin-Buch, Berlin, Germany; [2]Department of Psychiatry, Freie Universität Berlin, Berlin, Germany; [3]VolkswagenStiftung Research Group, Department of Experimental Neurology, Charité University Hospital, Humboldt University, Berlin, Germany

Adult hippocampal neurogenesis originates from precursor cells in the adult dentate gyrus and results in new granule cell neurons. A kinetic model of this development has been established before, but the exact dynamics of neuronal development in the dentate gyrus are unknown. To analyse the temporal pattern of adult hippocampal neurogenesis and quantitfy the development we have used transgenic mice expressing green fluorescent protein (GFP) under the nestin promoter and analyzed the relative number of type-1, type-2, type-3 and early postmitotic cells at different time points after BrdU injection. BrdU permanantly labels cells during S-phase of the cell cycle and allows to follow a cohort of new cells over time. Additionally we determined the absolut number of BrdU-positive, NestinGFP-positive and Doublecortin-positive cells over time. We found an increase in BrdU-positive cells within 48 hours after BrdU injection. Between 48 hours and 21 days the absolute number of BrdU-positive cells decreases again. These data leads to the assumption that BrdU labeled cells are highly proliferative within the first 48 hours followed by a prolonged phase of selective cell death. Based on these data a mathematical model will be established.

100 SUBCORTICAL CONTRIBUTIONS TO THE SYNTACTIC ANALYSIS OF PHRASES

M. Wahl[1,2]; F. Marzinzik[1]; A. Hahne[3]; A. Kupsch [4]; A. D. Friederici[3], G. Curio[1]; D. Saddy[2]; F. Klostermann[1]

[1] Department of Neurology, Charité, CBF; [2] Department of Linguistics, University of Potsdam; [3] MPI for Human Cognitive and Brain Sciences, Leipzig; [4] Department of Neurology, Charité, CVK

The syntax of phrases is a prerequisite of language comprehension. In EEG, two correlates of syntax analysis can be depicted with event related potentials (ERP): the early left anterior negativity (ELAN), presumed to reflect the automatic detection of phrase violations, and the centro-parietal 'P600', putatively mirroring phrase re-analysis. For studying subcortical contributions, we recorded syntactic error potentials directly from the thalamus in patients with deep brain stimulation (DBS).
In 8 patients with tremor diseases, EEG was recorded from 16 thalamic DBS electrodes, bilaterally implanted into the ventral intermediate nucleus (VIM). Simultaneously, scalp EEGs were derived from 20 scalp sites, due to the 10-20 system. Per patient, 148 correct and erroneous sentences were acoustically presented in randomized order (75% correct, 25% syntactically incorrect). 3s after the sentence the in-/correctness had to be indicated by a button press.
At scalp level, the classical 'syntactic' EEG pattern, the frontal ELAN and the parietal P600 peaked at 169 ± 34 ms and 803 ± 92 ms, respectively. In the thalamic recordings, two additional negative potentials were identified upon syntactic errors, peaking at 195 ± 45 ms and 591 ± 58 ms. The peak latencies of thalamic ERP differed significantly from those of scalp ERP.
According to the latencies obtained at either level, it is conceivable that the early thalamic negativity arises along a fronto-thalamic route along which automatic error detection is propagated. The late thalamic negativity is compatible with a thalamo-cortical route, initiating language re-analysis, suggesting a cortico-basal network of primary language comprehension.

101 ROLE OF MYOSIN XV IN SENSORY MECHANOTRANSDUCTION

R. Wang, G. R. Lewin

Growth Factor and Regeneration Group, Max-Delbrueck-Center, Berlin, Germany

Mutations in several unconventional myosin genes are known to underlie both syndromic and non-syndromic hearing loss in animals and humans. These unconventional myosin proteins, myosin VI, VIIa and XV, may have the function of organizing the actin cytoskeleton of the hair cell stereocilia bundle and regulating the adaptation behavior of mechanotransduction channels in sensory hair cells. Here we asked if these proteins might play a similar

role in cutaneous mechanoreceptors. Cutaneous mechanoreceptors have their cell bodies in the sensory or dorsal root ganglia (DRG). From a previous study in our laboratory, it was found that the adaptation behaviors of two types of rapidly adapting mechanoreceptors were dramatically altered in myosin VI and VIIa mutant mice, termed *Snells Waltzer* and *Shaker-1*, respectively. In the current study, I used an in vitro skin nerve preparation to investigate whether the third unconventional myosin mutation in the myosin XV gene that causes deafness in the mutant *Shaker-2*, can also alter the adaptation behavior of cutaneous mechanoreceptors. With real-time PCR, I also investigated further possible members of the molecular complexes underlying the mechanotransduction that might be common to sensory hair cells and DRG neurons. The present study showed that in *Shaker-2* mice, D-hair mechanoreceptors were endowed a novel slowly adapting behavior, which dramatically elevated the mechanical sensitivity of this receptor. Except for rapidly adapting mechanoreceptors, all the other tested receptors displayed delayed mechanical latencies an indicator of a higher threshold for activation. We also found that several hair-cell mechanotransduction related proteins were all detected in DRG and skin. We conclude that unconventional myosins may function as the adaptation motors in cutaneous mechanoreceptors. Thus hair cell and cutaneous mechanoreceptors may use common gene products to regulate their mechanotransduction function.

102 CHARACTERIZATION OF THE IMPAIRMENT IN CONGENITAL PROSOPAGNOSIA BY COMBINED ELECTROPHYSIOLOGICAL AND BEHAVIOURAL DATA

Joachim E. Weber[1], Tilmann Sander[2], Claus C. Carbon[3], Thomas Grueter[4], Martina Grueter[4], Lutz Trahms[2], Gabriel Curio[1] & Andreas Lueschow[1]

[1]Dpt. of Neurology, Charité-Universitätsmedizin Berlin, Germany; [2]Physikalisch-Technische Bundesanstalt, Berlin, Germany; [3]Faculty of Psychology, University of Vienna, Vienna, Austria; [4]Münster, Germany

Recently a form of prosopagnosia has attracted attention that is not accompanied by any discernible brain lesion. Because subjects complain a lifelong impairment and given a familial clustering this condition has been termed congenital prosopagnosia (cPA) although sensu stricto "congenital" requires the molecular establishment of a genetic basis. Without such determination of this neuropsychological condition as a discrete entity it is necessary to aim at a delineation by neuroimaging and behavioural data. In 14 subjects with cPA and 19 controls evoked responses were measured by simultaneous EEG and MEG recording in a viewing task with a sequence of faces and houses. A double dissociation between methodology and stimulus category was revealed: i) In the cPA group, only MEG (not EEG) showed an M170 (a component linked to structural encoding of faces) significantly reduced over the right hemisphere and delayed over the left hemisphere. ii) The M170 for houses was not altered, suggesting that the deficit is restricted to a face processing system. Additional analysis with accuracy data from three basic tests (face-familiarity, face recognition, face imagery) revealed a significantly negative correlation between hit rate and latency of M170 over the left hemisphere for subjects with cPA only. This suggests a link between strength of impairment as measured behaviourally and MEG-correlates of face processing in cPA. In summary electrophysiological measures alone and their combination with behavioural measures offer an objective criterion to dissociate cPA from normal face processing.

Supported by a grant of the Sonnenfeldstiftung to JW.

103 ANALYSIS OF MAFA AND C-MAF FUNCTION IN MOUSE EMBRYONIC DEVELOPMENT

Hagen Wende, Katja Reuter, Elvira Rhode und Carmen Birchmeier

Max Delbrück Center for Molecular Medicine, Berlin, Germany

c-Maf and MafA are two transcription factors, belonging to a family of related proteins with a conserved basic region/leucin zipper (bZIP) domain. Both genes were identified in two different large scale expression analysis of spinal cord tissue in our lab. Subsequent experiments confirmed the expression in the spinal cord, where the two genes are expressed in an overlapping fashion in postmitotic neurons predominantly in the dorsal horn, but also in the ventral spinal cord. Both genes are furthermore found in the brain stem, in dorsal root ganglion neurons and in a number of other tissues. c-Maf and MafA are evolutionary closely related and are mostly co-expressed in the CNS indicating a potential redundancy in function. In order to study the function of these proteins we employed gene targeting to mutate both genes and introduced a marker gene (GFP in MafA and LacZ in c-Maf), which should facilitate the phenotypic analysis. MafA mutant mice are viable and fertile and show no obvious phenotype. c-Maf mutant mice die shortly after birth, which has been described previously. c-Maf mutants show a phenotype in axonal pathfinding in the auditory brainstem. The compound mutants die around E15. We will be using tissue specific knock outs to further analyse the function of these two genes in CNS development.

104 INVESTIGATIONS OF PATHOMECHANISMS OF PARKINSON'S DISEASE AND SEARCH FOR NEUROPROTECTIVE THERAPIES

Wernicke C., Gille G., Lehmann J., Pavlovic S., Schulze G., Rommelspacher H.

Charité - Universitätsmedizin Berlin, Klinische Neurobiologie, Klinik und Hochschulambulanz für Psychiatrie und Psychologie, Berlin

1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine was described to induce irreversible Parkinson-like symptoms in humans. Beta-carbolines (BCs) resemble the neurotoxin in structure, specifically its active metabolite MPP^+. Natural BCs occur in plants, animal tissues, and human brains. They are metabolized via sequential di-*N*-methylation to 2,9-dimethylated carbolinium cations. Both steps are necessary to convert BCs into a potent complex-1-inhibitor and nigrostriatal toxin (Collins et al., 1992). The active transport of neurotoxins by the dopamine transporter (DAT) might contribute to the selective degeneration of dopaminergic neurons in the substantia nigra (SN), the main feature of Parkinson's disease.

DAT and OCT transfected HEK cells and native HEK cells were used as model to study the neurotoxicity of 27 BCs. Toxicity was studied by the MTT-method. Some BCs were tested in primary cell culture of embryonic mesencephalic mouse cells. Furthermore, the influence of BCs on [^{3}H]MPP^+ and [^{3}H]dopamine uptake was investigated in transfected cell lines.

Several of the tested BCs were neurotoxic, some only at high concentrations. The neurotoxic potential of a BC occurring naturally in human SN was in the same range as shown for MPP^+ in several tests. Detailed investigations revealed apoptosis as main mechanism of neurotoxicity (Pavlovic et al. 2006). One BC induced an increase in tyrosine hydroxylase immunostaining, dopamine and ATP levels, and a decrease in LDH release in primary cell cultures, suggesting neuroprotective effects. Uptake of [^{3}H]MPP^+ and [^{3}H]dopamine by hDAT was inhibited up to 70% by non-ionic BCs but not by ionic BCs, whereas most of the BCs inhibited the OCT up to 100%.

The results show that some BCs may contribute to the degeneration of dopaminergic neurons in Parkinson's disease, while at least one shows neuroprotective effects.

Supported: BMBF_01GZ0309.

105 SLP3 IS A MAMMALIAN STOMATIN-DOMAIN PROTEIN ESSENTIAL FOR TOUCH RECEPTOR FUNCTION

Christiane Wetzel[1], Anne Mannsfeldt[1], Jing Hu[1], Dieter Riethmacher[2], Lena Harder[1] and Gary R. Lewin[1]

[1]Growth Factors and Regeneration Group, Max-Delbrück Center for Molecular Medicine, Berlin-Buch, Germany; [2]Zentrum für Molekulare Neurobiologie Hamburg, Hamburg, Germany

A model for mechanotransduction has been proposed from the identification of genes essential for touch behaviour in *C.elegans*. One such gene is mec-2 and we have therefore looked for and found novel mec-2 orthologs in rodents one of which we is called SLP3 (stomatin like protein-3). To examine the role of this gene product in sensory mechanotransduction we used conventional techniques to generate a null mutation of this gene in mice. Homozygous SLP3 mutant mice are viable, fertile and seemingly healthy. Using an *in vitro* skin nerve electrophysiological assay we examined the physiological properties of wild type and mutant cutaneous sensory afferents to mechanical and thermal stimuli. We found that ~35% of Ab- and ~25% of Ad-mechanoreceptors in SLP3 -/- mice have no mechanosensitivity. In the present study we could show that the majority of the remaining rapidly adapting (RA) mechanoreceptors respond only poorly to mechanical stimuli as a brisk tap was the only effective stimulus. D-hair mechanoreceptors, Ad-mechanonociceptors and C-fiber mechanonociceptors on the other hand showed no substantial change in their stimulus response functions.

Moreover tactile driven behaviours are impaired in SLP3 mutant mice. In addition these animals are not able to develop a mechanical allodynia following chronic constriction injury (CCI) of the N ischiadicus. We therefore conclude that SLP3 is absolutely necessary for cutaneous mechanoreceptor function and we propose that it is an essential subunit of a mammalian mechanotransducer.

106 PROPERTIES OF HYPERPOLARIZATION-ACTIVATED INWARD CURRENTS OF HUMAN NEOCORTICAL NEURONES IN SLICES FROM EPILEPSY SURGERY SPECIMEN

Wierschke, S[1], Huggenberger, S[2], Lehmann, T-N[3], Meencke, H-J[4], Nitsch, R[1] and Deisz, RA[1]

[1]Charité University Medicine Berlin, Center for Anatomy, Institute of Cell- and Neurobiology; [2]University of Potsdam, Institute for Biochemistry and Biology; [3]Charité University Medicine Berlin, Department of Neurosurgery; [4]Epilepsy Centre Berlin-Brandenburg

Hyperpolarization-activated inward currents (I_H) of central neurones have diverse functions including e.g. stabilization of resting membrane potential and attenuation of temporal summation of EPSPs. The reduced I_H in epilepsy models (e.g. 1) and its augmentation by anticonvulsants (e.g. 2) indicates that reductions of I_H may contribute to hyperexcitability. We further evaluated I_H in resected human epileptogenic cortex (HEC) (3).

The methods have been described (1, 4). The inward

currents evoked by hyperpolarizing steps were reduced by the specific antagonist ZD7288 (n=4). Current densities averaged -3.5±2.3 pA/pF in HEC (at -140mV; n=158) and -6.3±3.2pA/pF in cortical neurones from healthy rats (n=44; P<0.0001). Application of Ba^{2+} yielded a slight increase of I_H in HEC (control: -335±237pA; Ba^{2+}: -419±289pA; n=39; P>0.05). The time constant of the fast activation (at -140mV) averaged 67.5±44.7ms in HEC (n=68) and 45.5±11.9ms in rat neurones (n=27; p=0.0138). The voltage of half-maximal activation ($V_{1/2}$) of isolated I_H averaged -101.1±8.7mV in HEC (n=8) and -92.5±4.7mV in rat neurones (n=8; p=0.029). Bath application of lamotrigine (100μM) caused no significant effects on I_H.

We conclude that neurones from human epileptogenic neocortex have smaller H-current densities than those from rat. The differences in kinetics and $V_{1/2}$ indicate a reduced contribution of HCN1 subunits in the human epileptogenic neocortex (see 1).

(1) Strauss U et al. 2004. Eur. J. Neurosci. 19:3048-3058.
(2) Poolos NP et al. 2002. Nature Neurosci. 5:767-773.
(3) Kole MHP 1999 Soc. Neuroscience 25:844.
(4) Deisz RA 1999 Neuropharmacology 38:1755-66.

107 DISTINCT ROLES FOR SELENOPROTEINS IN NEURONAL DEVELOPMENT AND FUNCTION

Wirth, E.; Bharathi, S.; Conrad, M.; Brielmeier, M.; Tessarollo, L.; Hatfield, D.; Köhrle, J.; Schweizer, U.

AG Neurobiologie des Selens, Charité, Berlin

Selenoproteins, i.e. proteins containing the rare amino acid selenocysteine, are among the key enzymes of cellular redox defense and regulation. Targeted ablation of Trsp, the gene encoding tRNA(Sec), leads to early embryonic lethality confirming the essentiality of selenoproteins for mammalian development. We abrogated selenoprotein biosynthesis in neurons by cell type-specific Cre mediated recombination of Trsp. Resulting knockout mice develop a devastating neurological phenotype in the second week of life with apparent neuronal dysfunction. In addition, marked cerebellar hypoplasia ensued, if Cre-mediated recombination occurred in the developing cerebellum. Analysis of postnatal cerebellar development revealed patterned Purkinje cell (PC) loss. A marked reduction of the external germinal layer suggests defective precursor cell proliferation compatible with cerebellar hypoplasia. More specifically, GABAergic interneurons (presumptive basket cells and stellate cells) are almost completely lost in neuron-specific Trsp knockout mice. The phenotypes of these mice were compared with several mouse strains deficient in individual selenoproteins, e.g. selenoprotein P and thioredoxin reductases. On the basis of these studies, conclusions can be drawn regarding the functions of individual selenoproteins within the brain. However, the specific mechanisms how these selenoproteins control neuronal development and survival require further study.

108 ELECTROPHYSIOLOGICAL CORRELATES OF CRAVING AFTER VISUAL AND AUDITORY CUE-EXPOSURE IN ALCOHOLISM

Wölfling, K.; Grüsser, S.M.

Interdisciplinary Research Group on Addiction, Institute for Medical Psychology, Charité - University Medicine, Berlin, Germany

In addiction research it is commonly agreed that craving - a specific emotional or motivational state - is a key symptom in the development and maintenance of alcohol dependence. Craving has been conventionally explained by behavioral approaches focussing on learning mechanisms (conditioning processes). This behavioral model is current supported by neurobiological findings which point to the fact that chronic drug intake is accompanied by neuroadaptive processes, e.g. changes in dopamine release in several brain regions (reward system). These findings contribute to explanations for the strong emotional and motivational responses to psychotropic substances. According to this model, we assume that due to conditioning processes alcohol-associated cues can elicit activation of drug memory, induce craving and motivate renewed alcohol intake. The aim of the present study is the comparison of psychophysiological responses to alcohol and neutral stimuli in 25 alcohol-dependents (AD) and 25 healthy controls (HC) in a cue-reactivity-paradigm. To take into consideration the complexity of the different modalities of alcohol-associated environmental cues to which alcohol-dependents are daily exposed, we used in this study standardized visual as well as auditory alcohol and neutral cues. Data analyses show that the enhanced emotional or motivational state to alcohol-specific cues is reflected by higher values of event-related potentials (P300, late positive complex) in AD compared to HC in both experimental (acoustic and visual) conditions. Additionally, within AD, the alcohol-associated category elicited significantly more arousal than neutral cues. Furthermore, AD reported significant higher craving. Our findings support that learning processes could be seen as the underlying mechanisms of a drug-specific emotional or motivational state induces craving and accentuate the close interaction between neurobiological and behavioral processes.

109 DYSFUNCTION OF THE REWARD SYSTEM CORRELATES WITH ALCOHOL CRAVING IN DETOXIFIED ALCOHOLICS

Jana Wrase[1], Florian Schlagenhauf[1], Thorsten Kienast[1], Torsten Wüstenberg[2], Anne Beck[1], Thorsten Kahnt[1], Brian Knutson[3], Andreas Heinz[1]

[1]Department of Psychiatry and Psychotherapy, Charité – Universitätsmedizin Berlin, Charité Campus Mitte (CCM), Berlin, Germany; [2]Department of Medical Psychology, Georg-August-University, Göttingen, Germany; [3]Department of Psychology, Stanford University ,CA

Objective: Alcohol dependence may be associated with dysfunction of the brain reward system, so that nonalcoholic reward cues fail to activate the ventral striatum, while alcohol cues continue to activate this area. Alcoholics may then crave the pharmacological effects of alcohol in order to stimulate the dysfunctional reward system. The present study aimed at investigating the neural mechanisms underlying these phenomena.

Methods: 16 detoxified male alcoholics and 16 age-matched healthy volunteers participated in two fMRI paradigms. In the first one alcohol-associated and affectively neutral pictures were presented, where as in the second one a monetary incentive delay task (MID) was performed, in which visual cues predicted that a rapid response to a subsequent target stimulus would result in monetary gain, avoidance of monetary loss or no consequence. For both paradigms the association with alcohol craving was assessed.

Results: Compared to healthy volunteers, detoxified alcoholics failed to activate the ventral striatum during the expectation of monetary reward. However, alcoholics did show increased activation of the ventral striatum when confronted with alcohol cues. Reduced activation in the ventral striatum during expectation of monetary reward, and increased activation during presentation of alcohol cues were correlated with alcohol craving in alcoholics, but not in healthy controls.

Conclusions: Our results suggest that the reward system in alcoholics is biased towards processing of alcohol cues. This might explain why alcoholics find it particularly difficult to focus on conventional reward cues and engage in other rewarding activities.

110 *IN VIVO* MRIMAGING OF TRIGEMINAL NERVE ROOT INFLAMMATION IN A MOUSE MODEL OF MULTIPLE SCLEROSIS

J. Wuerfel[1*], E. Tysiak[1*], O. Aktas[1], T. Prozorowski[1], A. Smorodzenko[1], S. Mueller[3], J. Schnorr[2], M. Taupitz[2] and F. Zipp[1]

[1]Institute of Neuroimmunolgy, [2]Dep. of Radiology and [3]BNIC, CCM, University Medicine Berlin, Germany
**equally contributing authors*

In the mouse model of multiple sclerosis (MS), experimental autoimmune encephalomyelitis (EAE), inflammation is commonly described as an ascending paralysis with initial spinal manifestation. Using high field strength MRImaging, we demonstrate cerebral blood brain barrier (BBB) leakage and cranial nerve involvement preceding or coinciding with first clinical signs of disease. These findings mimick MS, where cranial nerve inflammation, such as optic neuritis or trigeminal neuralgia, are common manifestations.

SJL/J-mice were imaged before and after disease onset. For the detection of BBB breakdown and the subsequent labelling of activated macrophages after particle internalization, we applied a novel very small citrate coated iron oxide particle (VSOP-C184; Ferropharm, Teltow, Germany). Leakage of the BBB was additionally assessed in Gadolinium-enhanced images. MRI findings were confirmed histologically and VSOP was detected by Prussian Blue staining. Macrophages and microglia were identified immunohistochemically.

Lesions could be precisely localised to the intracranial segment of the trigeminal nerve in 9 of 14 animals. Furthermore, we detected lesions in brain stem, midbrain, cerebellum, periventricular white matter, and the cortex. Although generally VSOP signal drop in T2*-weighted images colocalised with Gd-DTPA, VSOP appeared much more confined opposed to diffuse Gd-DTPA tissue enhancement. VSOP attributed hypointense spots shifted over time, indicating uptake by and subsequent migration of phagocytosing cells. In matching histological slices, VSOP was present diffusely in the perivascular tissue and internalised by macrophages.

VSOP-enhanced MRI indicated initial cerebral inflammation exceeding the spinal cord, with frequent trigeminal nerve involvement, accentuating BBB leakage and macrophage activity detection.

111 COMPETITION AND COOPERATION BETWEEN TENASCIN-R, LECTICANS AND CONTACTIN 1 REGULATE NEURITE GROWTH AND MORPHOLOGY

U. Zacharias[1], U. Rauch[2], F.G. Rathjen[1]

[1]Max-Delbrueck-Center for Molecular Medicine, Developmental Neurobiology, Berlin-Buch, Germany, [2]Department of Experimental Pathology, Institute for Clinical Sciences, Lunds University, Sweden

The extracellular matrix molecule tenascin-R and proteoglycans of the lectican family show an overlapping distribution in the developing brain, have been implicated in similar cellular processes and undergo a complex network of interactions. Previously, we have demonstrated that tenascin-R induces microprocesses along neurites and enlarged growth cones of tectal cells by interacting with the cell adhesion molecule contactin 1.

Here we describe competition and cooperation between tenascin-R, lecticans, and contactin 1 and their functional consequences for tectal cells. Aggrecan, brevican and neurocan inhibit the effects of tenascin-R on microprocess formation and growth

cone size. This blocking effect is due to competition of lecticans with binding of tenascin-R to its neuronal receptor contactin 1 as shown by a sandwich binding assay. Interaction of aggrecan with tenascin-R fibronectin type III domains 4-A is necessary for its inhibitory effect on both microprocess formation and tenascin-R binding to contactin 1. However, the chondroitin sulfate chains are not involved. Time lapse video microscopy showed that aggrecan has no acute effect on motility and morphology of microprocesses and growth cones but induces long-term neurite retraction after tenascin-R pretreatment. In contrast to the competition described above, tenascin-R cooperates with brevican and neurocan to induce tectal cell attachment and neurite outgrowth probably by forming a bridge between the lectican substrate and contactin 1 as the neuronal receptor. Our findings suggest that a complex network of protein-protein interactions within the brain extracellular matrix as shown here for tenascin-R and lecticans is important for the fine regulation of developmental processes like microprocess formation along the neurite and neurite outgrowth.

112 HIGH THROMBOPOIETIN CONCENTRATIONS IN THE CEREBROSPINAL FLUID OF NEONATES WITH SEPSIS AND INTRAVENTRICULAR HEMORRHAGE MAY CONTRIBUTE TO BRAIN DAMAGE

Juan Zhang[1], Anke Reinhold[1], Reinhard Gessner[2], Ursula Felderhoff-Mueser[1], Michael Obladen[1], Christof Dame[1,]

[1]Department of Neonatology, Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin; [2]Department of Clinical Chemistry, Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin

Thrombopoietin (Tpo) and its receptor (Tpo-R) are expressed in the developing and adult central nervous system (CNS). In mice, Tpo mRNA expression increases with postnatal development. Although Tpo shares significant homology with various neurotrophins, recent data indicate a pro-apoptotic function of Tpo in the CNS. In this study, Tpo concentrations were analyzed in the cerebrospinal fluid (CSF) of neonates. Human neuroblastoma-derived SH-SY5Y cells served as a model to elucidate the effects of inflammation and hypoxia on Tpo expression. Tpo was detectable in the CSF of 6/16 neonates with sepsis (including one patient with meningitis; median 140 pg/ml, range 2 to 613 pg/ml), 5/9 neonates with posthemorrhagic hydrocephalus (median 31 pg/ml, range 1.4 to 469 pg/ml), 3/4 neonates with posthemorrhagic hydrocephalus plus sepsis/meningitis (median 97 pg/ml, range 6 to 397 pg/ml), but not in controls. However, neither the presence of detectable Tpo nor its level in the CSF did significantly correlate with any clinical or laboratory parameter, including IL-6 concentrations in CSF. In SH-SY5Y cells Tpo and Tpo-R expression were detected by RT-PCR/real time PCR and Western Blot analysis. Under hypoxia (1% O_2), Tpo mRNA levels decreased significantly in a time-dependent manner to 23%, 47%, and 43% of control levels after 6, 12, and 24 hrs, respectively. In contrast to human hepatoma cells, which serve as a model of hepatic Tpo-production, IL-6 had no significant stimulatory effect on Tpo production in neuronal cells. Combined data provide evidence that in neuronal cells Tpo production is regulated by specific mechanisms. In conclusion, understanding of the regulation of Tpo in neuronal cells is important to judge on its relevance in brain development and function.

113 THE INVOLVEMENT OF THE NEURONAL CALCIUM SENSOR (NCS) PROTEIN VILIP-1 IN HIPPOCAMPAL PATHOPHYSIOLOGY IN SCHIZOPHRENIA: REGULATION OF EXPRESSION BY MGLURS IN HIPPOCAMPAL INTERNEURONS

Zhao, C.J. [a], Gierke, P. [a],Brackmann, M. [a], Bernstein, H.-G.[b], and Braunewell, K.-H. [,a]

[a] Signal Transduction Research Group, Neuroscience Research Center, Charité Berlin, Germany; [b] Department of Psychiatry, Otto-von-Guericke University Magdeburg, Germany

VILIP-1 is a member of the neuronal calcium sensor (NCS) protein family and has been implicated in many physiological as well as pathological processes in the brain. Recently, post mortem studies in the schizophrenic hippocampus have revealed a decreased expression of VILIP-1 in pyramidal neurons and an increased number of VILIP-1-positive interneurons. Similar results have been observed in the hippocampus of ketamine-treated rats, a glutamatergic hypofunction model for schizophrenia-like psychosis. Interestingly, the expression of VILIP-1 is also regulated in a form of hippocampal synaptic plasticity, long-term potentiation, and depends on glutamatergic transmission. These findings have raised the question of the regulation and the possible role of VILIP-1 in pathophysiological processes in the hippocampus probably leading to cognitive deficits. To address these questions we have examined the influence of glutamate on VILIP-1 expression in primary hippocampal cultures by immunocytochemistry which allowed to distinguish cell specific expression in pyramidal neurons and interneurons. Glutamate leads to an increase in the number of VILIP-1-positive interneurons. The use of DHPG, 4CPG and MPEP, specific mGluR group I agonist and antagonists, shows that mGluR1a regulates the glutamate-dependent increase in VILIP-1-expression in interneurons. Since mGluRs are known to regulate synaptic plasticity in the hippocampus the observed pathological changes in VILIP-1 expression in interneurons may partially explain

negative symptoms in schizophrenia including learning and memory deficits. Thus, we have investigated the effect of VILIP-1 expression on neuronal excitability using whole cell patch clamp recording.
Supported by grants of Deutsche Forschungsgemeinschaft to KHB.

114 NEURAL REPRESENTATION OF SURFACE WAVE PARAMETERS IN THE AQUATIC PREDATOR *XENOPUS LAEVIS*

U. Ziehm, F. Branoner, Z. Zhivkov, O. Behrend

Institute of Biology, Humboldt University Berlin

To decipher water movements, many aquatic vertebrates use mechano-sensory lateral lines. This study describes lateral line processing in the African clawed frog that utilizes surface waves for prey detection, recognition, and localization. The central organization of the lateral line shows similarities to the auditory system, indicating that information processing of both systems could be related: respective object representations, for instance, must be generated from patterns of particle motion across peripheral receivers. Thus, the lateral line offers insight into key features of neural computation beyond a specific sensory system.
To enable the experimental variation of single wave parameters, an algorithm was developed that minimized effects of source distance, frequency dependent propagation velocity, and amplitude dampening, based on reverse transfer functions and stepwise parameter adjustment. Responses to surface waves were recorded in 109 brainstem and midbrain units of *Xenopus*. The response pattern distribution differed significantly across the optic tectum and the torus semicircularis magnocellularis (chi-square test; $p<0.05$). Stimulus frequencies from 10–40 Hz were represented equally across lateral line nuclei, but best frequencies were systematically distributed along the rostrocaudal axis of the midbrain (chi-square test; $p<0.05$). 41% of 102 widely distributed units phase locked significantly to stimulus frequencies (Rayleigh test; $p<0.05$; vector strength >0.3). 41% of 39 tested units featured non-monotone rate-level functions. These neurons were registered mainly in the dorsal tectum and the magnocellular torus semicircularis (chi-square test; $p<0.05$). Across all tested nuclei, 16 of 17 discreetly distributed units showed a directional response to spatial stimulation. Midbrain subdivisions were apparent with respect to processing of stimulus timing, frequency and amplitude.

115 DEFINING A FUNCTION FOR THE ION CHANNEL TRPA1

[1]S. Zurborg,[1] B. Yurgionas,[1] O. Caspani,[1] P.A. Heppenstall.

[1]*Klinik für Anästhesiologie, CBF,*

the Transient Receptor Potential (TRP) family. It is expressed by a subset of nociceptive sensory neurons (*1*) and can be activated by several pungent, algesic compounds such as mustard oil and cinnamaldehyde (*2*). Despite the potential importance of TRPA1 in the pain pathway, its endogenous function remains to be elucidated. Data indicating that TRPA1 might act as a sensor for noxious cold (*1, 2)* or is a receptor-operated channel (*2*) are still controversial.
We have examined the cold sensitivity of TRPA1 in detail. Using calcium microfluorimetry we confirmed that HEK293 cells expressing TRPA1 respond to cold stimulation (15°C). However, we also measured a significant cold response in control untransfected HEK293 cells. Both of these responses had very similar activation thresholds (~17°C), whilst only TRPA1 containing cells were sensitive to the TRP channel blocker ruthenium red which reduced responses to control levels. This data suggests that the cold response in TRPA1 positive cells might be secondary to the rise in intracellular calcium seen in control HEK293 cells.
We tested this further using whole cell patch clamping. In experiments where we chelated intracellular calcium, we were not able to elicit a cold response. However, by raising intracellular calcium concentrations to 1μM, we observed robust activation of TRPA1. Our data indicates that TRPA1 is not directly activated by cold stimuli, but can be gated by increases in intracellular calcium concentration. This suggests that TRPA1 is likely to function as a receptor operated channel in nociceptive sensory neurons.
References: 1. Story GM *et al.*, *Cell* 112, 819-29 (Apr 21, 2003). 2. Jordt SE *et al.*, *Nature* 427, 260-5 (Feb 15, 2004).

SFB 507 "Role of non-neuronal cells in neurological disorders"

The Sonderforschungsbereich 507 is funded since 7/95 and investigates the role of non-neuronal cells in CNS disease. In particular, the role of astrocytes, microglia, and endothelial cells in neurological diseases such as stroke, multiple sclerosis, meningitis, and epilepsy is studied. Systems-physiological, molecular, and cellular strategies are utilized to understand the complex interaction of neurons and non-neuronal cells in models of neurological disorders. Special emphasis is put on clinical relevance, since it is the ultimate goal of this collaborative effort, which brings together clinical departments with basic research units, to develop new diagnostic and therapeutic tools.
The SFB 507 is coordinated by Ulrich Dirnagl (‚Sprecher', Charité Exp. Neurology), Uwe Heinemann (Charité Physiology), Frauke Zipp (Charité Neuroimmunology), Helmut Kettenmann (MDC), and Jens Dreier (Charité Neurology).

Projektbereich A
A1 ‚Cortical spreading ischemia', Dreier/Einhäupl
A5 Rekrutierung myeloider und lymphoider Zellen ins ZNS nach experimentellem Schlaganfall, Priller/Dirnagl
A9 Angiogenese und Vaskulogenese nach milder zerebraler Ischämie, Endres
Projektbereich B
B6 Zelluläre Schädigung der Blut-Hirn-Schranke - Ein Schlüsselmechanismus in der Schadenskaskade der bakteriellen Meningitis, Weber/Braun
B11 Die Rolle des Netzwerkes nicht-neuronaler Zellen bei axonalem Auswachsen, Nitsch/Müller-Röver
B14 Mechanismen der Immunzell-vermittelten Schädigung in der chronischen Entzündung des Zentralnervensystems, Zipp/Aktas
B16 Die Rolle der Mikroglia bei postläsionalen Veränderungen in Schichten anterograder axonaler Läsion, Bechmann
B18 Das Proteasom in Mikroglia und Astrozyten und seine Rolle bei Infektions- und Entzündungsprozessen im ZNS, Kloetzel/Dahlmann
Projektbereich C
C3 Funktionen von Gliazellen während epileptogener Prozesse, Heinemann/Kann
C7 In situ Untersuchungen zu physiologischen Mechanismen der Mikrogliaaktivierung unter pathophysiologischen Bedingungen, Schilling/Eder
C10 Kommunikation von Mikrogliazellen mit Astrozyten und Neuronen, Kettenmann
C12 Die Bedeutung von Bluthirnschrankenstörungen für Dysfunktionen des cerebralen Cortex, Friedman/Heinemann

Kontakt:
Prof. Dr. Ulrich Dirnagl
SFB 507
Charité
Neurologische Klinik
Schumannstr. 20/21
10098 Berlin
Tel.: +49 30 45056 0134
Fax: +49 30 45056 0942
EMail: ulrich.dirnagl@charite.de

SFB 618 "Theoretische Biologie: Robustheit, Modularität und evolutionäres Design lebender Systeme"

Zentrales Ziel des Sonderforschungsbereichs ist die Entwicklung von theoretischen Konzepten, mathematischen Modellen und Methoden der Datenanalyse, mit denen „Designprinzipien" lebender Systeme aufgedeckt und in ihrer funktionellen Bedeutung analysiert werden können. Hierzu untersuchen Theoretiker und Experimentatoren in aufeinander abgestimmten Kooperationsprojekten die Struktureigenschaften von zellulären Signalwegen, regulatorischen und neuronalen Netzwerken sowie organismischen Interaktionen. Projektübergreifend soll langfristig in einer vergleichenden Studie aufgezeigt werden, wie das Problem der Robustheit und Anpassungsfähigkeit in unterschiedlichen Systemen gelöst wird, welche Rolle die Modularität rückgekoppelter Systeme dabei spielt und welchen Einschränkungen die Evolution von Robustheit, Anpassungsfähigkeit und Modularität unterliegt. Die konkreten Projekte gelten verschiedenen Komponenten des Nerven-, Immun- und Reproduktionssystems, sowie der Regulation von Biorhythmen, Zelldifferenzierung und Genexpression. Ein Teil der Untersuchungen befasst sich gezielt mit der Genese pathologischer Zustände, an denen sich Grenzen der Robustheit lebender Systeme aufzeigen lassen.
Betrachtet werden in diesem Zusammenhang degenerative Erkrankungen des Nervensystems wie Chorea Huntington, Modulationen der Immunantwort durch parasitäre Nematoden und Eingriffe in das Reproduktionssystem von Wirten durch intrazelluläre Bakterien. In datenanalytischer Hinsicht gilt ein wesentliches Augenmerk des Sonderforschungsbereichs der Auswertung von Genexpressionsmustern und neuronalen Aktivitätszuständen. Insgesamt sollen neue Wege aufgezeigt werden, wie Biologie und Medizin mit Hilfe theoretischer Untersuchungen von der überwältigenden Datenflut profitieren können, und wie durch theoretische Konzepte und mathematische Modelle biologisches Wissen integriert werden kann.

Sprecher: Prof. Dr. Peter Hammerstein

Kontakt:
SFB 618: Theoretische Biologie
Institut für Biologie
Humboldt-Universität zu Berlin
Invalidenstr. 43
10115 Berlin
EMail: sfbtb@biologie.hu-berlin.de
http://www.biologie.hu-berlin.de/forschung/SFB_618/

SFB 665 "Entwicklungsstörungen im Nervensystem" („Developmental Disturbances in the Nervous System")

Seit Juli 2005 fördert die Deutsche Forschungsgemeinschaft (DFG) den Sonderforschungsbereich 665 »Developmental Disturbances in the Nervous System«, der von der Charité geleitet wird. 15 Forscherteams aus der Charité – Universitätsmedizin Berlin, der gemeinsamen Einrichtung der Freien Universität (FU), der Humboldt- Universität zu Berlin (HU), dem Max-Delbrück-Centrum für Molekulare Medizin (MDC) und dem Institut für Biologie der FU, forschen zusammen nach Wegen, Entwicklungsstörungen des Nervensystems aufzuklären.

Wie das Nervensystem während der Entwicklung ausgebildet wird, ist ausschlaggebend für seine spätere Funktion. Fortschritte in der Genetik und der Molekularbiologie in den letzten zwei Jahrzehnten haben es ermöglicht, Moleküle zu analysieren, welche die Entwicklung des zentralen Nervensystems steuern, und genetische Veränderungen zu identifizieren, die zu einer Störung dieses Prozesses führen. Wenn beispielsweise durch eine Mutationen kritische Zellfunktionen gestört sind, führt dies oft zu einer Kaskade weiterer Probleme, die schließlich zu einer Anzahl klinischer Syndrome führen können, wie z.B. Schwerhörigkeit, Epilepsie oder Sprachstörungen.

Wie neuronale Schaltungen gebildet und aufrechterhalten werden, ist jedoch bis jetzt nur teilweise aufgeklärt. Die Herausforderung für Grundlagenforscher und klinische Neurowissenschaftler ist deshalb, das Wissen über molekulare Mechanismen, welches durch Tiermodelle gewonnen wurde, in das Verständnis von Entwicklungsstörungen bei Patienten zu integrieren. Langfristiges Ziel des SFB 665 ist es deshalb, Kausalzusammenhänge zwischen Mutationen und neurologischen Phänotypen aufzuklären und dadurch eine Basis für zukünftige Verbesserungen therapeutischer Strategien zu schaffen. Der SFB 665 stellt sich diesen Herausforderungen, indem er Grundlagenforscher und Kliniker zusammenbringt, um die Funktionen des Nervensystems auf zellulären, biochemischen oder physiologischen Ebenen zu untersuchen und die genetischen Ursachen von Entwicklungsstörungen bei Patienten zu identifizieren.

Kontakt:
Prof. Dr. Robert Nitsch
SFB 665
Charité - Universitätsmedizin Berlin
Centrum für Anatomie
Institut für Zell- und Neurobiologie
Schumannstr. 20/21
10098 Berlin
Tel.: +49 30 450 528 072
Fax : +49 30 450 528 902
Email: robert.nitsch@charite.de, sfb665@charite.de
http://www.charite.de/sfb665

GRK 1123 "Zelluläre Mechanismen von Lernen und Gedächtniskonsolidierung in der hippokampalen Formation"

Das Graduiertenkolleg bietet die Möglichkeit, zelluläre Mechanismen von Lernen und Speicherung von Informationen im Gedächtnis sowie der Gedächtniskonsolidierung zu untersuchen. Ein Verständnis dieser Vorgänge ist von herausragender bio-medizinischer Bedeutung, da sie zum einen die Fähigkeit eines Organismus bestimmen, sich unabhängig von genetisch determinierten Verhaltensweisen an neue Umweltbedingungen anzupassen: das explizite Gedächtnis bestimmt entscheidend das menschliche Verhalten und ist Vorrausetzung für die eigene Individualität. Zum anderen sind die zugrunde liegenden Mechanismen störanfällig und damit in verschiedene neurologische und psychiatrische Krankheiten involviert. Hierzu zählen z. B. die Temporallappenepilepsie und die Alzheimersche Erkrankung. Zu den am intensivsten untersuchten zellulären Modellen für Lernen und Gedächtnis zählen die Langzeitpotenzierung (LTP) und Langzeitdepression (LTD). Allerdings sind noch viele der beteiligten prä- und postsynaptischen Mechanismen weitgehend unverstanden. Um langanhaltend Information zu speichern und Gedächtnisinhalte zu konsolidieren, bedarf es der Geninduktion und der Translation spezifischer Proteine, die die zugrunde liegenden Veränderungen in neuronalen Netzwerken ermöglichen. Auf zellulärer und neuronaler Netzwerkebene könnten an der Gedächtniskonsolidierung die Ausbildung von sharp wave ripple Komplexen, die Formierung von Frequenzgedächtnis und eine niederfrequent induzierte heterosynaptische LTP beteiligt sein. Zusätzlich könnten gespeicherte Informationen während des Traumschlafes wieder aktiviert werden, wobei die neuronale Aktivität von Theta- und Gammaoszillationen überlagert ist. Hierdurch können Veränderungen synaptischer Kopplung weiter verstärkt werden und schließlich aus dem Hippokampus in andere Hirnareale übertragen werden. Jeder der 11 am Graduiertenkolleg beteiligten Tutoren wird zu diesen Problemen spezifische Expertise beitragen. Elektrophysiologische, zellbiologische, genetische und verhaltensphysiologische Methoden sowie Modellierung von Netzwerkeigenschaften bieten den Studenten des Graduiertenkollegs die Möglichkeit, zu diesem aufregenden Gebiet der Neurowissenschaften beizutragen mit hervorragenden Chancen, eine exzellente Ausbildung in modernen neurobiologischen Methoden zu erhalten.

Sprecher: Prof. Dr. Dietmar Kuhl

Kontakt:
Barbara Neuhoff M.A.
Koordinatorin GRK 1123
Institut für Neurophysiologie
Tucholskystr. 2
10117 Berlin
Tel.: +49 30 450-528112
Fax: +49 30 450-528962
EMail: barbara.neuhoff@charite.de
www.charite.de/ch/physio/neuro/grk1123

GRK 429 "Doctoral Program on Neuropsychiatry and Psychology of Aging"

Central Themes of the Program:
It is generally agreed that, in order to understand the many aspects of old age and aging, it is important to strive for a transdisciplinary perspective and systematic integration. To this end, two main goals of the doctoral program on the neuropsychiatry and psychology of aging are:

- To integrate neuropsychiatric and psychological questions in research on aging
- To focus on issues of healthy and pathological aging.

In addition, the program seeks to integrate gerontological research and themes with studies and theoretical frameworks from health psychology.

Several topics serve as a forum for these integrative efforts. These include: brain aging and plasticity, pathological versus normal aging, the gain-loss dynamics of aging, the potential and limits of old age, cognition and sleep in elderly persons, and the nature of resilience in old age.

Speaker: Prof. Dr. Isabella Heuser

Contact:
Hu-Ping Chen
Department of Psychiatry
Charité
Campus Benjamin Franklin
Eschenallee 3
14050 Berlin
Tel: +49 30 84458701
EMail: hu-ping.chen@charite.de
www.charite.de/age

Neuropsychiatry and Psychology of Aging

GRK 1258 „Der Einfluss von Entzündungen auf die Funktion des Nervensystems“ („The impact of inflammation on nervous system function“)

There is increasing evidence that immunological processes are involved not only in the classical inflammatory disorders of the nervous system but also in primarily non-inflammatory injuries, such as trauma and ischemia, or even in functions of the nervous system, such as pain transmission. In all of these conditions or disorders, immune cells interact with cells of the nervous system. Although the initiating events differ considerably, we hypothesize common pathways in the crosstalk between immune and nervous system. The faculty of this graduate program studies this crosstalk by combining modern methods of molecular and cellular biology with imaging techniques (two photon microscopy, near-infrared fluorescence, and magnetic resonance imaging). We employ in vivo and in vitro approaches including animal models of neuroinflammation, ischemia, and arthritis, and in parallel we offer students experience in outpatient clinics and ward-rounds. Our aim is to elucidate the influence of both proinflammatory and regulatory immune cells, via contact or soluble mediators, on brain cells, namely astrocytes, microglial cells and neurons. We will analyse the immune-triggered responses of brain cells and study their impact on function, pathologic processes, damage cascades, and regeneration in nervous tissue. Studying the underlying mechanisms of these processes will be a challenge for motivated young students at the same time as providing them with an excellent opportunity to learn different approaches. The graduate program is integrated into the Humboldt University’s International Masters - MD/PhD Program Medical Neurosciences.

Speaker: Prof. Dr. Helmut Kettenmann, Prof. Dr. Frauke Zipp

Contact:
Stefanie Korthals
Max Delbrück Center for Molecular Medicine
Office Research Training Group ‚Inflammation’
Robert-Rössle-Str. 10
13122 Berlin
Tel.: +49 30 9406 3127
Fax: +49 30 9406 3819
MMail: korthals@mdc-berlin.de
http://neuroinflammation.glia.mdc-berlin.de/

Berlin NeuroImaging Center (BNIC)

Das Berlin NeuroImaging Center ist ein Berlin-weites Verbundprojekt, das die FU und die PTB einschließt und an der Charité koordiniert wird. Die übergeordneten Themen des Berlin Neuroimaging Center ergeben sich aus den langjährigen wissenschaftlichen Schwerpunkten der beteiligten neurowissenschaftlichen Institutionen in Berlin. Es sind dies die Erforschung zerebrovaskulärer Erkrankungen, insbesondere des Schlaganfalls und damit eng verknüpft das Forschungsgebiet der neurovaskulären Kopplung. Zerebrovaskuläre Erkrankungen stellen eine große medizinische Herausforderung dar. Zwar bedeuten neuere Verbesserungen im Bereich bildgebender Verfahren einen wichtigen Durchbruch für ihr besseres Management, allerdings besteht weiterhin ein unzureichendes Verständnis der physiologischen und pathophysiologischen Mechanismen beim (individuellen) Patienten mit Schlaganfall. Darüber hinaus können die zur Zeit eingesetzten bildgebenden Techniken nicht direkt am Patientenbett angewendet werden, so dass ihre Bedeutung hinsichtlich akuter Therapiemöglichkeiten in der Klinik eingeschränkt ist. Um diese methodischen Limitierungen zu überwinden, beabsichtigen wir mit dem hier vorgeschlagenen Zentrum Erkenntnisse zusammenzuführen, die in einem multimodalen Ansatz mit unterschiedlichen bildgebenden Verfahren gewonnen wurden. Damit sollen grundlegende physiologische und pathophysiologische Zusammenhänge aufgeklärt und neue Technologien zur Anwendung am Patientenbett entwickelt werden.

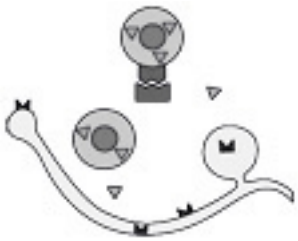
Sprecher: Prof. Arno Villringer

Kontakt:
Berlin NeuroImaging Center
Klinik und Poliklinik für Neurologie
Charité - Universitätsmedizin Berlin
Campus Charité Mitte
Charitéplatz 1
10117 Berlin
Tel.: +49 30 450 560142
Fax: +49 30 450 560952
EMail: julia.schlueter@charite.de
http://www.berlin-neuroimaging-center.de/

Klinische Forschergruppe 100 "Molekulare Mechanismen der Opioidanalgesie bei Entzündungsschmerz"

Beteiligte Fachrichtungen: Anaesthesiologie, Pharmakologie, Biochemie, Molekularbiologie, Rheumatologie, Immunologie, Anatomie.
Unser Forschungsprogramm beschäftigt sich mit der Kernfrage nach Mechanismen der Schmerzkontrolle durch Opioidwirkungen außerhalb des zentralen Nervensystems (ZNS), insbesondere bei Entzündungsschmerz. Opioidanalgetika sind in der pharmakologischen Behandlung akuter (z.B. postoperativer) und chronischer (z.B. Tumor-assoziierter) Schmerzen unübertroffen. Schwerwiegende unerwünschte Wirkungen wie Atemdepression, Sedierung, Toleranzentwicklung und Abhängigkeit limitieren jedoch ihren therapeutischen Einsatz. Experimentelle und klinische Untersuchungen unserer und anderer Forschergruppen zeigen potente antinozizeptive Wirkungen durch eine Aktivierung von Opioidrezeptoren außerhalb des ZNS. Opioidpeptide als endogene Liganden von Opioidrezeptoren werden in ortsständigen Immunzellen in entzündetem subkutanem Gewebe nachgewiesen. Verschiedene Stimuli wie z.B. Stress oder Corticotropin Releasing Factor können zur Freisetzung dieser Opioide und nachfolgender Analgesie führen. In achtTeilprojekten wird folgendes genauer untersucht: Im Teilprojekt 1 werden die Einwanderung von Opioid-produzierenden Immunzellen an den Ort einer Nervenläsion und der Einfluß sich daraus ergebender Wechselwirkungen zwischen Immun- und Nervensystem auf das Ausmaß neuropathischer Schmerzen aufgeklärt. Im Teilprojekt 2 werden potentielle Entzündungsmediatoren, wie z.B. Chemokine, formyl methionin leucin phenylalanin (fMLP) und Substanz P, auf ihre Rolle bezüglich der Rekrutierung Opioid-enthaltender Immunzellen und der Freisetzung endogener Opioidpeptide untersucht. Im Teilprojekt 3/4 werden mit Hilfe von genetisch modifizierten Mäusen die zelluläre Expression und Prozessierung endogener Opioidpeptide in Immunzellen untersucht. Im Teilprojekt 5 werden der akute und chronische Einfluß von Opioiden auf den TRPV1-Ionenkanal untersucht, dessen Modulation Auswirkungen auf die Transduktion und Fortleitung schmerzhafter Reize hat. Im Teilprojekt 6 geht es um die Bedeutung von TRPM8- und ANKTM1- Ionenkanälen und deren intrazellulären Signalwegen im Verlauf von neuropathischem Schmerz. Im Teilprojekt 7 wird die klinische Relevanz der lokalen Gabe von Opioiden (Morphin) und der Mobilisierung lokaler, körpereigener Opioidpeptide in einem entzündeten, schmerzhaften Kniegelenk von Arthritispatienten untersucht. Im Teilprojekt 8 werden potentielle Mediatoren des Entzündungsschmerzes identifiziert, die zu einer vermehrten Expression, G-Protein Kopplung und Funktion von Opioidrezeptoren sensorischer Neurone beitragen.

Kontakt:
Prof. Dr. Christoph Stein
Klinik für Anaesthesiologie und
Operative Intensivmedizin
Freie Universität Berlin
Charité - Campus Benjamin Franklin
Hindenburgdamm 30
D-12200 Berlin
Tel.: +49 30 84452731
Fax: +4930 84454469
EMail: christoph.stein@charite.de
www.medizin.fu-berlin.de/anae/index.phtml



International Graduate Program Medical Neurosciences MSc and PhD program in neuroscience with focus on translation from bench to bedside

Charité - Universitätsmedizin Berlin offers an interdisciplinary, international graduate program, which leads to the degrees of M.Sc., Ph.D. or M.D./Ph.D. in Medical Neurosciences. The program addresses both students of medicine and of life sciences (biology, biophysics, chemistry, psychology, etc.). Students are both German and international, the working language is English.

The main objective of the program is to bring together clinical and basic neurosciences in a comprehensive educational program by providing a structured education in basic neurosciences to medical students and by training students of the life sciences in medical topics and approaches concerning the central and peripheral nervous system.

The International Graduate Program in Medical Neurosciences is one of the International Postgraduate Programs (IPP) funded by the DAAD. The aim of this initiative is to reform doctoral education in Germany by introducing the graduate school system. These schools place a high emphasis on scientific excellency, provide a multidisciplinary research and learning environment and offer extensive supervision and tutoring allowing students to complete their projects within 3 - 4 years.

Sprecher: Prof. Dr. Ulrich Dirnagl

Kontakt:
Lutz Steiner
Klinik für Neurologie
Charité – Universitätsmedizin Berlin
Schumannstr. 20/21
10117 Berlin
www.medical-neurosciences.de

Berlin, Charité
International Graduate Program
Medical Neurosciences

Bernstein Center for Computational Neuroscience Berlin

Brain research has been flourishing for the last decades. Experimental breakthroughs - from novel genetic techniques to modern imaging methods - have advanced our understanding of cognitive processes in terms of the underlying neural dynamics and interactions. Yet, a thorough analysis of higher brain function continues to be an outstanding scientific challenge. This task requires focussed interdisciplinary cooperation between experimental and clinical neuroscientists, physicists, mathematicians and computer scientists.

Major insights are expected from the new discipline of Computational Neuroscience. It combines experiments with data analysis and computer simulation on the basis of well-defined theoretical concepts, and makes a scientific language available that can be used across disciplines and levels for neurobiology, cognitive science, systems biology and information technology. Computational Neuroscience may thus help to solve long-standing research questions, contribute to better prevention and treatment strategies for neural disorders, lead to unified concepts about biological processes, advance high-performing computers and, last but not least, provide new insight for designing efficient strategies for teaching and learning.

Integrating initiatives at the Charité, Freie Universität Berlin (FU), Humboldt-Universität zu Berlin (HU), Technische Universität Berlin (TU), Fraunhofer FIRST, the Max-Delbrueck-Center and the Wissenschaftskolleg zu Berlin, the Bernstein Center for Computational Neuroscience Berlin has been established with support from the Federal Ministry for Education and Research to reach these goals. The Bernstein Center Berlin is part of the German Network for Computational Neuroscience (see www.bernstein-zentren.de) which contains three further Centers in Freiburg, Goettingen and Munich.

Coordinators: Klaus Obermayer (TU)
Gabriel Curio (FU)
and Andreas Herz (HU, Lead Coordinator)

Contact:
Margret Franke
Bernstein Center for
Computational Neuroscience
Humboldt-University Berlin
Invalidenstr. 42
10115 Berlin
Germany
Tel: +49 30 2093-9110
Fax: +4930 2093-8801
www.bccn-berlin.de

BMBF Joint German-Israeli Research Program - 01GA0507 „Role of chemokines in neuroinflammation"

Im Mittelpunkt unseres Interesses steht die Erforschung von Chemokinen im Rahmen entzündlicher Schädigungen im Zentralen Nervensystem (ZNS) und die Anwendung dieser Erkenntnisse auf der Suche nach neuen Therapien für die Multiple Sklerose (MS). Wir beabsichtigen die Rolle von chemotaktischen Reizen zu untersuchen, die von ortsständigen ZNS-Zellen benutzt werden um Entzündungszellen ins ZNS zu leiten.
Bisherige gemeinsame Forschungsvorhaben betrachteten vor allem den entstehenden neuronalen Schaden, was in naher Zukunft durch mechanistische Studien mit Hilfe von Durchflussanalysen unter physiologischem Scherkraftstress und durch Multiphoton-Mikroskopie basierte Beobachtung von Zell-Zell-Interaktionen ex vivo und in vivo ergänzt werden wird. Wir erhoffen uns dadurch die Klärung der Rolle bestimmter Chemokine in der Pathophysiologie entzündlicher ZNS-Erkrankungen. Ergänzend planen wir eine klinische Studie, die die Wirksamkeit eines CCR-1 Antagonisten bei Patienten mit schubförmig verlaufender MS zum Gegenstand hat und somit die direkte Beeinflussung eines Chemokinweges in der menschlichen Erkrankung darstellt.
Wir sehen die Chemokin-abhängige Invasion und Aktivierung von ortsständigen und peripheren Immunzellen als entscheidende Ereignisse für MS-typische entzündliche Demyelinisierung und anschließende Glianarbenbildung an und halten die Beeinflussung der Zellmigration für eine vielversprechende Behandlungsoption der MS zur Minimierung des entstehenden neuronalen Schadens.

Koordinator: Prof. Dr. Frauke Zipp

Kontakt:
Institut für Neuroimmunologie
Neurowissenschaftliches Forschungszentrum
Charité – Universitätsmedizin Berlin
Schumannstraße 20/21
10117 Berlin
Tel.: +4930 450 539 028
Fax: +4930 450 539 906
EMail: frauke.zipp@charite.de
http://www.charite.de/nimmu/index.php

Centrum für Schlaganfall-Forschung Berlin (CSB)

The CSB is an initiative of the Charité – Universitätsmedizin Berlin and the Max-Delbrück-Centrum Berlin-Buch. Its opening symposium takes place in June 2006.
Stroke is the third leading cause of death in Germany. Moreover, it is the leading cause of palsy acquired in adulthood. But national and regional research centers for stroke research center are still lacking. CSB would like to use Berlin's stroke research resources and expertise to fill this gap.
The MDC is one of the leading centers in cardiovascular physiology and genetics, while clinical and basic stroke research as well as cerebrovascular physiology are emphasized at the Charité. The center's goal is to focus basic research activities as well as clinical research activities and to coordinate them. The translational approach shall give a fresh impetus: From bench to bedside and from bedside to bench. CSB's scientists are engaged in stroke diagnosis, prevention of the disease, the mechanisms of acute damage as well as its therapy, and the regeneration of brain function after stroke. Berlin's stroke research has an eminent position with respect to basic research, clinical care of stroke patients, and the development of innovative imaging techniques for the examination of brain function.
The CSB aims to bundle, focus, and support the activities of already existing institutions and structures in Berlin, and to supplement the network by strategic acquisition of collaborations, appointments and technology. The research groups "Vascular Biology" (located at the MDC) and "Translational Stroke Research" (located at the Charité, Campus Mitte) are key groups of the CSB initiative. The two groups are supported by means of the Helmholtz Gemeinschaft (HGF) as well as the coordinating office. The CSB is still in its founding phase. In the future we plan to expand the CSB's scope with institutions engaged in rehabilitation medicine, preventive medicine, and health care management research.

Leitung:
K.M. Einhäupl, U. Dirnagl, A. Villringer,
N. Hübner, H. Kettenmann

Kontakt:
Koordinierungssekretariat CSB
Dr. rer. nat. Corinna Pelz
Charité - Universitätsmedizin Berlin
Campus Mitte
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 450 560 096
Fax: +4930 450 560 942
EMail: corinna.pelz@charite.de
www.schlaganfallcentrum.de

CSB
Center for Stroke Research Berlin

Competence Network Dementia

Objectives
The Competence Network Dementia is a nationwide association of 14 leading university centers in the field of dementia research, and is funded by the German Federal Ministry of Education and Research (BMBF). The Network was founded in August 2002 and became a registered association in June 2003.
Focus of activities
About one million people in Germany today are suffering from some form of dementia. Given the increasing life expectancy, we can expect this number to double by the year 2040. The Competence Network Dementia sets out to improve the medical care of dementia patients by concentrating research activities and accelerating the transfer of current research findings into practical applications. The Network's goal is to improve the clinical instruments used for early and differential diagnosis of dementia and to develop more effective methods of treatment.
Uniform standards of diagnosis and therapy across the country
The Competence Network Dementia started out by developing standardized procedures for central aspects of dementia diagnosis. One of the key procedures to be standardized was the neuropsychological diagnosis of cognitive disorders. In the neurochemical diagnosis of dementia, standardized procedures were developed for obtaining, preparing and analyzing blood and cerebrospinal fluid samples used to identify dementia markers (such as amyloid-beta-peptides, phosphorylated tau protein). In the same way, standardized test records for MRI spectroscopic and volumetric examinations were devised and found to be effective. The central DNA bank currently holds over 4000 samples and is still being expanded. It will be used in identifying genetic risk factors that lead to dementia.
Optimization of treatment
A nationwide clinical infrastructure was set up to carry out double-blind pharmacological studies of dementia treatment. The most recent studies are investigating whether a combination therapy with two approved anti-dementia drugs is superior to monotherapy in treating Alzheimer's disease.

Speaker:
Prof. Dr. Wolfgang Maier

Contact:
Oliver Peters
Department of Psychiatry
Charité
Campus Benjamin Franklin
Eschenallee 3
14050 Berlin
Tel: +49 30 84458312,
EMail: oliver.peters@charite.de
www.charite.de

German Research Network on Schizophrenia

The German Research Network on Schizophrenia is funded by the German Federal Ministry of Education and Research (BMBF): it investigates the acute and long-term treatment of first-episode schizophrenic patients in a double-blind pharmacological treatment study (risperidone vs. haloperidol) over a period of two years, including pharmacokinetic, neurobiological and genetic parameters and additionally psychoeducation and psychotherapy (www.kompetenznetz-schizophrenie.de).

Speaker: Prof. Dr. Wolfgang Gaebel

Contact:
Maria Jockers-Scheruebl
Department of Psychiatry
Charité
Campus Benjamin Franklin
Eschenallee 3,
14050 Berlin
Tel: +49 30 84458707
EMail: maria.jockers-scheruebl@charite.de
www.charite.de

Neuroscience Research Center
Neurowissenschaftliches Forschungszentrum (NWFZ)

Neuroscience research groups at the Charité are involved in various collaborative research projects such as Collaborative Research Grants (SFBs), the Bernstein Center for Computational Neuroscience Berlin, Graduate Schools and others. Several members of these groups have joined in a neuroscience alliance, which operates the Neuroscience Research Center located at Charité Campus Mitte.
The Neuroscience Research Center supports in particular junior researchers in establishing their own independent research groups by providing labspace, financial support and a collaborative, interdisciplinary environment. Independent grant support is, however, an essential requirement for the establishment of a research group at the Center.
The Center is supervised by an Advisory Board of internationally renowned scientists, which advises the faculty in the search for suitable research groups.
Further informations can be found at: www.charite.de/nwfz.

Director: Prof. Dr. Dietmar Schmitz

Office Manager:
Iris Gerstenkorn
Neuroscience Research Center
Schumannstr. 20/21
10117 Berlin
Tel.: +4930 450 539002
EMail: iris.gerstenkorn@charite.de
www.charite.de/nwfz

Cortex – Cooperation in Research and Training for European Excellence in the Neurosciences

Under the acronym of cortex graduate schools in Berlin, Bochum, Helsinki, London, Oslo, Prague, Stockholm, Zurich offer a joint PhD training scheme funded by the EU under the Marie Curie Mobility Action Early Stage Training (EST).
Brain cells die following trauma, stroke and in chronic neurodegenerative disease. The mature brain cannot replace lost nerve cells in, and of, itself. An important goal of treatment and prevention is therefore to minimize nerve cell death. However, recently and quite unexpectedly, experimental strategies have emerged to foster regeneration in the CNS. In addition to understanding the complex mechanisms of brain damage, we must understand how the nervous system develops and continues to change throughout life. This information has profound implications for the treatment of nervous system diseases. Harnessing the capacity of the nervous system to adapt by reactivating developmental mechanisms allows for great hopes in regards to restoring function in the injured or diseased brain. Cortex scientists and students will study the basic mechanisms of damage of common brain disorders as well as the development of the CNS to harness the ability of the CNS to adapt when challenged.
The cortex neuroscience schools each cover a broad range of neuroscience expertise in the fields of brain damage, regeneration, and development of the CNS. Bridging from the molecular to the behavioral and clinical level is a common theme of the Cortex partners. However, each cortex member school has one or several unique areas of excellence. Bringing together these complementary fields of excellence within cortex offers young doctoral students the entire panoply of neuroscientific possibilities and technologies which are available in modern neuroscience, leading to an optimally structured PhD of the highest quality.
The Berlin program has a major focus on translational aspects of neuroscience: ‚bedside to bench', as well as ‚bench to bedside'. Acute neurodegeneration (stroke), neuroinflammation (MS) and neuroimaging, are key topics on the research agenda.

Speaker: Prof. Dr. Ulrich Dirnagl

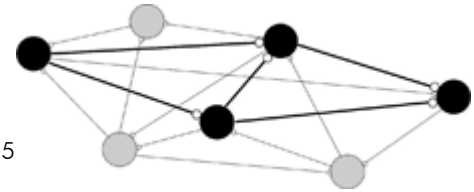
Contact:
Lutz Steiner
Klinik für Neurologie
Charité – Universitätsmedizin Berlin
Schumannstr. 20/21
10117 Berlin
www.cortex-training.net

cortex
Cooperation in Research and Training for European Excellence in the Neurosciences

Emmy Noether Programme (Ke 788/1-3)

The research group "Theoretical Neuroscience" is interested in the neural basis of learning and memory. Research involves the mathematical modeling and analysis of synapses, neurons and networks of neurons. Analysis and computer simulations are used to study the dynamics of synaptic short-term and long-term plasticity, the dynamics of single neurons, the interaction of neurons in recurrently coupled networks that store and process information. Of particular interest are mechanisms that control the development and functional stability of neural circuits of spiking neurons. Our main goal is to understand how neuronal networks can remain susceptible to learning, and, at the same time, be able to maintain a robust balance against instabilities. Understanding the underlying neural mechanisms that prevent neuronal tissue from developing pathological activity patterns may help to uncover origins of functional brain illnesses, and will lead to practical implications for designing remedial therapies. Research projects are always in close collaboration with experimental groups. Experimental models are the hippocampus and the early auditory system.
The junior research group "Theoretical Neuroscience" was established in January 2003 and is funded by the Deutsche Forschungsgemeinschaft (DFG, Emmy Noether).

Contact:
Richard Kempter
Theoretical Neuroscience Lab
Institute for Theoretical Biology (ITB)
Department of Biology
Humboldt-Universität zu Berlin
Invalidenstr. 43
10115 Berlin
Tel.: +49 30 20938925 Office: 2315
Fax: +49 30 20938801
EMail: r.kempter@biologie.hu-berlin.de
http://itb.biologie.hu-berlin.de/~kempter/



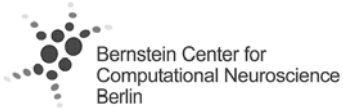
Master Program
Computational Neuroscience

The Berlin University of Technology and the Humboldt University of Berlin, Germany, solicit applications for a new international Master Program in Computational Neuroscience within the new Bernstein Center for Computational Neuroscience Berlin (www.bccn-berlin.de). The program is full-time for four semesters, and will start in October 2006. The program is taught by the faculty of the Bernstein Center, who represent departments ranging from biology and medicine to physics and computer science from all three universities in Berlin. Emphasis will be put on a broad, interdisciplinary education with strong interactions between experiment and theory. Students with a strong mathematical background,and a completed B.Sc. or equivalent degree at the time the courses start are welcome to apply. There are no tuition fees. Course language is English.

Application deadline: June 16th, 2006 for the winter term. For detailed information see www.computational-neuroscience-berlin.de or send an email to oby@cs.tu-berlin.de or l.wiskott@biologie.hu-berlin.de. Admission for the winter term 2006/2007 is dependent on the final approval of the program by the Senatsverwaltung für Wissenschaft, Forschung und Kultur.

Coordinators:

Klaus Obermayer
Technische Universität Berlin
Fakultät IV - Elektrotechnik und Informatik
Sekretariat FR 2-1
Franklinstr. 28/29
10587 Berlin
Tel.: +4930 31473442
Fax: +4930 31473121
EMail: sekr@ni.cs.tu-berlin.de
http://ni.cs.tu-berlin.de/



Laurenz Wiskott
Humboldt Universität zu Berlin
Institut für Theoretische Biologie
Invalidenstr. 43
D-10115 Berlin
Tel.: +4930 20938408
Fax: +4930 20938801
EMail: l.wiskott@biologie.hu-berlin.de
www.computational-neuroscience-berlin.de

Interdisciplinary Stroke Research (Lichtenberg-Professur der VolkswagenStiftung)

Stroke is the third leading cause of death and primary reason for long-term disability in western societies. Current treatment strategies, however, are disappointing and do not significantly reduce stroke morbidity and mortality. Within the scope of the professorship two scientific concepts will be targeted. The first deals with vascular mechanisms and interventions by analyzing whether increased nitric oxide-production is a feasible preventive strategy for stroke treatment in man, what the ideal therapeutic interventions are, whether endothelial progenitor cells contribute to stroke protection, and whether this can be visualized by imaging techniques. The second concept explores the finding that differentiated post-mitotic neurons can divide and give rise to two differential mature neurons when certain genes are expressed which may represent a novel approach for regenerative stroke treatment.

Contact:
Prof. Dr. Matthias Endres
Charité - Universitätsmedizin Berlin
Campus-Mitte
Klinik und Poliklinik für Neurologie
Schumannstraße 20/21
10117 Berlin
Tel.: +49 30 450 560 257
Fax: +49 30 450 560 932
http://www.charite.de/ch/neuro/expneuro/researchteams/team_endres.htm

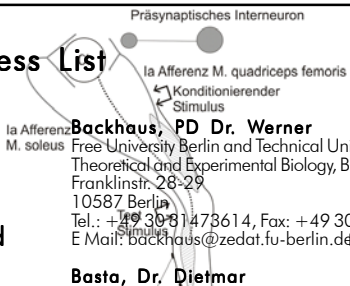
Keywords

(The numbers refer to page number)

Author Index

(The numbers refer to page number)

Address List



Aertsen, Prof. Dr. Ad
Albert-Ludwigs-Universität
Institut für Biologie III
Schänzlestr. 1
79104 Freiburg i. Br.
Tel.: +49 761 2032718, Fax: +49 761 2032745
E Mail: aertsen@biologie.uni-freiburg.de

Aktas, Dr. Orhan
Charité - Universitätsmedizin Berlin
Institute for Neuroimmunology
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 45053902, Fax: +49 30 45053990
E Mail: orhan.aktas@charite.de

Alasvand Zarasvand, Masoud
Medical Sciences University of Kurdestan
Physiology Department
Pasdaran - Sanandaj
Iran
Tel.: +989181719758, Fax: +988716660051
E Mail: alasvand@muk.ac.ir

Alexander, Christiane
Max Delbrück Zentrum für Molekulare Medicin (MDC)
Neurodegeneration
Robert-Rössle-Str. 10
13092 Berlin
Tel.: +49 30 94063830
E Mail: c.alexander@mdc-berlin.de

Altarche Xifro, Wassim
Charité - Hochschulmedizin Berlin
Signal Transduction Research Group, Neuroscience Research Center
Tucholskystr. 2
10117 Berlin
E Mail: wax5@hotmail.com

Appleby, Dr. Peter
Humboldt University of Berlin
ITB
Invalidenstraße 43
10115 Berlin
E Mail: p.appleby@biologie.hu-berlin.de

Armèlin, Anna
Markgrafenstr. 40
10117 Berlin
E Mail: a@logp.de

Aspeslagh, Sandrine
FMP
Robert Rössle Strasse 10
13125 Berlin Buch
Tel.: +49 30 94793300
E Mail: sandrine.aspeslagh@ugent.be

Baars, Dr. Jan
Charité Campus Mitte
Klinik für Anästhesiologie und Intensivmedizin
Schumannstr. 20-21
10117 Berlin
Tel.: +49 30 450531227, Fax: +49 30 4505319
E Mail: jan.baars@charite.de

Backhaus, PD Dr. Werner
Free University Berlin and Technical University Berlin
Theoretical and Experimental Biology, Bioinformatics
Franklinstr. 28-29
10587 Berlin
Tel.: +49 30 31473614, Fax: +49 30 31473614
E Mail: backhaus@zedat.fu-berlin.de

Basta, Dr. Dietmar
Unfallkrankenhaus Berlin
Otolaryngology
Warener Str. 7
12683 Berlin
Tel.: +49 30 56813874, Fax: +49 30 56912903
E Mail: dietmar.basta@ukb.de

Behrens, Dr. Christoph J.
Center for Physiology
Neurophysiology
Tucholskystrasse 2
10117 Berlin
Tel.: +49 30 45052814, Fax: +49 30 45052826
E Mail: christoph.behrens@charite.de

Benda, Dr. Jan
Humboldt University
ITB
Invalidenstr. 43
10115 Berlin
E Mail: j.benda@biologie.hu-berlin.de

Bert, Dr. Bettina
Freie Universität Berlin
Institute of Pharmacology and Toxicology, School of Veterinary Medicine
Koserstraße 20
14195 Berlin
Tel.: +49 30 83853478
E Mail: bert.bettina@vetmed.fu-berlin.de

Birchmeier, Prof. Carmen
Max-Delbrück-Center for Molecular Medicine
Mouse Genetics
Robert-Rössle-Str. 10
13125 Berlin
E Mail: cbirch@mdc-berlin.de

Blasig, PD Dr. Ingolf
Robert-Rössle-Str. 10
13125 Berlin-Buch
E Mail: iblasig@fmp-berlin.de

Boeck, Katharina
Charité, University Medicine Berlin
Signaltransduction Research Rroup, Neurosc. Res. Ctr
Tucholskystr. 2
10117 Berlin
Tel.: +49 30 450528358
E Mail: katharina.boeck@charite.de

Böddrich, Dr. Annett
MDC
Neuroproteomics / Wanker
Robert-Rössle-Str. 10
13125 Berlin
E Mail: a.boeddrich@mdc-berlin.de

Boehlen, Dipl.-Biol. Anne
Johannes-Müller-Institut
Institut für Neurophysiologie
Tucholskystrasse 1
10117 Berlin
E Mail: Anne.Boehlen@charite.de

Bounab, Yacine
Max Delbruck Center for Molecular Medicine (MDC)
Berlin-Buch
Neuroproteomics
Robert-Roessle-Strasse 10
13125 Berlin
Tel.: +49 30 94062636, Fax: +49 30 94062552
E Mail: bounab@mdc-berlin.de

Brackmann, Dr. Marian
Charité, University Medicine Berlin
Signal Transduction Res. Group; Neurosc. Res. Ctr.
Tucholskystr.2
10117 Berlin
Tel.: +49 30 450528358, Fax: +49 30 450528927
E Mail: marian.brackmann@charite.de

Bräuer, Dr. Anja U.
Centrum for Anatomy, Charité - Universitätsmedizin
Cell- and Neurobiology
Philippstr. 12
10115 Berlin
Tel.: +49 30 450528405, Fax: +49 30 450528908
E Mail: anja.braeuer@charite.de

Brakemeier, Dipl.-Psych. Eva-Lotta
Charité Universitätsmedizin, Campus Benjamin Franklin
Department of Psychiatry and Psychotherapy
Eschenallee 3
14050 Berlin
Tel.: +49 178 8159707, Fax: +49 30 84458233
E Mail: eva-lotta.brakemeier@charite.de

Brandt, Nicola
Institute of Cell- and Neurobiology
Center of Anatomy, Charite University Hospital Berlin
Philippstr.12
10115 Berlin
Tel.: +49 30 450528124, Fax: +49 30 450528902
E Mail: nicola.brandt@charite.de

Brandt, Alexander
Charité Universitätsmedizin Berlin
Institute of Neuroimmunology
Schumannstrasse 20/21
10117 Berlin
E Mail: alexander.brandt@charite.de

Braun, Mario
Freie Unviversität Berlin
Erziehungswissenschaften und Psychologie
Habelschwerdter Allee 45
14195 Berlin
Tel.: +49 30 8385519, Fax: +49 30 8385562
E Mail: mmbraun@zedat.fu-berlin.de

Braunewell, Dr. Karl-Heinz
Charité - Universitätsmedizin Berlin
SignalIransduction Research Group, Neuroscience Research Center
Tucholskystr. 2
10117 Berlin
E Mail: karl-heinz.braunewell@charite.de

Brecht, Michael
Erasmus MC
Neuroscience
Molewaterplein 50
3000 Rotterdam
Netherlands
Tel.: +31 10 4638049
E Mail: m.brecht@erasmusmc.nl

Britsch, Dr. Stefan
Max Delbrück Center for Molecular Medicine (MDC)
Berlin-Buch
Robert-Roessle-Str. 10
13092 Berlin
Tel.: +49 30 94063160, Fax: +49 30 94063449
E Mail: sbritsch@mdc-berlin.de

Brylka, Heike
Max-Delbrück-Zentrum für Molekulare Medizin
S.Britsch/AG C.Birchmeier
Robert-Rössle-Str.10
13092 Berlin
Tel.: +49 30 94063848
E Mail: heike.brylka@mdc-berlin.de

Caspani, Ombretta
Charité, Campus Benjamin Franklin
Anesthesiology
Krahmerstr. 6-12
12207 Berlin
Tel.: +49 30 84452131
E Mail: ombretta.caspani@charite.de

Cheung, Giselle
Max-Delbrueck-Center
Cellular Neuroscience
Robert-Rössele Str 10
13125 Berlin
Tel.: +49 30 94063503, Fax: +49 30 94063819
E Mail: gcheung@mdc-berlin.de

Chiang, M.Sc. Johnny Li-Yang
Max Delbrück Zentrum
Neuroscience
Robert-Rössle-Str.10
13125 Berlin-Buch
Tel.: +49 30 94063783
E Mail: li-yang.chiang@mdc-berlin.de

Cholewa, Jadwiga
Max-Delbrück-Centrum
Developmental Neurobiology
Robert-Rössle-Strasse 10
13092 Berlin
Tel.: +49 30 94063316

Conrad, Markus
Freie Universität Berlin
Allgemeine Psychologie
Habelschwerdter Allee 45
14195 Berlin
E Mail: markus_conrad@gmx.de

Craveiro, Rogério Bastos
Max-Delbrück-Centrum für Molekulare Medizin
Developmental Neurobiology
Robert-Rössler-Strasse 10
13092 Berlin
Tel.: +49 30 94063583
E Mail: craveiro@mdc-berlin.de

Creutzig, Felix
HU Berlin
Institute for Theoretical Biology
Invalidenstr. 43
10115 Berlin
E Mail: felix@creutzig.de

Curio, Prof. Dr. Gabriel
Campus Benjamin Franklin, Charité
Neurophysics Group, Dept. of Neurology
Hindenburgdamm 30
12200 Berlin
Tel.: +49 30 84452276, Fax: +49 30 84454264
E Mail: gabriel.curio@charite.de

Danóczy, Márton
HU Berlin
ITB
Invalidenstr. 43
10115 Berlin
Tel.: +49 30 20938838,
E Mail: m.danoczy@biologie.hu-berlin.de

Darna, Mahesh
Charité, Universitätsmedizin Berlin
Institut für Anatomie
Philippstr.12
10117 Berlin
Tel.: +49 30 450528428, Fax: +49 30 450528912
E Mail: mahesh.darna@charite.de

Decker, Jochen
Charité
Neurophysiology
Tucholskystr.2
10117 berlin
Tel.: +49 30 450528358
E Mail: jochen.decker@charite.de

Deisz, Dr. Rudolf
Center for Anatomy
Cell- and Neurobiology
Philippstr. 10
10098 Berlin
Tel.: +49 30 450528055, Fax: +49 30 450528902
E Mail: rudolf.deisz@charite.de

Dirnagl, Prof. Dr. Ulrich
Experimental Neurology
Schumannstr 20/21
10098 Berlin
E Mail: ulrich.dirnagl@charite.de

Drenckhahn, Christoph
Charité Campus Mitte
Department of Experimental Neurology
Schumannstr. 20/21
10098 Berlin
Tel.: +49 30 450560007, Fax: +49 30 450560932
E Mail: christoph.drenckhahn@charite.de

Eckart, Sarah Ann
Charité-University Medicine Berlin, Campus Benjamin Franklin
Department of Psychiatry
Akazienallee 36
14050 Berlin
Tel.: +49 30 84458241, Fax: +49 30 84458244
E Mail: sarah.eckart@charite.de

Engbert, Prof. Dr. Ralf
University of Potsdam
Department of Psychology
Karl-Liebknecht-Str. 24-25
14476 Golm (Potsdam)
Tel.: +49 331 97728, Fax: +49 331 97727
E Mail: engbert@uni-potsdam.de

Färber, Dr. Katrin
Max-Delbrueck-Center for Molecular Medicine
Cellular Neuroscience
Robert-Roessle-Str. 10
13125 Berlin
Tel.: +49 30 94063260
E Mail: kfaerber@mdc-berlin.de

Falcke, PD Dr. Martin
Hahn-Meitner-Institut
Department Theory
Glienicker Str. 100
14109 Berlin
Tel.: +49 30 80622627
E Mail: falcke@hmi.de

Fidzinski, Pawel
Charité Universitätsmedizin Berlin
Institute of Neurophysiology
Tucholskystr. 2
10117 Berlin
Tel.: +49 30 450528209, Fax: +49 30 450539941
E Mail: pawel.fidzinski@charite.de

Fink, Prof. Heidrun
Freie Universität Berlin
Institute of Pharmacology and Toxicology
Koserstr. 20
14195 Berlin
Tel.: +49 30 83853221, Fax: +49 30 83853112
E Mail: fink.heidrun@vetmed.fu-berlin.de

Foulle, Raphaele
Max Delbruck Center for Molecular Medicine (MDC)
Berlin-Buch
Neuroproteomics
Robert-Roessle-Str. 10
13125 Berlin
Tel.: +49 30 94062636, Fax: +49 30 94062552
E Mail: r.foulle@mdc-berlin.de

Frahm, Christina
Max-Delbrueck-Center for Molecular Medicine
Department of Neurosciences
Robert-Roessle-Str.10
13092 Berlin
Tel.: +49 30 94063848, Fax: +49 30 94063449
E Mail: c.schmidt@mdc-berlin.de

Franzius, Mathias
HU-Berlin
Institute for Theoretical Biology (ITB)
Invalidenstraße 43
10115 Berlin
E Mail: m.franzius@biologie.hu-berlin.de

Friedel, Michael
Institute of Neurophysiology
AG Behr
Tucholskystraße 2
10117 Berlin
Tel.: +49 30 450528209, Fax: +49 30 450539941
E Mail: friedel.michael@googlemail.com

Fuchs, Heiko
Institute of Cell Biology and Neurobiology
Center for Anatomy
Schumannstraße 20-21
10098 Berlin
Tel.: +49 30 450528278, Fax: +49 30 450528902
E Mail: biorad74@hotmail.com

Füchtemeier, Diplom-Biologin Martina
Charité Universitätsmedizin Berlin
Experimentelle Neurologie
Schumannstraße 20/21
10098 Berlin
Tel.: +49 30 40504860
E Mail: martina.fuechtemeier@web.de

Gallinat, Dr. Jürgen
Charité, CCM
Klinik für Psychiatrie und Psychotherapie
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 23112969, Fax: +49 30 23112903
E Mail: juergen.gallinat@charite.de

Garratt, Dr. Alistair
Max-Delbrueck-Center for Molecular Medicine
Department of Neurosciences
Robert-Roessle-Str.10
13092 Berlin
Tel.: +49 30 94063785, Fax: +49 30 94063449
E Mail: agarratt@mdc-berlin.de

Geist, Beate
Center of Anatomy
Institute of Cell- and Neurobiology
Philippstraße 12
10115 Berlin
Tel.: +49 30 450528008, Fax: +49 30 450528902
E Mail: beate.geist@charite.de

Ghani Kakhki, Dr. Mahdi
Institute of Human Genetics
Chromosomal Diagnostics
Augustenburger Platz 1
13353 Berlin
Tel.: +49 30 450566837, Fax: +49 30 450566933
E Mail: mahdi.ghani@charite.de

Glauser, Dipl. Zool. Samuel
Humboldt Universität zu Berlin
Institute for Theoretical Biology
Invalidenstrasse 43
10115 Berlin
Tel.: +49 30 20938649
E Mail: s.glauser@biologie.hu-berlin.de

Goebel, Prof. Rainer
Universiteit Maastricht
Dept. of Cognitive Neuroscience
Postbus 616
6200MD Maastricht
The Netherlands
Tel.: +31 43 3884014, Fax: +31 43 3884125
E Mail: r.goebel@psychology.unimaas.nl

Goswami, Chandan
Max Planck Institute for Molecular Genetics
Ihnestraße 63-73
14195 Berlin
E Mail: goswami@molgen.mpg.de

Grünewald, Dr. Bernd
Freie Universität Berlin
Institut für Biologie - Neurobiologie
Königin-Luise-Str. 28-30
14195 Berlin
Tel.: +49 30 83854298
E Mail: gruenewa@zedat.fu-berlin.de

Haesler, Sebastian
FU Berlin
Verhaltensbiologie
Takustrasse
14195 Berlin
Tel.: +49 30 84131291, Fax: +49 30 84131383
E Mail: haesler@molgen.mpg.de

Häusser, Dr. Michael
University College London
Wolfson Institute for Biomedical Research
Gower Street
WC1E 6BT London
UK
Tel.: +44 20 767932, Fax: +44 20 791685
E Mail: m.hausser@ucl.ac.uk

Hahner, Astrid
Charité Berlin
Inst. für Neuroimmunologie
Schumannstrasse 20/21
10117 Berlin
E Mail: astrid.hahner@charite.de

Harder, Lena
MDC
Neuroscience
Robert-Rössle-Strasse 10
13125 Berlin
Tel.: +49 30 94063789, Fax: +49 30 94062793
E Mail: lena-harder@freenet.de

Heine, Angela
Freie Universität Berlin
Dept. of Psychology
Habelschwerdter Allee 45
12043 Berlin
E Mail: aheine@zedat.fu-berlin.de

Heinemann, Prof. Dr. Uwe
Charité Universitaetsmedizin Berlin
Institute of Neurophysiology
Tucholskystr. 2
10117 Berlin
Tel.: +49 30 450528091, Fax: +49 30 450528962
E Mail: uwe.heinemann@charite.de

Hellmann, Julian
Charité-University Medicine Berlin
Dept. of Psychiatry
Eschenallee 3
14050 Berlin
Tel.: +49 30 844582410, Fax: +49 30 84458244
E Mail: julian.hellmann@charite.de

Hendrix, Dr. Sven
Center for Anatomy, Charité - Universitätsmedizin Berlin
Institute of Cell Biology and Neurobiology
Schumannstr. 20-21
10098 Berlin
Tel.: +49 30 45052840, Fax: +49 30 45052890
E Mail: sven.hendrix@charite.de

Herz, Prof. Andreas V.M.
Humboldt University
Inst. of Theoretical Biology
Invalidenstr. 43
10115 Berlin
Tel.: +49 30 20939103, Fax: +49 30 20938801
E Mail: a.herz@biologie.hu-berlin.de

Heuser, Prof. Dr. Isabella
Charité, Campus Benjamin Franklin
Psychiatry
Eschenallee 3
14050 Berlin
Tel.: +49 30 84458701, Fax: +49 30 84458726
E Mail: katharina.schmalfeld@charite.de

Hoene, Victoria
Charité Universitätsmedizin Berlin
Molekulare Neonatologie
Augustenburger Platz 1
13353 Berlin
Tel.: +49 30 450559509
E Mail: victoria.hoene@charite.de

Hörster, Henrik
Max-Delbrueck-Center for Molecular Medicine (MDC)
Berlin-Buch
Neuronal Stem Cells
Robert-Rössle-Str. 10
13125 Berlin
Tel.: +49 30 94063271
E Mail: henrik.hoerster@mdc-berlin.de

Hu, Dr. Jing
MDC
Neuroscience
Robert-Rössle-Str. 10
13092 Berlin
Tel.: +49 30 94063783, Fax: +49 30 94062793
E Mail: jinghu@mdc-berlin.de

Hucho, Dr. Tim
MPI für molekulare Genetik
Ropers
Ihnestrasse 73
14195 Berlin
Tel.: +49 30 8413 1243, Fax: +49 30 8413 1383
E Mail: hucho@molgen.mpg.de

Huchzermeyer, Christine
Charité-Universitätsmedizin Berlin
Institut für Neurophysiologie
Tucholskystraße 2
10117 Berlin
E Mail: christine.huchzermeyer@charite.de

Huggenberger, Stefan
University of Potsdam
Institute for Biochemistry and Biology
Karl Liebknecht Str. 24-26
14476 Golm
E Mail: huggen@rz.uni-potsdam.de

Ibanez-Tallon, Dr. Ines
Max Delbruck Center
Neurosciences
Robert Rössle Str. 10
13125 Berlin
Tel.: +49 30 94063411, Fax: +49 30 94063765
E Mail: ibanezi@mdc-berlin.de

Infante Duarte, Dr. Carmen
Charité - Universitätsmedizin Berlin
Institute of Neuroimmunology
Schumannstr. 20/21
10117 Berlin
E Mail: carmen.infante@charite.de

Jentsch, Prof. Thomas
Universität Hamburg
ZMNH
Falkenried 94
20246 Hamburg
Tel.: +49 40 428034741
E Mail: Jentsch@zmnh.uni-hamburg.de

Jockers-Scherübl, Dr. Maria
Charité, CBF
Psychiatry and Psychotherapy
Eschenallee 3
14050 Berlin
Tel.: +49 30 84458707, Fax: +49 30 84458341
E Mail: maria.jockers@charite.de

John, Anita
MDC Berlin
Dr. Stefan Britsch/ AG Prof. Carmen Birchmeier
Robert-Rössle-Str. 10
13092 Berlin
E Mail: ajohn@mdc-berlin.de

Jüttner, Dr. René
Max-Delbrueck Center
Developmental Neurobiology
Robert-Rössle-Str. 10
13092 Berlin
Tel.: +49 30 94062772
E Mail: r.juettner@mdc-berlin.de

Kann, Dr. Oliver
Inst. for Neurophysiology, Charité
Dept. of Mitochondrial Physiology and Pathology
Tucholskystr. 2
10117 Berlin
Tel.: +49 30 450528357, Fax: +49 30 450528962
E Mail: oliver.kann@charite.de

Kettenmann, Prof. Helmut
Max Delbrück Center for Molecular Medicine (MDC)
Berlin Buch
Cellular Neurosciences
Robert-Rössle-Str. 10
13092 Berlin
Tel.: +49 30 94063325, Fax: +49 30 94063819
E Mail: kettenmann@mdc-berlin.de

Kim, Simon
Charité University Medicine
Institute for Neurophysiology
Rubensstr. 3b
12159 Berlin
E Mail: simon.kim@charite.de

Klehmet, Dr. Juliane
Charité
Experimental Neurology
Schumannstraße 20/21
10117 Berlin
Tel.: +49 30 450560068, Fax: +49 30 450560913
E Mail: juliane.klehmet@charite.de

Kloetzel, Prof. Peter-Michael
Charité Berlin, CCM
Institute of Biochemistry
Monbijoustr.2
10117 Berlin
Tel.: +49 30 450528232
E Mail: p-m.kloetzel@charite.de

Kovács, Dr. Richard
Institute for Neurophysiology, Charité
Mitochondrial Physiology and Pathology
Tucholskystr. 2
10117 Berlin
Tel.: +49 30 450528357, Fax: +49 30 450528962
E Mail: mozsafa@gmx.net

Kuchinke, Lars
Freie Universität Berlin
Allgemeine Psychologie
Habelschwerdter Allee 45
14195 Berlin
E Mail: kuchinke@zedat.fu-berlin.de

Kunzmann, Volker
University Medicine Berlin, Charité, Campus Benjamin Franklin
Neurology
Hindenburgdamm 30
12200 Berlin
E Mail: volker.kunzmann@charite.de

Kuokkanen, MSc Paula
Humboldt Universität zu Berlin
Institute for Theoretical Biology
Invalidenstr. 43
10115 Berlin
Tel.: +49 30 20938633, Fax: +49 30 20938801
E Mail: p.kuokkanen@biologie.hu-berlin.de

Lauritzen, Prof. MD Martin
Glostrup Hospital and University of Copenhagen
Dept. of Clinical Neurophysiology
2600 Glostrup
Denmark
Tel.: +45 432 32500, Fax: +45 432 33933
E Mail: Marl@Glostruphosp.kdhamt.dk

Le Noble, Ferdinand
Max Delbrueck Center for Molecular Medicine
Laboratory for Angiogenesis and Cardiovascular Pathology
Robert Roessle Strasse 10
13125 Berlin
EMail: lenoble@mdc-berlin.de

Lechner, Dr. Stefan
MDC
Neuroscience
Robert Rössle Str.10
13092 Berlin
Tel.: +49 30 94062853
E Mail: stefan.lechner@mdc-berlin.de

Lehmann, Dr. med. Thomas-Nicolas
Charité Campus Virchow-Klinikum
Neurosurgery
Augustenburger Platz 1
13353 Berlin
E Mail: thomas-nicolas.lehmann@charite.de

Leistner, Dr. Stefanie
Charité - Universitätsmedizin Berlin, Campus Benjamin Franklin
Department of Neurology
Hindenburgdamm 30
12203 Berlin
Tel.: +49 30 84454705, Fax: +49 30 84454264
E Mail: stefanie.leistner@charite.de

Leithner, Dr. Christoph
Charite Universitätsmedizin Berlin
Experimentelle Neurologie
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 450660555
E Mail: christoph.leithner@charite.de

Lewin, Prof. Gary
MDC
Neuroscience
Robert Rössle Str. 10
13092 Berlin
E Mail: glewin@mdc-berlin.de

Lindauer, PD Dr. Ute
Charité Berlin
Experimental Neurology
Schumannstr. 20 / 21
10098 Berlin
Tel.: +49 30 450560198, Fax: +49 30 450560915
E Mail: ute.lindauer@charite.de

Lohmann, Peter
Charité University
Department of Psychiatry
Krahmerstr. 6-10
12207 Berlin
Tel.: +49 30 84453773
E Mail: peter.lohmann@charite.de

Lohrberg, Doerte
Leibniz-Institut für Molekulare Pharmakologie (FMP)
Signaltransduktion
Robert-Rössle-Str. 10
13125 Berlin
Tel.: +49 30 94793304
E Mail: lohrberg@fmp-berlin.de

Luborzewski, Alexander
Carité Campus Benjamin Franklin
Psychiatry
Eschenallee 3
14050 Berlin
E Mail: alexander.luborzewski@charite.de

Lueschow, Dr. Andreas
CBF, Charité-Universitätsmedizin Berlin
Neurology
Hindenburgdamm 30
12200 Berlin
Tel.: +49 30 84452276, Fax: +49 30 84454264
E Mail: andreas.lueschow@charite.de

Major, Sebastian
Charité - University Medicine Berlin
Neurology and Experimental Neurology
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 450560007, Fax: +49 30 450560915
E Mail: sebastian.major@charite.de

Mao, Xiaosong
Institute of Moleculare Neurobiology, Free University Berlin
Dept. Prof. Kuhl
Takustraße 6
14195 Berlin
Tel.: +49 30 83856973, Fax: +49 30 83856981
E Mail: xiaosong@neuroscience.fu-berlin.de

Meier, Dr. Jochen
Johannes Müller Centrum
Developmental Physiology
Tucholskystraße 2
10117 Berlin
Tel.: +49 30 450528156, Fax: +49 30 450528952
E Mail: jochen.meier@charite.de

Menzel, Prof. Randolf
Freie Universität Berlin
Neurobiologie
Königin Luise Str. 28/30
114195 Berlin
Tel.: +49 30 83853930, Fax: +49 30 83855455
E Mail: menzel@neurobiologie.fu-berlin.de

Mergenthaler, Philipp
Charite Universitaetsmedizin Berlin
Experimental Neurology
Schumannstrasse 20/21
10098 Berlin
E Mail: philipp.mergenthaler@charite.de

Merkl, Dr. Angela
Charité, CBF
Psychiatry
Eschenallee 3
14050 Berlin
Tel.: +49 30 84458752
E Mail: angela.merkl@charite.de

Milenkovic, Nevena
MDC
Neuroscience
Robert Rossle Str. 10
10092 Berlin
E Mail: Milenkovic@mdc-berlin.de

Müller, Dr. Thomas
Max-Delbrück-Center for Molecular Medicine
Medical Genetics
Robert-Rössle-Str.10
13125 Berlin
Tel.: +49 30 94062842, Fax: +49 30 94063765
E Mail: thomu@mdc-berlin.de

Naito, Aki
Charité, Campus Mitte, Humboldt University
Neurology
Schumannstrasse 20-21
10117 Berlin
E Mail: a.naito@biologie.hu-berlin.de

Nawrot, Dr. Martin
Free University Berlin
Neuroinformatics and Theoretical Neuroscience
Koenigin-Luise Strasse 28/30
14195 Berlin
E Mail: nawrot@neurobiologie.fu-berlin.de

Neuhaus, Dr. Andres
Charité University Medicine Berlin, Campus Benjamin Franklin
Psychiatry
Eschenallee 3
10405 Berlin
E Mail: andres.neuhaus@charite.de

Nitsch, Prof. Dr. Robert
Charité Universitätsmedizin Berlin
Institute for Cell Biology and Neurobiology
Schumannstr. 20/21
10098 Berlin
Tel.: +49 30 450528 00, Fax: +49 30 450528 90
E Mail: robert.nitsch@charite.de

Noack, Cornelia
Institut für Physiologie, AG Signaltransduktion
NWFZ
Tucholskystr. 2
10117 Berlin
E Mail: conny.noack@lycos.de

Offenhauser, Nikolas
Charité
Experimental Neurology
Schumannstr 20/21
10117 Berlin
Tel.: +49 30 450560206
E Mail: nikolas.offenhauser@charite.de

Parnavelas, PhD John
University College London
Anatomy & Development Biology
Gower Street
WC1E 6 BT London
UK
Tel.: +44 171 419 3366, Fax: +44 171 380 7349
E Mail: j.parnavelas@ucl.ac.uk

Pechstein, Arndt
Chemistry and Biochemistry
Chemistry-Biology-Pharmacy
Takustrasse 6
14195 Berlin
Tel.: +49 30 83856931
E Mail: arndtp@chemie.fu-berlin.de

Peters, Dr. Oliver
Charité - CBF
Department of Psychiatry
Eschenallee 3
14050 Berlin
Tel.: +49 30 84458312, Fax: +49 30 84458350
E Mail: oliver.peters@charite.de

Pflüger, Prof. Hans-Joachim
Freie Universität Berlin
Institut für Biologie, Neurobiologie
Königin-Luise-Strasse 28-30
14195 Berlin
Tel.: +49 30 83854676, Fax: +49 30 83855455
E Mail: pflueger@neurobiologie.fu-berlin.de

Piehl, Christian
Leibniz-Forschungsinstitut für molekulare Pharmakologie
Robert-Roessle-Str. 10
10437 Berlin
E Mail: piehl@fmp-berlin.de

Pohl, Dr. Elena
Charité
Institut für Zell und Neurobiologie
Schumannstr. 20/21
10117 Berlin
E Mail: elena.pohl@charite.de

Rathjen, Fritz G
MDC
Robert-Rössle-Str.10
13092 Berlin
E Mail: Rathjen@mdc-berlin.de

Raue, Claudia
Charité University Medicine
Institute for Neurophysiology
Stephanstr. 5
10559 Berlin
Tel.: +49 30 36726873
E Mail: craue@tiscalinet.de

Raza, Dr. Mohsin
Tarbiat Modares University
Physiology, School of Medical Sciences
Jalal Ale Ahmed Epxressway
14115 Tehran
Iran
Tel.: +9821 88011001
E Mail: mohsinrazahej@yahoo.com

Rentzsch, Johannes
Psychiatrische Klinik
Charité - Universitätsmedizin Berlin
Eschenallee 3
14050 Berlin
Tel.: +49 30 84458710, Fax: +49 30 84458262
E Mail: johannes.rentzsch@charite.de

Rex, Dr. André
Freie Universität Berlin
Institute of Pharmacology and Toxicology
Koserstr. 20
14195 Berlin
Tel.: +49 30 83853512, Fax: +49 30 83853112
E Mail: rex.andre@vetmed.fu-berlin.de

Rezaie, Dr. Mohamad Jafar
Medical Sciences University of Kurdestan
Departments of Anatomical Sciences and Histology
Pasdaran
1 Sananadaj
Iran
Tel.: +989123728582, Fax: +988716660051
E Mail: rezaiemj@hotmail.com

Prof. Matthias Riepe
Charité
Klinik für Psychiatrie und Psychotherapie
Klinik für Psychiatrie
Eschenallee 3
14050 Berlin
Tel.: +49 30 8445 8744
EMail: matthias.riepe@chaite.de

Rocca, Elena
Max-Delbrück-Centrum für Molekulare Medizin (MDC)
Robert-Rössle-Str. 10
13092 Berlin
E Mail: rocca@mdc-berlin.de

Roehner, Uwe
HU
ITB
Invalidenstr. 43
10115 Berlin
Tel.: +49 30 20938838
E Mail: u.roehner@biologie.hu-berlin.de

Roggenhofer, Elisabeth
Institut für Physiologie, Charité
AG Behr
Huebnerstr.4
10247 Berlin
Tel.: +49 30 25201400
E Mail: lisa.roggenhofer@gmx.de

Roland, Takeesha
Humboldt-Charité
Neuroscience
Wexstr 33
10715 Berlin
E Mail: tlrstarr@gmail.com

Royl, Dr. Georg
Charité
Department of Experimental Neurology
Schumannstr. 20 / 21
10098 Berlin
Tel.: +49 30 450560206
E Mail: georg.royl@charite.de

Rybak, Agnieszka
Institute of Cell Biology and Neurobiology
Center for Anatomy
Schumannstraße 20-21
10098 Berlin
Tel.: +49 30 450528278, Fax: +49 30 450528902
E Mail: ines_r@wp.pl

Sander-Thömmes, Dr. Tilmann
Physikalisch-Technische Bundesanstalt
AG 8.21
Abbestr. 2-12
10587 Berlin
Tel.: +49 30 34817436, Fax: +49 30 34817361
E Mail: tilmann.sander-thoemmes@ptb.de

Sangals, Dr. Jörg
Institut für Psychologie, Humboldt Univ. zu Berlin
Biological Psychology / Psychophysiology
Rudower Chaussee 18
10489 Berlin
Tel.: +49 30 20934826
E Mail: joerg.sangals@cms.hu-berlin.de

Schadt, Heiko
Center for Anatomy, Charité University Hospital
Institute of Cell Biology and Neurobiology
Philippstraße 12
10115 Berlin
Tel.: +49 30 450528124, Fax: +49 30 450528902
E Mail: heiko.schadt@charite.de

Schaette, Roland
Humboldt-Universität zu Berlin
Institute for Theoretical Biology
Invalidenstr. 43
10115 Berlin
Tel.: +49 30 20938926, Fax: +49 30 20938801
E Mail: r.schaette@biologie.hu-berlin.de

Schipke, Dr. Carola
Charité-Universitätsmedizin Berlin, Campus Benjamin Franklin
Psychiatrie und Psychotherapie
Eschenallee 3
14050 Berlin
E Mail: carola_schipke@hotmail.com

Schlagenhauf, Florian
Charité - Universitätsmedizin Berlin
Department of Psychiatry
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 450517257
E Mail: florian.schlagenhauf@charite.de

Schreiber, Susanne
Humboldt Universitaet zu Berlin
Institut fuer Theoretische Biologie
Invalidenstr. 43
10115 Berlin
Tel.: +49 30 20938652
E Mail: s.schreiber@biologie.hu-berlin.de

Schubert, Dipl.-Psych. Ruth
Charité Campus Benjamin Franklin
AG Neurophysik
Hindenburgdamm 30
12200 Berlin
Tel.: +49 30 450560195, Fax: +49 30 450560192
E Mail: ruth.schubert@charite.de

Schulte-Herbrüggen, Dr. Olaf
Charité, Campus Benjamin Franklin
Psychiatry and Psychotherapy
Eschenallee 3
14050 Berlin
Tel.: +49 30 84458328, Fax: +49 30 84458350
E Mail: olaf.schulte-herbrueggen@charite.de

Schulze Topphoff, Ulf
Charité Berlin
Institute of Neuroimmunology
Schumannstr. 20-21
10117 Berlin
E Mail: ulf.topphoff@charite.de

Schumacher, Dr. Stefan
Charité University Hospital
Institute of Cell Biology and Neurobiology, Center for Anatomy
Philippstrasse 12
10115 Berlin
Tel.: +49 30 45052832, Fax: +49 30 45052890
E Mail: stefan.schumacher@charite.de

Schweizer, Dr. Ulrich
AG Neurobiologie des Selens
Charité
Schumannstrasse 20/21
10117 Berlin
Tel.: +49 30 450539041, Fax: +49 30 450524922
E Mail: ulrich.schweizer@charite.de

Seifert, Diplom Biol. Stefanie
Max Delbrueck Center for Molecular Medicine (MDC)
Berlin-Buch
AG Kettenmann
Robert-Rössle-Str. 10
13125 Berlin
Tel.: +49 30 94063729
E Mail: s.seifert@mdc-berlin.de

Seifert, Alexandra
Max-Delbrück-Centrum für Molekulare Medizin
Robert-Rössle-Str.10
13125 Berlin
E Mail: alexandra.seifert@mdc-berlin.de

Seo, Eun-Yeong
Max-Delbrück Center for Molecular Medicine
Growth Factors and Regeneration Group
Robert-Rössle-Strasse 10
13122 Berlin
E Mail: eyseo@sogang.ac.kr

Siffrin, Dr. Volker
Charité
Institute of Neuroimmunology
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 450539057
E Mail: volker.siffrin@charite.de

Sigrist, Dr. Stephan
European Neuroscience Institute Göttingen
Waldweg 3
37073 Göttingen
E Mail: ssigris@gwdg.de

Skupin, Alexander
Hahn-Meitner-Institut
Department Theory
Glienicker Str. 100
14109 Berlin
Tel.: +49 30 80623198
E Mail: alexander.skupin@hmi.de

Smirnova, Lena
Institute of Cell and Neurobiology
Charite University Hospital
Center for Anatomy
Philippstr. 12
10115 Berlin
Tel.: +49 30 450528300
E Mail: lena.smirnova@charite.de

Smorodchenko, Dr. Alina
Neuroimmunology
Neuroscience Research Center
Neuroimmunology
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 450539051, Fax: +49 30 450539906
E Mail: alina.smorodchenko@charite.de

Soriguera i Farrés, Anna
Center for Anatomy
Institute of Cell Biology and Neurobiology
Philippstr. 12
10115 Berlin
Tel.: +49 30 450528406, Fax: +49 30 450528908
E Mail: annasoriguera@charite.de

Sprekeler, Henning
HU Berlin
Institute for Theoretical Biology
Invalidenstr. 43
10115 Berlin
Tel.: +49 30 20938630
E Mail: h.sprekeler@biologie.hu-berlin.de

Stonkute, Agne
Max Delbrueck Center for Molecular Medicine
Developmental Neurobiology
Robert Roessle Str.
13092 Berlin
E Mail: stonkute@mdc-berlin.de

Ströhle, PD Dr. Andreas
Campus Charité Mitte, Charité – Universitätsmedizin Berlin
Department of Psychiatry and Psychotherapy
Schumannstr. 20/21
10117 Berlin
E Mail: andreas.stroehle@charite.de

Strube, PhD Martin
Freie Universität Berlin
Neurobiologie
Königin Luise Strasse 26-28
14195 Berlin
Tel.: +49 30 83856597
E Mail: martin_strube@web.de

Telenczuk, Bartosz
Institute for Theoretical Biology
Humboldt University of Berlin
Invalidenstraße 43
10115 Berlin
E Mail: b.telenczuk@biologie.hu-berlin.de

Thaler, Mag. Verena
FU Berlin, Fachbereich Erziehungswissenschaften und Psychologie
Allgemeine und Neurokognitive Psychologie
Habelschwerdter Allee 45
14195 Berlin
Tel.: +49 30 83855626, Fax: +49 30 83855620
E Mail: thalerv@zedat.fu-berlin.de

Trimbuch, Thorsten
Charité - University Hospital Berlin
Institute of Cell- and Neurobiology
Philippstr. 12
10115 Berlin
Tel.: +49 30 450528008, Fax: +49 30 450528902
E Mail: thorsten.trimbuch@charite.de

Tysiak, Eva
Torstr. 94
10119 Berlin
Tel.: +49 30 450539057
E Mail: eva-kristin.tysiak@charite.de

Tzschentke, PD Dr. Barbara
Humboldt-University of Berlin
Biology
Philippstr. 13
10115 Berlin
Tel.: +49 30 20936276, Fax: +49 30 20936008
E Mail: barbara.tzschentke@rz.hu-berlin.de

Uhlenberg, Dr. Birgit
Charité Children's Clinic
Neuropediatrics
Augustenburger Platz 1
13353 Berlin
Tel.: +49 30 450566112, Fax: +49 30 450566920
E Mail: birgit.uhlenberg@charite.de

Velmans, Tanja
Centrum of Anatomy
Institute of Cell Biology and Neurobiology
Philippstr. 12
10115 Berlin
Tel.: +49 30 450528406, Fax: +49 30 450528908
E Mail: Tanja.Velmans@charite.de

Vierk, Dipl.-Biologe Ricardo
Institute for Neurobiology
Biology/Chemistry/Pharmacy Department
Königin-Luise-Strasse 28/30
14195 Berlin
Tel.: +49 30 83854916
E Mail: vierk@zedat.fu-berlin.de

Vogt, Dr. Johannes
Charité
Institute of Cell and Neurobiology
Philippstr. 12
10115 Berlin
Tel.: +49 30 450528429, Fax: +49 30 450528009
E Mail: johannes.vogt@charite.de

Vollmar, Imke
Max-Delbrück-Centrum für Molekulare Medizin (MDC)
Berlin-Buch
AG Kempermann
Robert-Rössle-Str. 10
13092 Berlin
Tel.: +49 30 94062364
E Mail: Imke.Vollmar@mdc-berlin.de

Wahl, Michael
Charité - University Medicine Berlin
Department of Neurology, CBF
Hindenburgdamm 30
12200 Berlin
E Mail: michael.wahl@charite.de

Wang, Ms. Rui
Max Delbrück Center for Molecular Medicine
Department of Neuroscience
Robert-Rössle-Str 10
13092 Berlin
Tel.: +49 30 94062853
E Mail: ruiwang@mdc-berlin.de

Wanker, Prof. Erich E.
Max Delbruck Center for Molecular Medicine (MDC)
Berlin-Buch
Neuroproteomics
Robert-Roessle-Str. 10
13125 Berlin
Tel.: +49 30 94062157, Fax: +49 30 94062552
E Mail: ewanker@mdc-berlin.de

Weber, Joachim E.
Charité Campus Benjamin Franklin
Department of Neurology and Neurophysiology
Hindenburgdamm 30
12200 Berlin
Tel.: +49 30 8445-2412, Fax: +49 30 8445-3144
E Mail: j.e.weber@t-online.de

Wende, Dr. Hagen
MDC
AG C. Birchmeier
Robert-Rössle-Str. 10
13125 Berlin
E Mail: hagen.wende@mdc-berlin.de

Wernicke, Dr. Catrin
Charité - Universitätsmedizin Berlin
Klinische Neurobiologie, Klinik und Hochschulambulanz für Psychiatrie und Psychotherapie
Eschenallee 3
14050 Berlin
Tel.: +49 30 84458257, Fax: +49 30 84458244
E Mail: catrin.wernicke@charite.de

Wetzel, Christiane
MDC
Growth Factor and Regeneration Group
Robert-Rössle-Str. 10
13092 Berlin
E Mail: cwetzel@mdc-berlin.de

Wierschke, Stephan
Center for Anatomy
Institute of Cell- and Neurobiology
Phillipstraße 10
10098 Berlin
E Mail: stephan.wierschke@charite.de

Wirth, Eva
AG Neurobiologie des Selens
Charité
Schumannstrasse 20/21
10117 Berlin
Tel.: +49 30 450539041, Fax: +49 30 450524922
E Mail: eva.wirth@charite.de

Wölfling, Dipl.-Psych. Klaus
Institute for Medical Psychology, Charité - University Medicine
Interdisciplinary Research Group on Addiction
Tucholskystr. 02
10117 Berlin
Tel.: +49 30 450529525, Fax: +49 30 450529923
E Mail: kwoelfling@gmx.de

Wrase, Dr. Jana
Charité Campus Mitte
Psychiatry
Schumannstr. 20 /21
10117 Berlin
Tel.: +49 30 450517153
E Mail: jana.wrase@charite.de

Wuerfel, Dr. Jens
Charité
Institute of Neuroimmunology
Schumannstr.20/21
10117 Berlin
Tel.: +49 30 450 539028, Fax: +49 30 450539906
E Mail: jens.wuerfel@charite.de

Wulczyn, Dr. F. Gregory
Charité
Institute for Cell and Neurobiology, Center for Anatomy
Schumannstrasse 20/21
10098 Berlin
Tel.: +49 30 450528459
E Mail: gregory.wulczyn@charite.de

Zacharias, Dr. Ute
MDC
Developmental Neurobiology
Robert Rössle Str.10
13125 Berlin
E Mail: uzachar@mdc-berlin.de

Zhang, Dr. rer. nat. Juan
Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin
Department of Neonatology
Augustenburger Platz 1
13353 Berlin
Tel.: +49 30 450559509, Fax: +49 30 450559906
E Mail: juan.zhang@charite.de

Ziehm, Ulrike
Humboldt University Berlin
Institute of Biology
Invalidenstr.43
10115 Berlin
Tel.: +49 30 20939066, Fax: +49 30 20938491
E Mail: rike.z@gmx.net

Zipp, Prof. Dr. Frauke
Charité - Universitaetsmedizin Berlin
Institute of Neuroimmunology
Schumannstr. 20/21
10117 Berlin
Tel.: +49 30 45053902, Fax: +49 30 45053990
E Mail: frauke.zipp@charite.de

Zurborg, M.Sc. Sandra
CBF, Charité-Universitätsmedizin
Forschungseinrichtung für Experimentelle Medizin FEM
Krahmerstraße 6-10
12207 Berlin
Tel.: +49 30 84452131, Fax: +49 30 8339389
E Mail: sandra.zurborg@charite.de