ISSN 0065-1400 (PRINT)
ISSN 1689-0035 (ONLINE)

2023 Volume 83
Supplement

ACTA NEUROBIOLOGIÆ EXPERIMENTALIS

www.ane.pl

NENCKI INSTITUTE OF EXPERIMENTAL BIOLOGY, WARSAW, POLAND

CONTENTS

ORGANIZATION

Organizer:

Polish Neuroscience Society (PTBUN)

Co-organizers:

Nicolaus Copernicus University in Toruń	Neurobiology Committee of the Polish Academy of Sciences

PARTNERS, SPONSORS, FINANCIAL SUPPORT

Ministry of Education and Science	International Brain Research Organization	Polish Academy of Sciences
Kujawsko-Pomorskie Region	TZMO S.A.	RWD Life Science Co.
GenoPlast Biotech S.A.	BESA GmbH	Science Products GmbH
Labsoft Nanotechnology Experts Sp. z o.o.	Interlab Sp. z o.o.	Elmiko Biosignals Sp. z o.o.

PARTNERS, SPONSORS, FINANCIAL SUPPORT

Merck Life Science Sp. z o.o.	Noldus Information Technology BV	Elsevier BV Science Direct
TK BIOTECH Sp. z o.o.	Medisoft	

COMMUNITY PARTNER

Polonium Foundation

HONORARY PATRONAGE

Mayor of the City of Toruń Michał Zaleski	Marshal of Kujawsko-Pomorskie Region	Nicolaus Copernicus University in Toruń Rector Magnificus prof. dr hab. Andrzej Sokala
Mayor of the City of Toruń Michał Zaleski	Marshal of Kujawsko-Pomorskie Region	UNIWERSYTET MIKOŁAJA KOPERNIKA W TORUNIU JM Rektor prof. dr hab. Andrzej Sokala

MEDIA PATRONAGE

Polskie Radio Pomorza i Kujaw (Radio PiK)	TVP Nauka	TVP3 Bydgoszcz
PiK POLSKIE RADIO	TVP NAUKA	TVP3 BYDGOSZCZ

SCIENTIFIC PROGRAM COMMITTEE

Chairperson:

Elżbieta Pyza, Jagiellonian University

Members:

Jarosław Barski, Medical University of Silesia in Katowice
Anna Błasiak, Jagiellonian University
Grzegorz Hess, Jagiellonian University
Ewelina Knapska, Nencki Institute of Experimental Biology Polish Academy of Sciences
Ewa Kublik, Nencki Institute of Experimental Biology Polish Academy of Sciences
Irena Nalepa, Maj Institute of Pharmacology, Polish Academy of Sciences
Michał Ślęzak, Łukasiewicz Research Network – PORT Polish Center for Technology Development
Marta Wiśniewska, Warsaw University
Agnieszka Zelek-Molik, Maj Institute of Pharmacology, Polish Academy of Sciences

ORGANIZING COMMITTEE

Chairperson:

Małgorzata Gut, Nicolaus Copernicus University in Toruń

Members:

Anna Błasiak, Jagiellonian University
Sławomir Czachowski, Nicolaus Copernicus University in Toruń
Joanna Gorgol, Warsaw University
Monika Lewandowska, Nicolaus Copernicus University in Toruń
Rafał Milner, Nicolaus Copernicus University in Toruń
Justyna Rogalska, Nicolaus Copernicus University in Toruń
Rafał Ryguła, Maj Institute of Pharmacology, Polish Academy of Sciences
Agnieszka Siejka, Nicolaus Copernicus University in Toruń
Jakub Słupczewski, Nicolaus Copernicus University in Toruń
Tytus Sosnowski, Nicolaus Copernicus University in Toruń

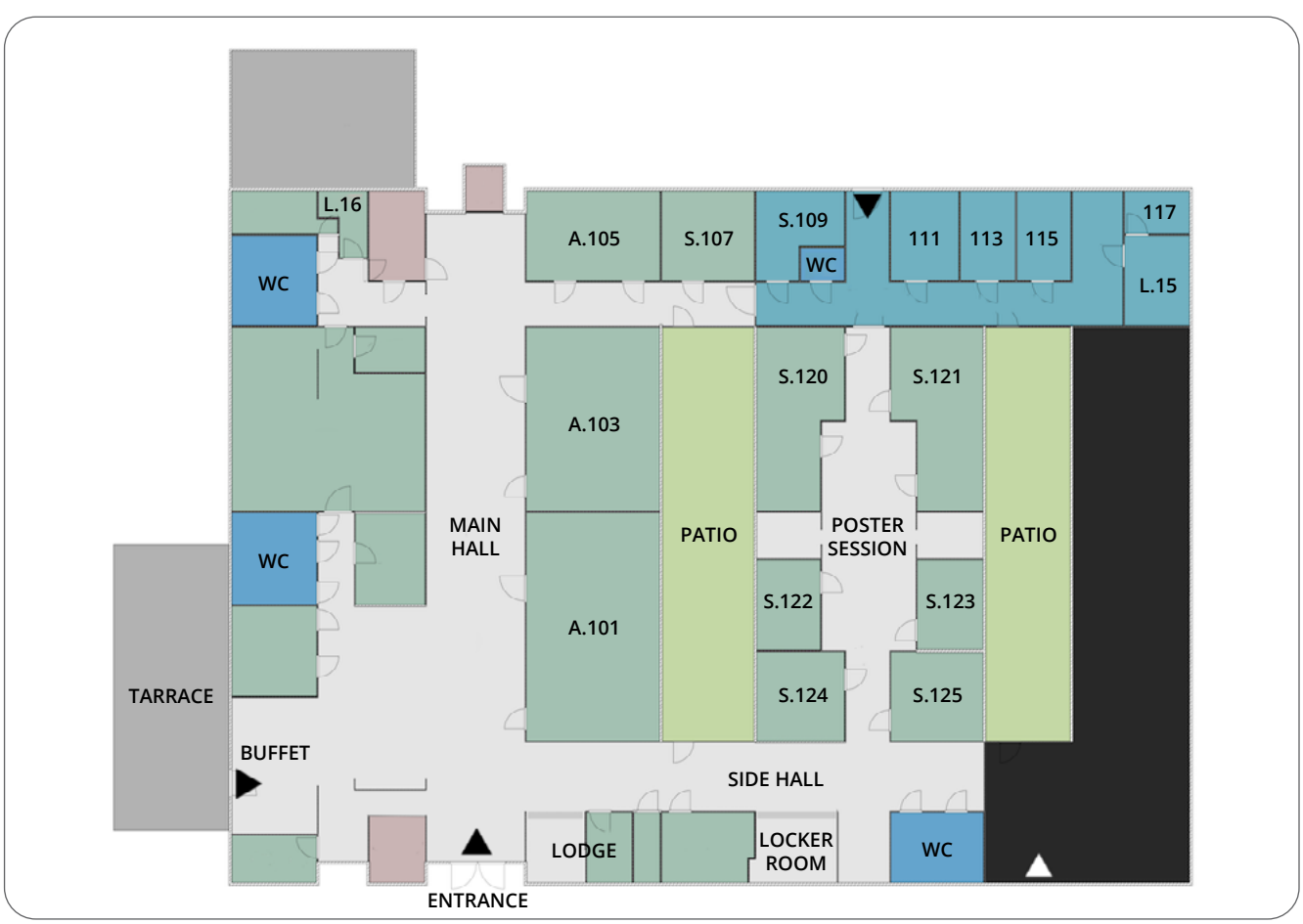
ORGANIZING COMMITTEE

Students and PhD Students
volunteers involved in the organization of the conference:

Julia Adamczyk, Nicolaus Copernicus University in Toruń
Milena Celebucka, Nicolaus Copernicus University in Toruń
Gabriela Czerniak, Jagiellonian University
Julia Garstka, Jagiellonian University
Emilia Goszczyńska, Jagiellonian University
Łukasz Grabowski, Nicolaus Copernicus University in Toruń
Maja Hiszpańska, Nicolaus Copernicus University in Toruń
Joanna Jędrusik, Jagiellonian University
Julia Kawczyńska, Nicolaus Copernicus University in Toruń
Bartłomiej Kiljanek, Nicolaus Copernicus University in Toruń
Anna Zofia Leśniewska, Jagiellonian University
Agata Machaczka, Jagiellonian University
Daria Makurat, Nicolaus Copernicus University in Toruń
Karolina Nowalińska, Jagiellonian University
Martyna Olszewska, Nicolaus Copernicus University in Toruń
Natalia Pawlaczyk, Nicolaus Copernicus University in Toruń
Gabriela Rajtar, Jagiellonian University
Gabriela Stopka, Jagiellonian University
Krzysztof Tołpa, Nicolaus Copernicus University in Toruń
Karolina Warzecha, Jagiellonian University

PLAN


INSTITUTE OF PSYCHOLOGY
ACADEMIC CENTER OF CULTURE AND ART "OD NOWA"


L.16
WC
A.105
S.107
S.109
WC
111
113
115
117
L.15
A.103
S.120
S.121
WC
MAIN HALL
PATIO
POSTER SESSION
PATIO
A.101
S.122
S.123
TARRACE
S.124
S.125
BUFFET
SIDE HALL
LODGE
LOCKER ROOM
WC
ENTRANCE

PROGRAMME

20.09.2023, WEDNESDAY

11.00 – 13.00 **Workshop "Effective Scientific Communication Skills – PAT your RAT metod"** [IP, room 120]

11.00 – 13.00 **Workshops "ScienceDirect – find your path from hypothesis to discovery. How can I use the world's scientific databases to advance my research? Discover Scopus and ScienceDirect "** [IP, room 121]

11.00 – 13.00 **Workshop "BESA: EEG signal analysis software and its possible applications"** [IP, room 016]

13.00 – 18.00 **Registration**

14.00 – 16.00 **General Assembly of PTBUN** [IP, room 101]

16.00 – 16.30 **Coffee Break** [IP]

16.30 – 17.00 **Opening Ceremony** [ON]

17.00 – 18.00 **Plenary Lecture 1 (PL1)** [ON]

Speaker: **Zoltan Molnar**, Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, United Kingdom
Title: "Evolution of thalamocortical development"
Introduced by: **Marta Wiśniewska**

18.00 – 18.30 **Flash Talks** [ON]
Chairpersons: **Anna Błasiak and Michał Ślęzak**

18.30 – 20.00 **Welcome Reception** [IP]

21.09.2023, THURSDAY

9.00 – 10.00 **Plenary Lecture 2 (PL2)** [ON]

Speaker: **Carl Petersen**, EPFL Brain Mind Institute, Lausanne, Switzerland
Title: "Neural circuits for goal-directed sensorimotor transformation"
Introduced by: **Ewa Kublik**

[IP] – Institute of Psychology, Gagarina Street 39; [ON] – Academic Center of Culture and Art "Od Nowa", Gagarina Street 37a

10.00 – 11.00 **Jerzy Konorski Award Ceremony** [ON]

Speakers: **Natalia Ochocka-Lewicka**, Computational Genomics Group, International Centre for Translational Eye Research, Institute of Physical Chemistry, Polish Academy of Sciences, Warsaw, Poland
Agnieszka Grabowska, Laboratory of Molecular Basis of Cell Motility, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland
Matylda Roszkowska, Laboratory of Neurobiology, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland
Milena Damulewicz, Department of Cell Biology and Imaging, Institute of Zoology and Biomedical Research, Faculty of Biology, Jagiellonian University, Krakow, Poland
Chairperson: **Irena Nalepa**

11.00 – 11.30 **Coffee Break** [IP]

11.30 – 13.30 **Symposia 1-3** [IP]

Symposium 1 "Altered brain rhythms, psychoactive compounds and models of psychiatric disease" (S1) [IP, room 101]

Chairperson: **Mark J. Hunt**, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Speakers: **Pawel M. Matulewicz**, Department of Pharmacology, Medical University of Innsbruck, Austria
"Disruption of mGlu5 receptors in somatostatin-expressing neurons affects anxiety-like behaviors and neuronal oscillations in prefrontal cortex and ventral hippocampus during fear memory retrieval" (**S1.1**)

Kjartan Herrik, Department of Circuit Biology, Lundbeck Research, Lundbeck, Valby, Denmark
"Translating NMDA receptor antagonism effects from rodent to human and back again" (**S1.2**)

Pär Halje, Group for Integrative Neurophysiology and Neurotechnology, Department of Experimental Medical Science, Lund University, Lund, Sweden
"Synchronised high-frequency oscillations in the cortex-basal ganglia system induced by psychedelic drugs" (**S1.3**)

Mark Hunt, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland
"Modulation of ketamine-dependent high-frequency oscillations by nasal respiration" (**S1.4**)

Symposium 2 "In sickness and in health: the role of astrocytes in the brain function" (S2) [IP, room 103]

Chairpersons: **Łukasz M. Szewczyk** and **Anna Malik**, University of Warsaw, Poland

Speakers: **Łukasz M. Szewczyk**, Centre of New Technologies, University of Warsaw, Poland
"Astrocytic ß-catenin pathway – a new player in the regulation of behavior" (**S2.1**)

Nilhan Gunhanlar, Erasmus University Rotterdam, Medical Center, The Netherlands
"Thyroid hormone signaling in a human cellular model for early brain development" (**S2.2**)

Anna Malik, Faculty of Biology, University of Warsaw, Poland
"Intracellular protein sorting in astrocytes shapes their properties in post-ischemic brain" (**S2.3**)

Christoph Harms, Charité – Universitätsmedizin Berlin, Center for Stroke Research (CSB), Department of Experimental Neurology, Germany
"Paracrine interleukin-6 signaling in post-stroke recovery" (**S2.4**)

Symposium 3 "Advances in neuromodulation – spinal motoneurons and beyond" (S3) [IP, room 105]

Chairperson: **Marcin Bączyk**, Poznań University of Physical Education, Poland

Speakers: **Guillaume Caron**, Saints-Pères Paris Institute for the Neurosciences (UMR 8003), Faculty of Exact and Biomedical Sciences, Université Paris Cité, Paris, France
"β-adrenergic receptors increase motoneuron excitability in adult WT and SOD mice" (**S3.1**)

Francesco Roselli, Department of Neurology, Ulm University, German Center for Neurodegenerative Diseases (DZNE), Ulm, Germany
"Chemogenetic control of motoneurons: new windows into neurodegeneration" (**S3.2**)

Piotr Krutki, Department of Neurobiology, Poznan University of Physical Education, Poznań, Poland
"Modulation of motoneuron properties by trans-spinal direct current stimulation (tsDCS)" (**S3.3**)

Marcin Bączyk, Department of Neurobiology, Poznan University of Physical Education, Poznań, Poland
"TsDCS in Amyotrophic Lateral Sclerosis – Intrinsic excitability and synaptic excitation" (**S3.4**)

13.30 – 14.00 **Lunch Break** [IP]

14.00 – 15.30 **Poster session 1** [IP]

15.30 – 17.30 **Symposia 4-6** [IP]

Symposium 4 "Molecular biology of autism spectrum disorders" (S4) [IP, room 101]

Chairperson: **Leszek Kaczmarek**, BRAINCITY & Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Speakers: **Claudia Bagni**, Vice-Dean Research and Innovation, Faculty of Biology and Medicine, University of Lausanne, Switzerland & Department of Fundamental Neurosciences, Switzerland
"An altered gene function in autism spectrum disorders" (**S4.1**)

Sumantra Chattarji, Tata Institute of Fundamental Research, Bangalore, Karnataka, India
"Fear and Fragile X Syndrome" (**S4.2**)

Magdalena Dziembowska, Laboratory of Molecular Basis of Synaptic Plasticity, Centre of New Technologies, University of Warsaw, Poland
"The role of mitochondria in the pathomechanism of autism-associated neurodevelopmental disorder" (**S4.3**)

Alicja Puścian, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Center of Excellence for Neural Plasticity and Brain Disorders: BRAINCITY, a Nencki-EMBL Partnership, Warsaw, Poland
"Targeted, symptom-specific, and mechanism-based strategy to remedy cognitive deficits in Fmr1 knock-out mouse model of autism" (**S4.4**)

Symposium 5 "The multifaceted roles of CNS glia: from tumours to neurodegeneration" (S5)
[IP, room 103]

Chairperson: **Aleksandra Rutkowska**, Medical University of Gdańsk, Poland

Speakers: **Aleksandra Rutkowska**, Medical University of Gdańsk, Brain Diseases Center, Gdańsk, Poland
"Can we stimulate remyelination in vivo? A glance at novel therapeutic targets" **(S5.1)**

Maria Velasco-Estevez, H12O-CNIO Hematological Malignancies Group, Clinical Research Unit, Centro Nacional de Investigaciones Oncologicas (CNIO), Madrid, Spain
"DePIEZing the brain: the role of mechanoreceptor Piezo1 in CNS pathological state" **(S5.2)**

Ana Belen Lopez-Rodriguez, Molecular Neuroinflammation and Neuronal Plasticity Research Laboratory, Hospital Universitario Santa Cristina, Instituto de Investigación Sanitaria-Hospital Universitario de la Princesa, Madrid, Spain
"Microglia and Astrocytes: the brain whisperers and keepers" **(S5.3)**

Przemysław Kowiański, Department of Anatomy and Neurobiology,
Medical University of Gdańsk, Poland
"The stimulus-specific character of neuroglial response to cerebral ischemia – a new perspective on old problems?" **(S5.4)**

Symposium 6 "Electrophysiological correlates of the altered states of consciousness" (S6)
[IP, room 105]

Chairperson: **Marek Binder**, Jagiellonian University, Cracow, Poland

Speakers: **Marek Binder and Róża Krycińska**, Institute of Psychology,
Jagiellonian University, Cracow, Poland
"Sensitivity of the gamma-range auditory steady-state responses to fluctuations of awareness following severe brain injury and during general anaesthesia" **(S6.1)**

Urszula Górska-Klimowska, University of Wisconsin-Madison, USA
"Neural signatures of conscious and unconscious seizures as compared to natural sleep" **(S6.2)**

Inga Griskova-Bulanova, Life Sciences Centre, Vilnius University, Vilnius, Lithuania
and National Institute of Mental Health, Klecany, Czechia
"Psilocybin-mediated changes of gamma-range auditory steady-state responses" **(S6.3)**

Čestmír Vejmola, National Institute of Mental Health, Klecany and Third Faculty of Medicine, Charles University, Prague, Czechia
"Psilocin-induced alterations of visual perception in rats evaluated by visual evoked potentials" **(S6.4)**

17.30 – 18.00 **Coffee Break** [IP]

18.00 – 19.00 **Adolf Beck Award Ceremony. Special Lecture** [ON]

Speaker: **Daniel Wójcik**, Laboratory of Neuroinformatics, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland
Title: "What we can and what we cannot see with extracellular multielectrodes in the brain"
Introduced by: **Grzegorz Hess**

20.00 – 22.00 **Tour of Toruń (Old Town) or Astronomical Observatory**

22.09.2023, FRIDAY

9.00 – 10.00 **Plenary Lecture 3 (PL3)** [ON]

Speaker: **Inbal Goshen**, Edmond and Lily Safra Center for Brain Sciences (ELSC), The Hebrew University of Jerusalem, Israel
Title: "Astrocytes in high brain function"
Introduced by: **Michał Ślęzak**

10.00 – 11.00 **Young Investigator Award Ceremony** [ON]

Chairperson: **Elżbieta Pyza**

Speakers: **Paulina Kamińska**, Warsaw PhD School in Natural and Biomedical Sciences at the Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Klaudia Radoszkiewicz, Doctoral School of Translational Medicine run by the Center for Postgraduate Medical Education and the Mossakowski Medical Research Institute PAS, Warsaw, Poland

Martyna Podgajna, Doctoral School of Translational Medicine run by the Center for Postgraduate Medical Education and the Mossakowski Medical Research Institute PAS, Warsaw, Poland

11.00 – 11.30 **Coffee Break** [IP]

11.30 – 13.30 **Symposia 7-9** [IP]

Symposium 7 "Regulation of Brain Metabolism and Neural Networks by Astrocytes" (S7) [IP, room 101]

Chairperson: **Katarzyna Terejko**, Łukasiewicz – PORT Polish Center for Technology Development, Poland

Speakers: **Amit Agarwal**, The Chica and Heinz Schaller Research Group, Institute for Anatomy and Cell Biology, Heidelberg University, Germany
*"Decoding mitochondrial structure and calcium dynamics in astrocytes" (**S7.1**)*

Olga Barca Mayo, Circadian and Glial Biology Lab, Physiology Department, Molecular Medicine and Chronic Diseases Research Centre (CiMUS), University of Santiago de Compostela, Santiago de Compostela, Spain
*"Astrocytic nutrient signaling pathways and entrainment of circadian behavior" (**S7.2**)*

Magdalena Zielińska, Department of Neurotoxicology, Mossakowski Medical Research Institute Polish Academy of Sciences, Warsaw, Poland
*"Dysregulation of astrocytic glutamine transport in hyperammonemic brain edema" (**S7.3**)*

Dominika Drulis-Fajdasz, Department of Molecular Physiology and Neurobiology, University of Wroclaw, Poland
*"Age-related decline in memory formation is accompanied by the changes in proteomic and metabolic profile" (**S7.4**)*

Symposium 8 "From Retina to Cortex: Processing of the visual information in healthy and diseased conditions" (S8) [IP, room 103]

Chairperson: **Andrzej Foik**, International Centre for Translational Eye Research, ICTER & Institute of Physical Chemistry PAS, Poland

Speakers: **Patrycja Orłowska-Feuer**, The University of Manchester, Manchester, United Kingdom
*"The circadian/visual system of diurnal rodents – exciting times ahead" (***S8.1***)*

Andrea Curatolo, International Centre for Translational Eye Research, Institute of Physical Chemistry PAS, Warsaw, Poland
*"Ultrafast volumetric imaging of the mouse retina for monitoring hemodynamic changes and the functional response to light stimulation" (***S8.2***)*

Henri Leinonen, University of Eastern Finland, Kuopio, Finland
*"Retinal homeostatic plasticity" (***S8.3***)*

Andrzej Foik, International Centre for Translational Eye Research, ICTER & Institute of Physical Chemistry PAS, Warsaw, Poland
*"Visual responses characteristics in healthy, diseased and treated animals" (***S8.4***)*

Symposium 9 "Artificial intelligence, machine learning and other modern techniques in neurobiological research" (S9) [IP, room 105]

Chairperson: **Anna Błasiak**

Speakers: **Andrzej Opala**, Institute of Experimental Physics, Faculty of Physics, University of Warsaw, Warsaw, Poland and Institute of Physics, Polish Academy of Sciences, Warsaw, Poland
*"Optical neural networks" (***S9.1***)*

Marieke van Vugt, University of Groningen, The Netherlands
*"Using machine learning to detect mind-wandering" (***S9.2***)*

Ellen Boven, Neural Dynamics Transition fellow, School of Physiology, Pharmacology & Neuroscience, University of Bristol, United Kingdom
*"AI-driven modelling for brain-wide credit assignment" (***S9.3***)*

Melisa Maidana Capitan, Neural Networks of Memory Lab, Donders Institute, Nijmegen, The Netherlands; Laboratory of Sensory Perception Mechanisms, Center for Social and Affective Neuroscience, Linköping University, Sweden
*"Latent variables estimation for studying complex behaviors in mice" (***S9.4***)*

13.30 – 14.00 **Lunch Break** [IP]

14.00 – 15.30 **Poster session 2** [IP]

15.30 – 17.30 **Symposia 10-12** [IP]

Symposium 10 "Neural and real-life correlates of social interactions" (S10) [IP, room 101]

Chairperson: **Agnieszka Pluta**, University of Warsaw and University of California, Los Angeles, USA

Speakers: **Gianluca Esposito**, Nanyang Technological University, Singapore & University of Trento, Italy
"Exploring neural correlates of role-play using hyperscanning fNIRS" **(S10.1)**

Bear Goldstein, University of California, Los Angeles, USA
"Neural synchrony when executives pitch each other ideas: Effects of group composition and perceptions of value" **(S10.2)**

Grace Qiyuan Miao, University of California, Los Angeles, USA
"Shallow or deep conversations? Interpersonal neural synchronization as biological mechanism for emergence of good social relationships" **(S10.3)**

Agnieszka Pluta, University of Warsaw, Poland; Bioimaging Research Center, Institute of Physiology and Pathology of Hearing, Kajetany/Warsaw, Poland; University of California, Los Angeles, USA
"Theory of mind and parental mental-state talk in children with cochlear implants" **(S10.4)**

Symposium 11 "mTOR in physiology and pathology of the nervous system" (S11) [IP, room 103]

Chairpersons: **Marcin Lipiec and Adam Gorlewicz**, BRAINCITY & Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Speakers: **Manuel F. López-Aranda**, University of California, Department of Neurobiology, Gonda Neuroscience and Genetics Center Los Angeles (UCLA), USA
"Post-natal immune activation in a mouse model of tuberous sclerosis results in sexual dimorphic microglia dependent social memory deficits" **(S11.1)**

Jacek Jaworski, Laboratory of Molecular and Cellular Neurobiology, International Institute of Molecular and Cell Biology, Warsaw, Poland
"Contribution of nuclear mTOR activities to neuronal physiology and mTORopathies" **(S11.2)**

Helen Bateup, Department of Molecular & Cell Biology, University of California, Berkeley, USA
"Manipulating Raptor as a therapeutic strategy for Tuberous Sclerosis Complex" **(S11.3)**

Katarzyna Kotulska, Department of Neurology and Epileptology, The Children's Memorial Health Institute, Warsaw, Poland
"mTOR and epilepsy in humans: from pathology to treatment of seizures and preventive strategies" **(S11.4)**

Symposium 12 "Understanding the Blind Brain" (S12) [IP, room 105]

Chairperson: **Artur Marchewka**, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Speakers: **Stefania Mattioni**, Department of Experimental Psychology, UGent; Center for Cognitive Neuroscience (CCN), UGent, Gent, Belgium
Categorical coding in the ventral occipito-temporal cortex (VOTC) following transient early blindness" (**S12.1**)

Maria Czarnecka, Institute of Psychology, Jagiellonian University, Cracow, Poland
"The correlation between the cortical thickness and the functional activation in language tasks in the occipital cortex of Blind adults" (**S12.2**)

Łukasz Bola, Institute of Psychology, Polish Academy of Sciences, Warsaw, Poland
"Decoding spoken words in visual cortex of sighted and blind individuals" (**S12.3**)

Jacek Matuszewski, Łukasz Bola, Olivier Collignon, Artur Marchewka, Institute for Research in Psychology (IPSY), Université Catholique de Louvain, Louvain-la-Neuve, Belgium
"Sensory-specific computations of the occipital cortex during reading and speech processing in congenital blindness" (**S12.4**)

17.30 – 18.00 **Coffee Break** [IP]

18.00 – 19.00 **Plenary Lecture 4 (PL4)** [ON]

Speaker: **Christian Keysers**, Netherlands Institute for Neuroscience, KNAW, Amsterdam, The Netherlands and Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands
Title: "A cross-species approach to empathy and prosociality"
Introduced by: **Ewelina Knapska**

20.00 – ... **Gala Dinner**

23.09.2023, SATURDAY

9.00 – 10.00 **Plenary Lecture 5 (PL5)** [ON]

Speaker: **Maria Grazia Spillantini**, Department of Clinical Neurosciences, Clifford Allbutt Building, Cambridge University, United Kingdom
Title: "Protein aggregates and their role in neurodegenerative diseases"
Introduced by: **Grzegorz Kreiner** and **Agnieszka Zelek-Molik**

10.00 – 11.00 **IBRO-sponsored session: „Funding programs available within IBRO"** [ON]

Speaker: **José L. Lanciego**, CNS Gene Therapy Program, Center for Applied Medical Research (CIMA), University of Navarra, Pamplona, Spain. A director of the Pan-European Committee of the International Brain Research Organization (PERC-IBRO)
Introduced by: **Rafał Ryguła**

11.00 – 11.30 **Coffee Break** [IP]

11.30 – 13.30 **Symposia 13-15** [IP]

Symposium 13 "Neuronal mechanisms underlying social behaviors" (S13) [IP, room 101]

Chairperson: **Jan Rodriguez Parkitna**, Institute of Pharmacology PAS, Cracow, Poland

Speakers:

Diego Scheggia, Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy
*"Neural circuits for social decision-making" (**S13.1**)*

Cristina Marquez, DYNABrain ERA Chair holder Center for Neuroscience and Cell Biology, CNC-UC, Coimbra, Portugal
*"Social decision-making in foraging contexts" (**S13.2**)*

Zofia Harda, Department of Molecular Neuropharmacology, Maj Institute of Pharmacology of the PAS, Cracow, Poland
*"Social reward changes in adolescence" (**S13.3**)*

Daniel Wójcik, Laboratory of Neuroinformatics, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland
*"Modeling social effects in mice learning in intelligent cages" (**S13.4**)*

Symposium 14 "Clock ticking in health and disease" (S14) [IP, room 103]

Chairperson: **Milena Damulewicz**, Jagiellonian University, Cracow, Poland

Speakers:

Kazue Semba, Department of Medical Neuroscience, Dalhousie University, Halifax, Canada
*"Sleep/wake-dependent astrocytic plasticity at synapses to orexin and MCH neurons" (**S14.1**)*

Marco Brancaccio, Department of Brain Sciences, Imperial College, London, United Kingdom
*"Circadian timekeeping in glia in brain health and disease" (**S14.2**)*

Ezio Rosato, Department of Genetics, Leicester University, Leicester, United Kingdom
*"The clock gene period is required for genome integrity in neuronal progenitor cells in Drosophila" (**S14.3**)*

Milena Damulewicz, Department of Cell Biology and Imaging, Jagiellonian University, Cracow, Poland
*"Multicellular regulation of circadian neuronal plasticity" (**S14.4**)*

Symposium 15 "The advanced methods of EEG signal processing in clinical neuropsychology" (S15) [IP, room 105]

Chairpersons: **Tomasz Piotrowski and Monika Lewandowska**, Nicolaus Copernicus University in Toruń, Poland

Speakers: **Maryna Kapitonova**, Neuromedical AI Lab, Department of Neurosurgery, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany; IMBIT//BrainLinks-BrainTools, Albert-Ludwigs-University, Freiburg, Germany
"EEG Brain Mapping with Interpretable Deep Learning" **(S15.1)**

Tomasz M. Rutkowski, RIKEN AIP, Tokyo, Japan, The University of Tokyo, Tokyo, Japan; Nicolaus Copernicus University in Toruń, Torun, Poland
"Machine Learning Application to Process EEG for Multisensory Reactive BCI for Control and Passive Mode for Dementia Neuro-biomarker Elucidation" **(S15.2)**

Jacek Rogala, Bioimaging Research Center, World Hearing Center, Institute of Physiology and Pathology of Hearing, Warsaw/Kajetany, Poland; The Center for Systemic Risk Analysis, Faculty of 'Artes Liberales', University of Warsaw, Warsaw, Poland
"Decoding working memory-related information from repeated psychophysiological EEG experiments using convolutional and contrastive neural networks" **(S15.3)**

Michał Konrad Komorowski, Faculty of Philosophy and Social Sciences, Institute of Information and Communication Research, Nicolaus Copernicus University in Toruń, Poland; Neurocognitive Laboratory, Centre for Modern Interdisciplinary Technologies, Nicolaus Copernicus University, Toruń, Poland; Department of Informatics, Faculty of Physics, Astronomy, and Informatics, Nicolaus Copernicus University, Toruń, Poland
"ToFFi Toolbox for EEG/MEG-based brain spectral fingerprinting" **(S15.4)**

13.30 – 14.30 **Lunch Break** [IP]

14.30 – 15.30 **Plenary Lecture 6 (PL6)** [ON]

Speaker: **Bożena Kamińska-Kaczmarek**, Nencki Institute of Experimental Biology, Warsaw, Poland
Title: "New insights of the roles of microglia in neuroinflammation, depression and aging brain – enlightenments from single-cell omics"
Introduced by: **Elżbieta Pyza**

15.30 – 16.00 **Closing Ceremony**

Chairpersons: **Irena Nalepa and Elżbieta Pyza**

16.30 – 19.00 **Workshop "Biostatistics – Made Ridiculously Simple"** [IP, room 120]

16.30 – 19.00 **Workshops "ScienceDirect – find your path from hypothesis to discovery. How can I use the world's scientific databases to advance my research? Discover Scopus and ScienceDirect"** [IP, room 121]

POSTER SESSION I

P1. DEVELOPMENT

P1.1. **In utero electroporation of TBC1D5-GAP impairs multipolar to bipolar transition in migrating neurons**
Oliver Tkaczyk, Jacek Jaworski

P1.2. **Maternal, embryonic, and placental contributions to neurodevelopmental programming in the BTBR mouse model of autism: a multi-developmental stage study**
Silvestre Sampino, Maria Pia Viscomi, Joanna Czyrska, Dominika Żbikowska, Elżbieta Wenta-Muchalska, Agnieszka Bernat-Wójtowska, Karolina Król-Szmajda, Małgorzata Cybulska, Dawid Winiarczyk, Marta M. Ziętek

P1.3. **Neural correlates of changes in the rewarding properties of social interactions occurring during adolescence**
Karolina Przyborowicz, Klaudia Misiołek, Marta Klimczak, Łukasz Szumiec, Magdalena Chrószcz, Maria Kaczmarczyk-Jarosz, Barbara Ziółkowska, Julia Netczuk, Rafał Ryguła, Jan Rodriguez Parkitna, Zofia Harda

P1.4. **Quality of dyadic interaction and theta power distribution in occipital and frontal areas of infant brain can be used as early indicators of autism outcomes at 3 years of age at an elevated likelihood for ASD**
Tanaya Batabyal, Rianne Haartsen, Eirini Papageorgiou, Ming Wei Wan, Greg Pasco, Tony Charman, Przemysław Tomalski, Anna Anzulewicz, Kalinka Timmer, Mark H. Johnson, Emily J.H. Jones

P1.5. **Serum response factor is essential for developmental synaptic maturation in the hippocampus**
Matylda Roszkowska, Anna Krysiak, Anna Beroun, Karolina Nader, Martyna Pekala, Jacek Jaworski, Tomasz Wojtowicz, Ludwika Kondrakiewicz, Alicja Puścian, Ewelina Knapska, Leszek Kaczmarek, Katarzyna Kalita

P2. GENETICS IN NEUROPATHOLOGY

P2.1. **KIF3A, KIF3C and KIF21B are involved in tuberous sclerosis complex abnormal neuronal phenotype**
Jan Węsławski, Joanna Lipka, Jacek Jaworski

Flashtalks' session

P3. NEUROSCIENCE METHODS

P3.1. **Do they talk? Novel approach to study neuronal maturation in brain organoids**
Bogna Badyra, Matylda Roszkowska, Karolina Protokowicz, Dominika Kurpiewska, Marcin Barański, Ewa Liszewska, Jacek Jaworski, Leszek Kaczmarek

P3.2. **Impaired modulation of movement-related EEG beta oscillations is associated with dopamine deficiency in the posterior putamen and with declined manual dexterity in Parkinson's disease**
Karolina Lorek, Joanna Mączewska, Leszek Królicki, Małgorzata Chalimoniuk, Józef Langfort, Magdalena Siemiatycka, Katarzyna Kisiel-Sajewicz, Jarosław Marusiak

P3.3. **Unveiling the *in vivo* antidepressant properties of gyrophoric acid, a lichen secondary metabolite**
Nicol Urbanska, Patrik Simko, Rastislav Jendzelovsky, Zuzana Jendzelovska, Terezia Kiskova

P3.4. **Utilizing a novel bioorthogonal probe to study the dynamics of certain post-translational modification in hippocampal subregions in response to excitotoxic stimuli**
Aleksandra Owczarek, Remigiusz Serwa, Michał Węgrzynowicz

P4. COGNITION AND BEHAVIOR

P4.1. **The effect of phencyclidine administration in the early postnatal period on the levels of glutathione and sulfur amino acids in the rat brain as a potential causative factor underlying schizophrenia-like behavior in adulthood**
Zofia Rogóż, Kinga Kamińska, Magdalena Górny, Małgorzata Iciek, Elżbieta Lorenc-Koci

P4.2. **Coming together – the neural dynamics of transition from out-group reserve to in-group fellowship**
Anjaly Yadav, Mateusz Rycerz, Fahmida Haque, Anna Bryksa, Alicja Puścian

P4.3. **Is the triple network dynamics a frame associated to the disturbance of temporal experience in schizophrenia? A kinaesthesia based phenomenological hypothesis**
Camilo Sanchez, Marcin Moskalewicz, Drozdstoj Stojanov
POSTER WITHDRAWN

P4.4. **MMP-9 mediates behavioral alterations after bacteria-like inflammation in early life**
Karolina Protokowicz, Leszek Kaczmarek

P4.5. **Impact of regular cycling training on cognitive control: a preliminary data from a longitudinal randomized controlled trial**
Gabriela Rajtar, Michał Marzec-Remiszewiski, Tomasz S. Ligęza

P4.6. **Effects of atranorin on behavioral patterns in experimental animals: investigating the pharmacological properties and potential antidepressant applications**
Patrik Simko, Simona Mattova, Nicol Urbanska, Terezia Kiskova

P4.7. **Peer influence on reward learning of mice in Intellicages allows to recover their social structure**
Michał Lenarczyk, Bartosz Jura, Zofia Harda, Magalena Ziemiańska, Łukasz Szumiec, Jan Rodriguez Parkitna, Daniel Wójcik

P4.8. **Lexical search based on letter cues is more demanding than based on category cues: evidence from fMRI**
Piotr Górniak, Agata Wolna, Zofia Wodniecka

P4.9. **ERP similarities and differences between Simon, flanker and multi-source conflicts: the same sequence but conflict-specific intensity of cognitive processes**
Ingrida Antonova, Katarzyna Paluch, Patrycja Dzianok, Jan Nikadon, Jakub Wojciechowski, Katarzyna Jurewicz, Ewa Kublik

P4.10. **Synaptic plasticity impairment rescue in an idiopathic model of autism spectrum disorder**
Ksenia Meyza, Tomasz Nikolaev, Tomasz Górkiewicz, Klaudia Nowicka, Maciej Winiarski, Maria Wołyniak, Małgorzata Śliwińska, Joanna Jędrzejewska-Szmek, Ewelina Knapska

P4.11. **Chemogenetic inhibition of the VTA-ACC pathway decreases motivation for social interaction in C57BL/6 mice**
Marcin Lipiec, Asia Macaione, Mohammad Abdelfattah, Anju Cyriac, Ewelina Knapska

P4.12. **Changes in appetitive associative learning in compulsive sexual behavior disorder – fMRI study**
Jakub Wojciechowski, Małgorzata Draps, Ewa Kublik, Tomasz Wolak, Mateusz Gola

P4.13. **Social Box as a tool to study complex social behavior in mice**
Bartosz Zglinicki, Patrycja Ziuzia, Mathias Schmidt, Michał Ślęzak

P4.14. **Effect of chronotype on sleep deprivation tolerance**
Karolina Warzecha, Halszka Kontrymowicz-Ogińska

P5. NEUROPSYCHOLOGY

P5.1. **From genes to brain function: Unveiling the impact of Alzheimer's disease risk-genes on resting-state EEG/fMRI features in non-demented middle-aged individuals**
Patrycja Dzianok, Jakub Wojciechowski, Tomasz Wolak, Ewa Kublik

P5.2. **The relationship between general cognitive functioning, numerosity comparison ability and cognitive strategies in elderly people**
Jakub Słupczewski, Małgorzata Gut, Jacek Matulewski, Adam Tarnowski

P5.3. **Altered gait parameters under spatial navigation task in older adults with subjective cognitive complaints and medial temporal atrophy**
Natalia Anna Pawlaczyk, Rafał Milner, Magdalena Szmytke, Bartłomiej Kiljanek, Bibianna Bałaj, Monika Lewandowska

P5.4. **Electrophysiological assessment of bio-behavioral personality systems? Revised Reinforcement Sensitivity Theory and Feedback Related Negativity**
Julia Zaborowska, Sławomir Duda, Krzysztof Tołpa, Joanna Dreszer, Rafał Milner

P5.5. **BOLD correlates of Simon and flanker conflicts and time-on-task effects in extended multi-source interference task**
Jakub Wojciechowski, Katarzyna Jurewicz, Patrycja Dzianok, Ingrida Antonova, Katarzyna Paluch, Tomasz Wolak, Ewa Kublik

P5.6. **Effectiveness of the cognitive training with the use of the mathematical computer game in children with dyscalculia risk**
Małgorzata Gut, Katarzyna Mańkowska, Jakub Słupczewski, Jacek Matulewski

P5.7. **Neurodynamics of divergent thinking: an EEG microstate analysis**
Ewa Ratajczak, Martyna Olszewska

P6. DISORDERS OF THE NERVOUS SYSTEM

P6.1. **Induced mTOR pathway hyperactivity in dentate granule cells leads to the impairment of pattern separation in mice**
Farzad Khanipour, Karol Sadowski, Adam Gorlewicz

P6.2. **The role of Brg1 in the development of seizure-like behavior in zebrafish larvae**
Roberto Pagano, Justyna Zmorzyńska, Jacek Jaworski

P6.3. **Comparative transcriptomic analysis of mature rat neuron models of induced instability of the dendritic arbors**
Juan Zeng, Magdalena Mlostek, Katarzyna Misztal, Malgorzata Urbanska, Jacek Jaworski

P6.4. **Anxiolytic and antidepressant activity of new pyrrolidine derivative with 5-HT1A receptor interaction in mice**
Jolanta Orzelska-Górka, Claudia Sorbi, Silvia Franchini, Marta Kruk-Słomka, Ewa Kędzierska, Grażyna Biała

P6.5. **Synthesis and pharmacological evaluation of some novel arylpiperazine derivatives**
Ewa Kędzierska, Jolanta Orzelska-Górka, Marta Kruk-Słomka, Jolanta Kotlińska

P6.6. **Changes in brain orexin system in a rat model of depression induced by prenatal administration of dexamethasone**
Katarzyna Głombik, Magdalena Kukla-Bartoszek, Katarzyna Curzytek, Agnieszka Basta-Kaim

P6.7. **Region specific alteration and activation of protein tyrosine kinase 2 beta in temporal lobe epilepsy**
Ozasvi R Shanker, Sonali Kumar, Jyotirmoy Banerjee, Manjari Tripathi, Sarat P. Chandra, Aparna Banerjee Dixit
POSTER WITHDRAWN

P6.8. **Searching for epileptogenesis/epilepsy biomarkers – circulating microRNA levels changes in the rat model of temporal lobe epilepsy**
Kinga Szydłowska, Anna Bot, Karolina Nizińska, Maciej Olszewski, Katarzyna Łukasiuk

P6.9. **A new pathogenic mechanism for a rare genetic form of hereditary spastic paraplegia (aka SINO syndrome): mutated Kidins220 accumulates in cells and disrupts intracellular interactions *via* liquid-liquid phase separation**
Alicja Krawczun-Rygmaczewska, Martina Albini, Fabio Benfenati, Fabrizia Cesca

P6.10. **Altered histone deacetylase 4 (HDAC4) levels and dysregulated interaction with a non-histone substrate in temporal lobe epilepsy**
Sonali Kumar, Ozasvi R Shanker, Jyotirmoy Banerjee, Manjari Tripathi, Sarat P. Chandra, Aparna Banerjee Dixit
POSTER WITHDRAWN

P6.11. **The lipopolysaccharide-evoked systemic inflammatory response enhances the transcription of CD33 in the mouse hippocampus; the role of the BET proteins**
Grzegorz A. Czapski, Marta Matuszewska, Magdalena Cieślik, Joanna Strosznajder

P6.12. **Bioelectrical brain activity differences in patients with psychosomatic diseases during resting-state paradigm**
Łukasz Grabowski, Marek Chełstowski, Marta Nowacka, Maja Hiszpańska, Krzysztof Tołpa, Monika Lewandowska, Rafał Milner, Jakub Kopowski

P6.13. **Energy metabolism disruption accompanies brain cancer progression in Sprague-Dawley rats**
Terezia Kiskova, Andrea Leskanicova, Zuzana Porvazova, Nicol Urbanska, Patrik Simko, Nela Zidekova, Martin Kertys

P6.14. **Ketogenic diet prevents neuronal loss in contralateral hippocampus but does not change gliosis around lesion site after traumatic brain injury**
Zuzanna Rauk, Gabriela Hatala, Zuzanna Setkowicz-Janeczko

P6.15. **Are interoception processes altered among patients suffering from psychosomatic disorders? A Heart Evoked Potentials study**
Marek Chełstowski, Łukasz Grabowski, Marta Nowacka, Maja Hiszpańska, Krzysztof Tołpa, Monika Lewandowska, Rafał Milner

P7. NEURODEGENERATION AND PROTECTION

P7.1. **HuR silencing promotes retinal ganglion cells degeneration and alleviates the activity of exogenous neuroprotection in glaucoma**
Anna Pacwa, Joanna Machowicz, Piotr Rodak, Bartosz Machna, Klaudia Bugara, Saeed Akhtar, Marialaura Amadio, Joanna Lewin-Kowalik, Adrian Smedowski

P7.2. **Intrastriatal injection of α-synuclein oligomers into mice triggers a decrease in parkin level and evokes an inflammatory response in the striatum and substantia nigra pars compacta**
Anna Wilkaniec, Eva Ruiz-Ortega, Gabriela Olech-Kochańczyk, Grzegorz A. Czapski, Elżbieta Gawinek, Carsten Culmsee, Agata Adamczyk

P7.3. **On the way to a new model of neurodegeneration? First evidence of the expression of GATA1 in the brain**
Martyna Podgajna, Aleksandra Kaczyńska, Francesco Bellomi, Claudia Caturano, Paola Verachi, Michał Węgrzynowicz, Maria Zingariello, Mario Falchi, Anna Rita Franco Migliaccio, Giorgio Vivacqua

P7.4. **Effects of swim training on the skeletal muscles of ALS model mice**
Anbarieh Saadat, Emilia Białobrodzka, Ewa Rodziewicz-Flis, Damian Flis, Wiesław Ziółkowski, Elżbieta Pyza

P7.5. **Ghrelin receptor agonist MK-0677 rescues motor impairments and protects substantia nigra dopamine neurons in mouse α-synuclein aggregation model**
Katarzyna Maziarz, Monika Jankowska–Kiełtyka, Justyna Barut, Gabriela Burda, Małgorzata Figiel, Piotr Chmielarz

P7.6. **Graphene Quantum Dots (GQDs) as a novel approach in preventing α-syn aggregations in α synucleinopathy model of Parkinson's disease**
Anna Alwani, Katarzyna Maziarz, Małgorzata Figiel, Małgorzata Kujawska, Piotr Chmielarz

P7.7. **Evaluation of neurite outgrowth induced by low-basicity 5-HT7 agonists in human neuroblastoma SH-SY5Y cells**
Klaudia Jakubowska, Sławomir Gołda, Adam Hogendorf, Danuta Jantas

P7.8. **Spermidine restores the number of peripheral blood leukocytes and their subsets in rat model of Parkinson's disease**
Beata Grembecka, Joanna Dunacka, Oliwia Harackiewicz, Daria Korewo-Labelle, Irena Majkutewicz, Danuta Wrona

P7.9. **Investigating the CHIP/STUB1 pathway and its impact on neurodegeneration**
Dominika Bedran, Erisa Nita, Ailish Tynan, Artur Piróg, Jakub Faktor, Georges Bedran, Sachin Rote, Kathryn Ball, Ted Hupp

P7.10. **Overexpression of myristoylated Akt protect neurons from alpha-synuclein aggregation independently of its kinase activity**
Piotr Chmielarz, Gabriela Burda, Katarzyna Maziarz, Małgorzata Figiel

P8. GLIAL CELLS

P8.1. **Pro-tumorigenic properties of microglia during glioblastoma progression are promoted by SorLA**
Paulina Kaminska, Peter L. Ovesen, Mateusz Jakiel, Magda Bakun, Tomasz Obrebski, Michal Draminski, Vanessa Schmidt, Bozena Kaminska, Michal Dadlez, Thomas E. Willnow, Anna R. Malik

P8.2. **Role of glial pituicytes in neurohypophyseal synaptic morphogenesis**
Naveen Nedunchezhian

P8.3. **Modulation of HIF1-α signaling pathway affects oligodendrocyte maturation in the *in vitro* model of perinatal asphyxia**
Justyna Janowska, Joanna Sypecka

P8.4. **Induction of clock genes by GR stimulation of astrocytes *in vitro***
Tansu Göver, Paweł Hanus, Agnieszka Krzyżosiak, Kamila Środa-Pomianek, Michał Ślęzak

P8.5. **SorCS2 protects astrocytes from amyloid beta (Ab) – induced stress by modulating p75 NTR signaling**
Ewelina Ziemlińska, Tomasz Obrębski, Vannesa Schmidt, Thomas E. Wilnow, Anna R. Malik

P8.6. **Investigating the mediating role of astrocytes in noradrenergic transmission for neuroprotection**
Justyna Barut, Katarzyna Rafa-Zabłocka, Michał Wilczkowski, Monika Bagińska, Rosanna Parlato, Grzegorz Kreiner

P9. NEURONAL METABOLISM

P9.1. **TCF7L2 thalamic deletion leads to alterations in mice's behavioral profile and brain energy metabolism**
Suelen Baggio, Andrzej Nagalski, Kamil Koziński, Łukasz Szewczyk, Marcin Lipiec, Ben Hur Mussulini, Ksenia Meyza, Ewelina Knapska, Agnieszka Chacińska, Marta Wiśniewska

P10. MOTOR SYSTEMS

P10.1. **Muscle spindles in rat medial gastrocnemius muscle and Ia proprioceptive input to spinal motoneurons in male and female animals**
Jan Celichowski, Magdalena Piotr, Hanna Drzymała-Celichowska, Hanna Jackowiak, Marcin Bączyk, Piotr Krutki

P10.2. **Cortical sources of electrical activity, related to the switching to an alternative motor program in humans**
Olha Korzhyk, Alevtyna Morenko

P10.3. **Effect of locomotor exercise on distribution of VGluT1 and VGluT2 in the lumbar spinal cord of rats with complete spinal cord transection**
Magdalena Paradowska, Karolina Godlewska, Małgorzata Skup, Olga Gajewska-Woźniak

P10.4. **Targeted activation of extensor soleus motoneurons using AAV-mediated TrkB receptor enrichment enhances motor function recovery after spinal cord transection**
Anna Głowacka, Olga Gajewska-Woźniak, Karolina Godlewska, Magdalena Paradowska, Sylwia Wieczorek, Małgorzata Skup

P10.5. **Combined stimulation of extensor soleus motoneurons *via* DREADDs with intermittent treadmill training prevails over long-term locomotor training in maintenance of plantar foot stepping after spinal cord transection**
Olga Gajewska-Woźniak, Benjun Ji, Karolina Godlewska, Magdalena Paradowska, Małgorzata Skup

P11. NEURONAL SYGNALING

P11.1. **Zebrafish synaptosome-post synaptic density ligand-receptor interactome atlas**
Miłosz Chodkowski, Andrzej Zieleziński, Savani Anbalagan

P11.2. **Disinhibition of ryanodine receptors and their overexpression might support calcium wave propagation in neurons and contribute to aberrant calcium homeostasis in the dendritic branch**
Joanna Jędrzejewska-Szmek

P11.3. **Activity-dependent polyadenylation of mRNAs in the rat brain**
Bozena Kuzniewska, Pawel Krawczyk, Francois Pauzin, Jacek Milek, Clive Bramham, Andrzej Dziembowski, Magdalena Dziembowska

P12. PERIPHERAL NERVOUS SYSTEM

P12.1. **Deletion of Diaphanous related formin 1 preserves diabetic peripheral neuropathy in mice – A preliminary study**
Kamila Zglejc-Waszak, Agnieszka Korytko, Andrzej Pomianowski, Judyta Juranek

POSTER SESSION II

P13. STRESS RESEARCH

P13.1. **Lack of mitochondrial chaperone TRAP1 in mice affects neuronal response to stress and mitochondria metabolism**
Aleksandra Stawikowska, Bożena Kuźniewska, Magdalena Dziembowska

P13.2. **The power of model: development of depressive-like behavior in mice exposed to Chronic or Subchronic Social Defeat Stress**
Patrycja Ziuzia, Laura Bergauer, Michał Ślęzak

P13.3. **Effect of variable doses of nickel oxide nanoparticles on behavior, blood biochemistry and markers of oxidative stress from the vital organs of albino mice in a sex specific manner**
Furhan Iqbal
POSTER WITHDRAWN

P13.4. **Distinct microRNA signatures of childhood trauma in human serum and sperm: Implications for potential intergenerational transmission**
Magdalena Gomółka, Weronika Tomaszewska, Adria-Jaume Roura Canalda, Bożena Kamińska-Kaczmarek, Ali Jawaid

P13.5. **Electromagnetic field exposure: adaptive stimulant or co-factor for stress-related diseases?**
Maciej Klimiuk, Hanna Kletkiewicz, Angelika Klimek, Agnieszka Siejka, Justyna Maliszewska, Joanna Wyszkowska, Milena Jankowska, Paulina Idczak, Anna Nowakowska, Maria Stankiewicz, Justyna Rogalska

P13.6. **The immune checkpoint expression in the brain and blood cells is associated with the occurrence of depressive symptoms: a study in an animal model of depression based on Wistar Kyoto rats**
Katarzyna Curzytek, Anna Gąsiorek, Stanisław Malicki, Marta Kubera

P13.7. **Inactivation of α1A-adrenergic receptor affects anxiety- and depressive-like behavior of mice in chronic restraint stress-induced model of depression and modulates citalopram effect on expression of some genes: insights from female α1A knockout mice**
Michał Wilczkowski, Katarzyna Chorązka, Piotr Chmielarz, Katarzyna Maziarz, Adam Bielawski, Katarzyna Rafa-Zabłocka, Monika Bagińska, Agnieszka Zelek-Molik, Irena Nalepa

P13.8. **Potential effect of sleep deprivation on the gut – *Drosophila melanogaster* model**
Joanna Jędrusik, Karolina Warzecha, Milena Damulewicz

P13.9. **Behavioral characteristics of chronic psychosocial crowding stress model in rats**
Agnieszka Zelek-Molik, Weronika Surdej, Agnieszka Potasiewicz, Agnieszka Nikiforuk, Michał Wilczkowski, Irena Nalepa, Grzegorz Kreiner

P14. HOMEOSTATIC AND NEUROENDOCRINE

P14.1. **Effects of a mother's cafeteria diet on histological parameters and the expression of receptors belonging to the kisspeptin system in the testes of the offspring**
Emilia Grzeda, Julia Matuszewska, Dominika Kawka, Monika Kaczmarek, Joanna Śliwowska

P14.2. **Effect of corticosterone on the gene expression in the context of global hippocampal transcription**
Grzegorz Juszczak, Adrian Stankiewicz, Aneta Jaszczyk

P15. NOVEL METHODS AND TECHNOLOGY DEVELOPMENT

P15.1. **Deep learning approaches to identification and delineation of cortical areas in the marmoset cortex**
Agata Kulesza, Sylwia Bednarek, Marcello G.P. Rosa, Piotr Majka

P15.2. **Identification of genes and signaling pathways regulating proliferation and differentiation of rat spinal cord central canal neural progenitor cells**
Krzysztof Miazga, Urszula Sławińska, Marek Bekisz, Małgorzata Zawadzka

P15.3. **Deep learning approaches in observer-independent exploration of cytoarchitectural properties of the non-human primate cerebral cortex**
Adam Datta, Agata Kulesza, Sylwia Bednarek, Marcello G.P. Rosa, Piotr Majka

P15.4. **Analysis of transcriptomes and differentiation fate of embryonic brainstem progenitor cells grown *in vitro* under different experimental conditions**
Urszula Sławińska, Anna Kwaśniewska, Marek Bekisz, Krzysztof Miazga, Małgorzata Zawadzka

P15.5. **Modeling neuroscientific research using virtual reality environments, and examples of VR application areas**
Beata Sokołowska, Ewa Sokołowska

P15.6. **Novel data on the tolerance of cerebellar vessels for temporary occlusion using awake testing**
Natalia Lehman, Chiara Spezzani, Matan Bone, Yana Al-Inaya, Fariba Amiri, Jack Wellington, Monika Martinek, Raghuram Sampath, Kathleen Spears, Meghan Rodriquez, Saleem Abdulrauf
POSTER WITHDRAWN

P16. DISEASE MODELS

P16.1. **Characterization of novel mouse models of tuberous sclerosis for the study of developmental basis of autism spectrum disorder**
Marcin Lipiec, Mohammad Abdelfattah, Karolina Bogaj, Joanna Urban-Ciećko, Mateusz Grabowski, Jarosław Barski, Ewelina Knapska

P16.2. **Social position effect on plasma pro-inflammatory cytokine level after subthalamic nucleus deep brain stimulation applied in a rat model of Parkinson's disease**
Oliwia Harackiewicz, Beata Grembecka, Irena Majkutewicz, Wojciech Glac, Danuta Wrona

P16.3. **N-acetylcysteine and aripiprazole improve social behavior and cognition, and modulate brain BDNF levels in a rat model of schizophrenia**
Elżbieta Lorenc-Koci, Kinga Kamińska, Zofia Rogóż

P16.4. **Increased neuronal activity and mTOR hyperactivation leads to degradation of BAF complex subunit – Brg1**
Shiwani Kumari, Karolina Bogusz, Matylda Macias, Ewa Liszewska, Magdalena Bakun, Justyna Jackiewicz, Weronika Zajko, Jacek Jaworski

P16.5. **The influence of KML-29, inhibitor of endocannabinoids enzymatic degradation, on the different stages of memory and memory disorders provoked by an acute injection of MK-801 in mice**
Marta Kruk-Slomka, Ewa Kedzierska, Jolanta Orzelska-Gorka, Grazyna Biala

P16.6. **NMDA antagonist enhanced-high frequency oscillations (130-180 Hz) in the piriform cortex are driven by the olfactory bulb in freely moving rats**
Jacek Wróbel, Władysław Średniawa, Daniel K. Wójcik, Mark J. Hunt

P16.7. **Role of CXCR4/CXCL12 and CXCR2/CXCL1 signalling in the crosstalk of glial cells in the *in vitro* rat model of neonatal asphyxia**
Justyna Gargas, Justyna Janowska, Malgorzata Ziemka-Nalecz, Joanna Sypecka

P16.8. **Activation of intracellular signaling pathways in motoneurons by synaptic excitation in presymptomatic SOD1-G93A ALS mouse model**
Kamil Grycz, Francesco Roselli, Daniel Zytnicki, Marcin Bączyk

P16.9. **The impact of selective phosphodiesterase-4 inhibitor – Rolipram, and AMPA receptor agonist - ampakine on spinal motoneuron electrophysiological profile in SOD1 G93A mouse model of ALS**
Piotr Zawistowski, Kamil Grycz, Francesco Roselli, Daniel Zytnicki, Marcin Bączyk

P16.10. **The role of PARKIN protein in maintaining circadian rhythmicity in *Drosophila melanogaster***
Kamila Zientara, Milena Damulewicz

P16.11. **TRAP-1 mutant mice – a novel mouse model of autism-associated neurodevelopmental disorder manifest alterations in synaptic mitochondria number**
Marta Magnowska

P17. ELECTROPHYSIOLOGY

P17.1. **Working memory content outside the focus of attention: evidence from single-neuron recordings in humans**
Katarzyna Paluch, Mikołaj Magnuski, Władysław Średniawa, Davor Ivanovski, Wojciech Fortuna, Katarzyna Smarzewska, Paweł Tabakow, Harish Babu, Jan Kamiński

P17.2. **The influence of the cholinergic and relaxin-3 signalling on the activity of interpeduncular nucleus neurons – a possible neuronal substrate for the familiarity/novelty processing**
Gabriela Stopka, Patryk Sambak, Aleksandra Trenk, Anna Gugula, Andrew Gundlach, Mohammad Akhter Hossain, Anna Blasiak

P17.3. **Influence of procaine injection into the unilateral olfactory bulb on the behavioral response elicited by contralateral electrical stimulation of the ventral tegmental area**
Grażyna Jerzemowska, Aleksandra Piwka, Jolanta Orzeł-Gryglewska

P17.4. **Shining the light on the dopaminergic system: electrophysiological insights from VTA/SNc**
Karolina Nowalińska, Magdalena Walczak, Martyna Marzec, Tomasz Błasiak

P17.5. **Learning influences the synaptic inputs and outputs of GABAergic interneurons in the barrel cortex of mice**
Dominik Kanigowski, Joanna Urban-Ciećko

P17.6. **The visual temporal order threshold is positively associated with the multivariate MultiScale Entropy of resting-state EEG activity**
Monika Lewandowska, Marcin Hajnowski, Krzysztof Tołpa, Tomasz Piotrowski, Joanna Dreszer

P17.7. **The physiological and morphological effects of perinatal exposure to fluoxetine in mouse dorsal raphe nucleus serotonergic neurons**
Agnieszka Kania, Bartosz Bobula, Nikola Multan, Michał Kiełbiński, Marcin Siwiec, Grzegorz Hess

P17.8. **Clonidine inhibits interictal epileptiform events in prefrontal cortex pyramidal neurons**
Weronika Kołba, Bartłomiej Szulczyk

P17.9. **Protein S-palmitoylation in hippocampal synaptic plasticity**
Tomasz Wójtowicz, Agata Pytyś, Anna Buszka, Matylda Roszkowska, Eli Kerstein, Rhonda Dzakpasu, Katarzyna Kalita-Bykowska, Jakub Włodarczyk

P17.10. **The boost in initial force developed by fast motor units stimulated with pulses at variable intervals in the rat medial gastrocnemius muscle**
Katarzyna Kryściak, Hanna Drzymała-Celichowska, Jan Celichowski

P17.11. **The effect of TENT2 cytoplasmic poly(A) polymerase knockout on electrophysiological properties of neurons**
Patrycja Wardaszka, Tomasz Wojtowicz, Magdalena Dziembowska

P17.12. **Electrophysiological type-specific modulation of VIP-expressing interneurons through gababrs in the primary somatosensory cortex**
Karolina Bogaj, Joanna Urban-Ciećko

P17.13. **Changes in electrophysiological properties of spinal motoneurons in response to altered levels of BDNF in blood serum and hindlimb muscles. Studies on wild-type and BDNF knockout rats**
Norbert Grzelak, Piotr Krutki, Marcin Bączyk, Dominik Kaczmarek, Włodzimierz Mrówczyński

P17.14. **Short-lasting anosmia in rats after gadolinium infusion to the nares: Preliminary findings**
Wiktoria Podolecka, Mark Hunt

P17.15. **The possible role of NGF and relaxin-3 modulation of interpeduncular nucleus in the control of anxiety and stress related behaviors**
Sylwia Drabik, Aleksandra Trenk, Anna Guguła, Patryk Sambak, Angelika Kaleta, Gabriela Stopka, Anna Błasiak

P18. LEARNING AND BEHAVIOR

P18.1. **Understanding functional brain reorganisation for naturalistic piano playing in novice pianists**
Alicja Olszewska, Maciej Gaca, Dawid Droździel, Agnieszka Widlarz, Aleksandra Herman, Artur Marchewka

P18.2. **Preserved selectivity in occipitotemporal but not temporoparietal cortices in children with reading and spelling deficits**
Agnieszka Dębska, Marta Wójcik, Katarzyna Jednoróg

P18.3. **Involvement on antarior cingulate cortex in social buffering during fear memory extinction**
Tomasz Górkiewicz, Konrad Danielewski, Ksenia Meyza, Ewelina Knapska

P18.4. **Input specificity of NMDA-dependent GABAergic plasticity in the hippocampus**
Grzegorz Wiera, Jadwiga Jabłońska, Jerzy Mozrzymas

P19. MEMORY AND BEHAVIOR

P19.1. **The central role of dopamine in learning and motivation – a theoretical review**
Olgierd Borowiecki

P20. NEURODEGENERATION AND PROTECTION

P20.1. **SUMO-specific protease SENP3 interacts with tau under long-term mitochondrial stress**
Lukasz Samluk, Piotr Ostapczuk, Magdalena Dziembowska

P20.2. **Long-term mitochondrial stress induces early steps of Tau aggregation and triggers responses counteracting Tau aggregation on a bigger scale**
Piotr Ostapczuk, Magdalena Dziembowska, Łukasz Samluk

P20.3. **Depletion of neurodegeneration-associated protein TDP-43 perturbs cellular energy metabolism in motor neurons**
Ismail Gbadamosi, Ali Jawaid

P20.4. **Lipids modulate microglial phagocytosis of amyloid beta**
Izabela Lepiarz-Raba, Taufik Hidayat, Sandra Binias, Bartłomiej Gielniewski, Ali Jawaid

P20.5. **The importance of compartmentation of polyamine metabolism in the hippocampus for the differential sensitivity of CA1-3 regions to excitotoxicity**
Aleksandra Kaczyńska, Małgorzata Beręsewicz-Haller, Aleksandra Owczarek, Katarzyna Skowrońska, Magdalena Zielińska, Barbara Zabłocka, Michał Węgrzynowicz

P20.6. **Protective effect of selected natural compounds against erastin-induced mitochondrial dysfunction in BV2 microglial cells**
Agata Adamczyk, Anna Wilkaniec, Renata Wolińska, Magdalena Bujalska-Zadrożny

P20.7. **GPR183 antagonist prevents immune cell migration to the blood-brain barrier *in vitro* during inflammation**
Fionä Caratis, Bartosz Karaszewski, Tomomi Furihata, Aleksandra Rutkowska

P20.8. **Long-term hyperglycemia affects expression of Diaph1 and its cytoskeleton ligands in epidermis of diabetic patients**
Bernard Kordas, Robert Modzelewski, Wojciech Matuszewski, Jarosław Szuszkiewicz, Michał Załęcki, Joanna Wojtkiewicz, Elżbieta Bandurska-Stankiewicz, Judyta Juranek

P21. THERAPY

P21.1. **Idiosyncrasy of antisense oligonucleotide targeting protein-coding gene embedded with non-coding RNA *in vivo***
Md Hasan Ali, Savani Anbalagan

P21.2. **The influence of cerebrospinal fluid on the therapeutic potential of neural stem cells**
Klaudia Radoszkiewicz, Anna Sarnowska

P22. VISUAL SYSTEM

P22.1. **Tunnel vision in retinitis pigmentosa patients leads to negative contrast motion-acuity impairment: behavioral and fMRI evidence**
Marco Ninghetto, Tomasz Gałecki, Kamil Szulborski, Artur Marchewka, Kalina Burnat
POSTER WITHDRAWN

P22.2. **Usage of novel TRP ion channels combined with Melanopsin to signal transduction**
Anna Galińska, Bartłomiej Bałamut, Jagoda Płaczkiewicz, Andrzej T. Foik

P22.3. **Shedding light on calcium dynamics and membrane potential control with optogenetics**
Bartłomiej Bałamut, Jagoda Płaczkiewicz, Karolina Saran, Andrzej T. Foik

P22.4. **New approach for delivery of gene therapy to cones, using modified rabies virus**
Jagoda Płaczkiewicz, Lucyna Piórkowska, Samuel Du, Krzysztof Palczewski, Andrzej T. Foik

P22.5. **Neural underpinnings of visual awareness investigated with transcranial magnetic stimulation**
Justyna Hobot, Kristian Sandberg, Michał Wierzchoń

P22.6. **Improvement of retinal conductivity by the increase of synaptophysin expression in a mouse model of diabetic retinopathy**
Marita Pietrucha-Dutczak, Radosław Dutczak, Iwona Matuszek

P22.7. **Effect of cholinergic modulation on the visual processing in rat**
Katarzyna Kordecka, Anna Galińska, David Lyon, Andrzej T. Foik

P22.8. **Asymmetry in selective and non-selective covert and overt attention. An EFRP study**
Agnieszka Fudali-Czyż, Marta Szewczyk, Łukasz Grzeczkowski, Paweł Augustynowicz

P23. OTHER

P23.1. **Impact of maternal childhood trauma on metabolic composition and microRNA content of human milk**
Magdalena Gomółka, Patrycja Chudzicka-Ormaniec, Weronika Tomaszewska, Anna Ziomkiewicz-Wichary, Ali Jawaid

P23.2. **Measuring individual preferences for diverse tastes in group-housed mice**
Mateusz Rycerz, Maria Kalinowska, Joanna Sadowska, Alicja Puścian, Fahmida Haque, Anna Bryksa

PLENARY LECTURES

PL1. EVOLUTION OF THALAMOCORTICAL DEVELOPMENT

Zoltan Molnar

Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, United Kingdom

Conscious perception in mammals depends on precise circuit connectivity between the cerebral cortex and thalamus; the evolution and development of these structures are closely linked. During the wiring of reciprocal connections between cortex and thalamus, thalamocortical axons (TCAs) first navigate forebrain regions that had undergone substantial evolutionary modifications. In particular, the organization of the pallial subpallial boundary (PSPB) diverged significantly between mammals, reptiles, and birds. In mammals, transient cell populations in internal capsule and early corticofugal projections from subplate neurons closely interact with TCAs to enable PSPB crossing. Prior to TCA arrival, cortical areas are initially patterned by intrinsic genetic factors. TCAs then innervate cortex in a sensory modality specific manner to refine cortical arealization and form primary sensory areas. Here, I shall review the mechanisms underlying the guidance of TCAs across forebrain boundaries, the implications of PSPB evolution for TCA pathfinding, and the reciprocal influence between TCAs and cortical areas during development.

PL2. NEURAL CIRCUITS FOR GOAL-DIRECTED SENSORIMOTOR TRANSFORMATION

Carl Petersen

EPFL Brain Mind Institute, Lausanne, Switzerland

Precisely wired neuronal circuits process sensory information in a learning- and context-dependent manner in order to govern behavior. Simple whisker-dependent sensory decision-making tasks in mice reveal contributions of distinct cell types and brain regions participating in the conversion of sensory information into goal-directed motor output through reward-based learning. Task learning is accompanied by target-specific routing of sensory information to specific downstream brain regions. Current evidence from investigations of whisker-deflection detection tasks, in which thirsty head-restrained mice learn to lick a reward spout to obtain a water reward, is consistent with the hypothesis of learning-dependent changes in signalling from primary somatosensory barrel cortex to secondary somatosensory cortex and dorsolateral striatum, indirectly recruiting tongue-jaw motor cortex and higher-order cortical regions, such as medial prefrontal cortex and hippocampus. An important challenge for the future is to understand the brainwide neural circuit mechanisms underlying reward-based learning connecting cell type-specific processing of sensory information with the motor neurons ultimately responsible for goal-directed action initiation and motor control.

PL3. ASTROCYTES IN HIGH BRAIN FUNCTION

Inbal Goshen

Edmond and Lily Safra Center for Brain Sciences (ELSC), The Hebrew University of Jerusalem, Israel

In addition to their well characterized supportive and homeostatic roles, pioneering studies have shown that astrocytes directly affect neuronal activity. In recent years, groundbreaking research revealed many surprising roles for astrocytes in modulating neuronal activity and even behavior. To directly and specifically modulate astrocytic activity we employed a chemogenetic approach: We expressed the Gq-coupled designer receptor hM3Dq or the Gi-coupled designer receptor hM4Di in astrocytes, which allowed their time-restricted activation or inhibition (respectively) by the application of the designer drug clozapine-N-oxide. We discovered that *in vivo*, astrocytic Gq activation enhanced memory allocation, and memory performance, also in Alzheimer mice (non-published data). On the other hand, astrocytic Gi pathway activation during memory acquisition impairs remote, but not recent, recall. We show that this effect is mediated by a specific disrupting of the projection from the hippocampus to the anterior cingulate cortex by astrocytes.

What other high brain functions can astrocytes affect? We chronically imaged dozens of CA1 astrocytes using 2-photon microscopy, in mice that ran on a linear treadmill and proceed in a virtual environment to

obtain water rewards. We find that astrocytic activity persistently ramps towards the reward location in a familiar environment. When the reward location was changed in the same environment or when mice were introduced to a novel context, the ramping was not apparent. Following additional training, as the mice were familiarized with the new reward location or novel context, the ramping was reestablished, suggesting that spatial modulation of astrocytic activity is experience dependent. This is the first indication that astrocytes can encode position related information in learnt spatial contexts, thus broadening their known computational abilities, and their role in cognitive functions. We are continuing to look for higher brain function (now – memory engrams!, another piece of non-published data that I will present) in which astrocytes are involved.

PL4. A CROSS-SPECIES APPROACH TO EMPATHY AND PROSOCIALITY

Christian Keysers[1,2]

[1]Netherlands Institute for Neuroscience, KNAW, Amsterdam, The Netherlands, [2]Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands

How does our brain make us feel what others feel? How does it motivate us to help others? In humans, the somatosensory, insular and cingulate cortices are activated both when experiencing pain and while witnessing other do so. How and whether such vicarious activations cause us to share the distress of others and help remains difficult to test in humans. I will present a series of experiments showing that altering brain activity in these brain regions does alter emotional contagion and prosociality. In humans, activity in the somatosensory cortex of observers predicts helping and perturbing that activity perturbs helping. Single cell recordings in rats show that neurons involved in an animal's own pain become reactivated while the animal witnesses another animal in pain. Strikingly, this occurs in area 24, the rodent homologue of the anterior cingulate cortex in which humans show activations while witnessing the pain of others. Rats normally freeze while witness a conspecific receiving footshocks – evidence of emotional contagion – and deactivating area 24 reduces such vicarious freezing demonstrating the causal role of this region in sharing the emotions of others. These data show the existence of an evolutionarily conserved mechanism that maps the pain of others onto an observer's own pain circuitry and trigger emotional contagion. Finally, when a rat can choose between a lever that produces food for the rat itself, and one that produces food and triggers a footshock to another animal, rats learn to avoid the shock-lever. Deactivating area 24 abolishes this harm aversion, suggesting a causal link between emotional contagion and helping. In the light of these experiments, I will suggest that emotion sharing is an evolutionarily conserved mechanism that allows animals and humans to better prepare for yet unseen dangers by tuning into the state of those that have already detected them. This selfishly beneficial mechanism can promote prosociality, but does so in fewer animals and situations than the emotional contagion itself.

PL5. PROTEIN AGGREGATES AND THEIR ROLE IN NEURODEGENERATIVE DISEASES

Maria Grazia Spillantini

Department of Clinical Neurosciences, Clifford Allbutt Building, University of Cambridge, Cambridge, United Kingdom

Several neurodegenerative diseases of the brain are characterized by the presence of intracellular protein inclusions. These inclusions were described at the beginning of last century as characteristic neuropathological features for diseases such as Alzheimer's disease, Pick's disease, Parkinson's disease. Now we know that the main component of the Lewy pathology of Parkinson's disease is the protein alpha-synuclein; the same is also true of dementia with Lewy bodies and multiple system atrophy. In Alzheimer's disease, Pick's disease and a number of other diseases, the abnormal filamentous inclusions are made of the microtubule-associated protein tau. Structural studies using cryo-EM have allowed a more refined classification of neurodegenerative diseases based on how tau or alpha-synuclein fold in the aggregates in the various conditions. They have also led to identification of the novel TMEM106B aggregates of yet unclear function. The importance of tau and alpha-synuclein in their specific diseases is supported by findings that genetic mutations in their genes cause neurodegeneration. Study on the distribution of Lewy bodies have suggested that alpha-synuclein aggregation starts at the periphery and spreads to the brain leading on the way to pre-motor and motor symptoms. In the brain of Parkinson's patients, besides the large Lewy body inclusions in the substantia nigra, alpha-synuclein smaller aggregates are present at the synapse and by impairing neurotransmitter release they contribute to the early stages of neurodegeneration. We have reproduced the alpha-synuclein pathology observed in Parkinson's

disease in transgenic models where progressive neurodegeneration can be investigated. Similarly, transgenic mice reproducing tau aggregation reveal that not only neurons are involved in the pathological process but that glial cells also greatly contribute to tau-related neurodegeneration. The link between protein inclusions and neurodegeneration supports them as a target for the treatment of neurodegenerative diseases.

PL6. NEW INSIGHTS OF THE ROLES OF MICROGLIA IN NEUROINFLAMMATION, DEPRESSION AND AGING BRAIN – ENLIGHTENMENTS FROM SINGLE-CELL OMICS

Bożena Kamińska-Kaczmarek

Nencki Institute of Experimental Biology, Warsaw, Poland

Microglia are the resident immune cells of the central nervous system (CNS) that have distinct ontogeny from other tissue macrophages and play a pivotal role in health and disease. Microglia rapidly react to the changes in their microenvironment and adapt a context-specific phenotype. Recent advances in transcriptomics and single-cell technologies allow studying microglia at high resolution and demonstrate the unforeseen heterogeneity of microglia and immune infiltrates in brain pathologies. A precise definition of microglia states is essential to design future immune-modulating therapies. Transcriptomics studies revealed both heterogeneity and plasticity of microglia and myeloid cells in stroke-neuroinflammation. Depression-like behavior is associated with a distinct microglia activation and triggers specific changes in gene expression in experimental mice. The changes could be modulated by behavioral strategies. Survival of microglia in CNS depends on colony stimulating factor 1 receptor (CSF1R) signaling and CSF1R inhibitors depletes 99% of microglia in a few weeks. Microglia repopulate within 1 week upon cessation of treatment in adult mice as demonstrated by TMEM119 immunohistochemical staining and flow cytometry. We investigated the origin and functionality of repopulated microglia in young and old mouse brains using single-cell RNA sequencing (scRNA-seq), flow cytometry and immunohistochemistry. Interestingly, confocal and Scholl analysis of microglial cell body and branching revealed that repopulated cells display distinct morphology. Repopulated microglia originating by proliferation from precursor microglia reconstitute the functional clusters but vary in morphology and express higher levels of pro-inflammatory genes than controls. Intriguingly, in old mice more repopulated microglia persist as proliferating cells and do not reach mature microglia phenotype. The results highlight subtle differences in the repopulation of microglia in aged brains that might contribute to deterioration of its protective functions with aging.

SYMPOSIA LECTURES

S1.1. DISRUPTION OF mGlu5 RECEPTORS IN SOMATOSTATIN-EXPRESSING NEURONS AFFECTS ANXIETY-LIKE BEHAVIORS AND NEURONAL OSCILLATIONS IN PREFRONTAL CORTEX AND VENTRAL HIPPOCAMPUS DURING FEAR MEMORY RETRIEVAL

Pawel M. Matulewicz

Department of Pharmacology, Medical University of Innsbruck, Austria

Altered function of mGlu5 receptors is associated with several neuropsychiatric disorders. Here, we examined the effect of disruption of mGlu5 receptors in somatostatin (SOM)+ neurons on medial prefrontal cortex (mPFC) and ventral hippocampus (vHPC) neuronal oscillatory activity (local field potentials) during a fear memory task. We assessed also the social and anxiety-like behaviors in a sequential battery of behavioral tests. Our results indicate that conditional knockout of mGlu5 receptors in SOM+ neurons affects social processing and anxiety-like behaviors, alters mPFC/vHPC neuronal oscillatory activity and disrupts mPFC-vHPC theta synchronization associated with aversive state processing.

References: Matulewicz, P.; Ramos-Prats, A.; Gómez-Santacana, X.; Llebaria, A.; Ferraguti, F. Control of Theta Oscillatory Activity Underlying Fear Expression by mGlu5 Receptors. Cells 2022, 11, 3555.

S1.2. TRANSLATING NMDA RECEPTOR ANTAGONISM EFFECTS FROM RODENT TO HUMAN AND BACK AGAIN

Kjartan Herrik

Department of Circuit Biology, Lundbeck Research, Lundbeck, Valby, Denmark

Inhibition of NMDA receptor function has been shown to be effective in the treatment of therapy resistant episodes of major depression and prevention of suicidal ideation. However, block of NMDA receptors may also induce acute side effects like hallucinations, vomiting and impaired motor function. To improve antidepressive treatment options there is a need to better our understanding of the acute mode of action as well as downstream longlasting effects. We have attempted to bridge rodent and human studies with resting state EEG as a translational biomarker of the acute effects of NMDA receptor modulation.

References: Nottage JF, Gabay A, De Meyer K, Herrik KF, Bastlund JF, Christensen SR, Gijsen S, Mehta MA. The effect of ketamine and D-cycloserine on the high frequency resting EEG spectrum in humans. Psychopharmacology (Berl). 2022 Nov 19. doi: 10.1007/s00213-022-06272-9. Epub ahead of print.

Bowman C, Richter U, Jones CR, Agerskov C, Herrik KF. Activity-State Dependent Reversal of Ketamine-Induced Resting State EEG Effects by Clozapine and Naltrexone in the Freely Moving Rat. Front Psychiatry. 2022 Jan 27;13: 737295. doi: 10.3389/fpsyt.2022.737295.

Disclosure of potential conflicts of interests: Kjartan Herrik is a Lundbeck A/S employee.

S1.3. SYNCHRONISED HIGH-FREQUENCY OSCILLATIONS IN THE CORTEX-BASAL GANGLIA SYSTEM INDUCED BY PSYCHEDELIC DRUGS

Pär Halje

Group for Integrative Neurophysiology and Neurotechnology, Department of Experimental Medical Science, Lund University, Lund, Sweden

We investigated the effects of classic psychedelics (LSD, DOI) and dissociative psychedelics (ketamine, PCP) on neuronal firing rates and LFPs in several brain structures in freely moving rats. While firing rate modulations were disparate for the two classes of psychedelics, the local field potentials revealed a shared pattern of synchronized high-frequency oscillations. Remarkably, the phase differences between structures were close to zero, corresponding to delays smaller than 1 ms. We propose that the observed hypersynchrony is a key contributor to changes in perception and cognition during psychedelic drug use. Potentially, similar mechanisms induce hallucinations and delusions in psychotic disorders and would constitute promising targets for new antipsychotic treatments.

References: Brys, I., Barrientos, S., Ward, J. E., Wallander, J., Petersson, P., Halje, P. (2022, preprint). Classic and dissociative psychedelics induce simi-

lar hyper-synchronous states in the cognitive-limbic cortex-basal ganglia system. bioRxiv, https://doi.org/10.1101/2022.09.27.509527.

Halje, P., Brys, I., Mariman, J. J., da Cunha, C., Fuentes, R., & Petersson, P. (2019). Oscillations in cortico-basal ganglia circuits: implications for Parkinson's disease and other neurologic and psychiatric conditions. Journal of Neurophysiology, 122(1), 203–231. https://doi.org/10.1152/jn.00590.2018.

S1.4. MODULATION OF KETAMINE-DEPENDENT HIGH-FREQUENCY OSCILLATIONS BY NASAL RESPIRATION

Mark J Hunt

Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Subanesthetic doses of ketamine are widely reported to induce high frequency oscillations (HFO) in diverse brain regions of freely moving rodents. How these oscillations are generated remains a mystery. We have shown previously that the olfactory bulb (OB) plays a crucial role in the generation of ketamine-enhanced HFO. Here, we show that under ketamine-xylazine anesthesia, delivery of air to the nares reliably increases HFO power in the OB, whilst odor delivery had little impact. In freely moving rats, unilateral naris blockade reduced ketamine-enhanced HFO power in the OB, and also the accumbens, and PFC. We conclude that nasal airflow is essential for the emergence of ketamine-enhanced HFO and that activity of the OB can orchestrate HFO in other brain areas.

References: Wróbel J, Średniawa W, Jurkiewicz G, Żygierewicz J, Wójcik DK, Whittington MA, Hunt MJ. Nasal respiration is necessary for ketamine-dependent high frequency network oscillations and behavioral hyperactivity in rats. Sci Rep. 2020 Nov 4;10(1): 18981. doi: 10.1038/s41598-020-75641-1.

S2.1. ASTROCYTIC β-CATENIN PATHWAY – A NEW PLAYER IN THE REGULATION OF BEHAVIOR

Łukasz M. Szewczyk

Centre of New Technologies, University of Warsaw, Poland

The β-catenin pathway is a central regulator of brain development and plays ubiquitous roles across cell types and developmental stages. Genes encoding β-catenin and its nuclear effector – the TCF7L2 transcription factor, contain multiple high-confidence risk mutations linked to neurodevelopmental disorders including autism, what implicates its impact on behavior. However, its omnipresent roles point that overall behavioral might be the resultant of β-catenin action in different brain cell lineages and structures. We showed that the β-catenin *via* TCF7L2 effector plays a central and astrocyte lineage-specific role in brain function and social performance. We found out that coordination of a gliogenic program required for postnatal astrocyte development and functional maturation is tightly regulated by TCF7L2. Deletion in TCF7L2 in postnatal astrocytes led to alterations in astrocyte morphology, physiology, and expression of synapse support genes. Mice lacking TCF7L2 in astrocytes had increased number of excitatory synapses in the somatosensory cortex, increased neuronal activity and exhibited hypersocial behavior when exposed to social stimuli. Our work revealed a new role for developmental β-catenin/TCF7L2 signaling in restricting behavior pointing to its lineage-dependent function in social performance and behaviors.

References: Bem J, Brożko N, Chakraborty C, Lipiec MA, Koziński K, Nagalski A, Szewczyk ŁM, Wiśniewska MB. Wnt/β-catenin signaling in brain development and mental disorders: keeping TCF7L2 in mind. FEBS Lett. 2019 Jul;593(13): 1654-1674. doi: 10.1002/1873-3468.13502.

Szewczyk LM, Lipiec MA, Liszewska E, Urban-Ciecko J, Kondrakiewicz L, Puscian A, Knapska E, Inoue H, Nowakowski TJ, Molofsky AV, Wiśniewska MB. β-catenin signaling *via* astrocyte-encoded TCF7L2 regulates neuronal excitability and social behavior. This article is a preprint on bioRxiv.org; doi: https://doi.org/10.1101/2020.11.28.402099.

S2.2. THYROID HORMONE SIGNALING IN A HUMAN CELLULAR MODEL FOR EARLY BRAIN DEVELOPMENT

Nilhan Gunhanlar

Erasmus University Rotterdam, Medical Center, The Netherlands

Disrupted thyroid hormone (TH) signaling has devastating effects on human neurodevelopment. The molecular mechanisms underlying TH regulation are largely based on animal models. However, animal models are limited in revealing some of the most fundamental aspects of human neurodevelopment. We employed human induced pluripotent stem cell (iPSC) technology to study the effects of TH in a human cellular model for fetal brain development. We observed that TH has a critical role in iPSC-derived neural networks and different TH concentrations change neuron to glia ratio, regulation of gene expression, morphology, synaptogenesis and neuronal functionality. This study provides the molecular underpinnings of the actions of TH in human brain and advance the understanding of TH signaling in human brain in health and disease.

References: Gunhanlar N, Shpak G, van der Kroeg M, Gouty-Colomer LA, Munshi ST, Lendemeijer B, Ghazvini, M, Dupont C, Hoogendijk WJG, Gribnau J, de Vrij FMS, Kushner SA. A simplified protocol for differentiation of electrophysiologically mature neuronal networks from human induced pluripotent stem cells. Mol Psychiatry. 2018 May;23(5): 1336-1344. doi: 10.1038/mp.2017.56.

S2.3. INTRACELLULAR PROTEIN SORTING IN ASTROCYTES SHAPES THEIR PROPERTIES IN POST-ISCHEMIC BRAIN

Anna Malik

Faculty of Biology, University of Warsaw, Poland

Astrocytes actively contribute to brain physiology and pathology. They maintain homeostasis and shape synaptic transmission in the healthy brain, while in brain pathologies they get activated, proliferate and infiltrate damaged tissue to influence the final outcome of the insult. Astrocytes' actions in the diseased brain highly depend on the release of cytokines, chemokines, ECM-remodeling molecules and growth factors. In particular, proteins secreted by astrocytes activated after ischemic stroke take part in regulating angiogenesis, tissue remodeling and inflammation. We have recently discovered that the expression of a 'neuronal' sorting receptor SorCS2 is induced specifically in astrocytes in the post-ischemic brain. We demonstrated a mechanism whereby SorCS2 controls release of angiogenesis-related factor endostatin from astrocytes and influences angiogenesis. Thus, we provided evidence that intracellular protein sorting exerted by SorCS2 shapes astrocytes activity after stroke. Now, we further elucidate the astrocytic roles of SorCS2 with use of *in vitro* and *in vivo* models combined with unbiased mass spectrometry-based approaches.

References: Malik AR, Willnow TE. VPS10P domain receptors: sorting out brain health and disease. Trends Neurosci. 2020 Nov;43(11): 870-885. doi: 10.1016/j.tins.2020.08.003.

Malik AR, Lips J, Gorniak-Walas M, Broekaart DWM, Asaro A, Kuffner MTC, Hoffmann CJ, Kikhia M, Dopatka M, Boehm-Sturm P, Mueller S, Dirnagl U, Aronica E, Harms C, Willnow TE. SorCS2 facilitates release of endostatin from astrocytes and controls post-stroke angiogenesis. Glia. 2020 Jan 3. doi: 10.1002/glia.23778.

S2.4. PARACRINE INTERLEUKIN-6 SIGNALING IN POST-STROKE RECOVERY

Christoph Harms

Charité – Universitätsmedizin Berlin, Center for Stroke Research (CSB), Department of Experimental Neurology, Germany

Paracrine cerebral interleukin 6 (IL-6) is relevant for stroke recovery, but systemic IL-6 elevation may worsen outcome. Hence, paracrine IL-6 response modulation within the neurovascular unit has emerged as an attractive therapeutic approach. We developed a mouse model for inducible astrocytic IL-6 expression (Cx30-Cre-ERT2; FLEX-IL6) and induced IL-6 two days after common carotid artery occlusion. Mass spectrometry of laser capture micro-dissected tissues examined hypo-perfused striatum and contralateral motor cortex proteomes. Cerebral remodeling by paracrine IL-6 increased inter-hemispheric and motor system connectivity. Lithium modulates IL-6 responses and improves stroke outcome. However, lithium may cause serious adverse effects. We discovered that lithium affects IL-6 signaling *via* Zinc finger protein 580 (Zfp580). Zfp580 inactivation was not neurotoxic-free, unlike lithium. Lithium and hypoxia disinhibited IL-6 *via* Zfp580 sup-

pression and post-translational modification by small ubiquitin-like modifier (SUMO). After stroke in mice, loss of Zfp580 reduced paracrine IL-6 and increased IL-6 trans-signaling. Aside from modulating IL-6 signaling, Zfp580 loss improved endothelial resilience to ischemia and was highly neuroprotective, resulting in smaller infarcts and enhanced use-dependent neuroplasticity, all of which led to improved functional outcome. In conclusion, Zfp580 inactivation improved multiple key mechanisms without significant side effects, making it a potentially better stroke recovery treatment target than lithium.

References: Hoffmann CJ, Harms U, Rex A, Szulzewsky F, Wolf SA, Grittner U, et al. Vascular signal transducer and activator of transcription-3 promotes angiogenesis and neuroplasticity long-term after stroke. Circulation. 2015;131: 1772-1782.

Kuffner MTC, Koch SP, Kirchner M, Mueller S, Lips J, An J, et al. Paracrine interleukin 6 induces cerebral remodeling at early stages after unilateral common carotid artery occlusion in mice. Front Cardiovasc Med. 2022;8: 805095.

S3.1. β-ADRENERGIC RECEPTORS INCREASE MOTONEURON EXCITABILITY IN ADULT WT AND SOD MICE

Guillaume Caron

Saints-Pères Paris Institute for the Neurosciences (UMR 8003), Faculty of Exact and Biomedical Sciences, Université Paris Cité, Paris, France

We recently found that enhancing motoneuron excitability through cAMP/PKA pathway confers some neuroprotection in amyotrophic lateral sclerosis (ALS). We now identified β2 and β3 adrenergic receptors (Gs-protein coupled receptors) as new players that provide neuromodulation of motoneuron firing. We used intracellular recordings of spinal motoneurons in anesthetized mice to find that an acute delivery of blood-brain barrier permeable β2 and β3 agonists increases the motoneuron excitability both in WT and mSOD presymptomatic mice. Furthermore, transcriptomic experiments showed an increase of cFos in motoneurons of WT and SOD mice indicating an enhancement of motoneuron activity. We discuss whether β2 and β3 adrenergic receptors might be new therapeutics targets for the treatment of ALS.

References: Bączyk M, Alami NO, Delestrée N, Martinot C, Tang L, Commisso B, Bayer D, Doisne N, Frankel W, Manuel M, Roselli F, Zytnicki D. Synaptic restoration by cAMP/PKA drives activity-dependent neuroprotection to motoneurons in ALS. J Exp Med. 2020 Aug 3;217(8): e20191734. doi: 10.1084/jem.20191734.

S3.2. CHEMOGENETIC CONTROL OF MOTONEURONS: NEW WINDOWS INTO NEURODEGENERATION

Francesco Roselli

Department of Neurology, Ulm University, German Center for Neurodegenerative Diseases (DZNE), Ulm, Germany

Achieving control of individual biological features *in vivo* is critical to dissect pathogenic pathway in animal models without compromising the complexity of the pathophysiology in reduced systems (such as cultured cells). We have used chemogenetics systems based on ligand-gated ion channels or GCPR with mutually orthogonal pharmacology to control excitability and signaling in motoneurons as well as in glial cells in a murine model of ALS, with cell-autonomous or multiplexed, multicellular designs. We have now extended the toolset to include intrabodies and non-conventional chemogenetic systems to control synaptic integrity and intracellular trafficking. We have used these tools to investigate the role of excitability, synaptic integrity, signaling and cell biology in motoneuron degeneration.

References: Bączyk M, Alami NO, Delestrée N, Martinot C, Tang L, Commisso B, Bayer D, Doisne N, Frankel W, Manuel M, Roselli F, Zytnicki D. Synaptic restoration by cAMP/PKA drives activity-dependent neuroprotection to motoneurons in ALS. J Exp Med. 2020 Aug 3;217(8): e20191734. doi: 10.1084/jem.20191734. PMID: 32484501; PMCID: PMC7398175.

Ouali Alami N, Tang L, Wiesner D, Commisso B, Bayer D, Weishaupt J, Dupuis L, Wong P, Baumann B, Wirth T, Boeckers TM, Yilmazer-Hanke D, Ludolph A, Roselli F. Multiplexed chemogenetics in astrocytes and motoneurons restore blood-spinal cord barrier in ALS. Life Sci Alliance. 2020 Sep 8;3(11): e201900571. doi: 10.26508/lsa.201900571.

S3.3. MODULATION OF MOTONEURON PROPERTIES BY TRANS-SPINAL DIRECT CURRENT STIMULATION (tsDCS)

Piotr Krutki

Department of Neurobiology, Poznan University of Physical Education, Poznań, Poland

Externally applied electrical currents gained recognition as a neuromodulatory technique in motor rehabilitation, though our knowledge of how tsDCS affects neuronal networks remains limited. We have performed intracellular motoneuron recordings coupled with spinal polarization *in vivo* in rats to investigate short-term, long-lasting and chronic tsDCS-induced alterations of motoneuron electrophysiological properties. TsDCS evokes polarity-dependent changes in threshold and firing properties of motoneurons which appear immediately after onset of polarization and considerably outlast its duration. The effects of anodal polarization are generally more pronounced and uniform than those evoked by cathodal polarization. Moreover, chronic tsDCS elicits adaptive changes in electrophysiological properties of motoneurons due to repeated alterations in the activity of spinal circuitry.

References: Bączyk M, Drzymała-Celichowska H, Mrówczyński W, Krutki P. Motoneuron firing properties are modified by transspinal direct current stimulation in rats. Journal of Applied Physiology, 2019, 126 (5), 1232-1241. DOI10.1152/japplphysiol.00803.2018.

Bączyk M, Drzymała-Celichowska H, Mrówczyński W, Krutki P. Polarity-dependent adaptations of motoneuron electrophysiological properties after 5-wk transcutaneous spinal direct current stimulation in rats. Journal of Applied Physiology, 2020, 129(4): 646-655. DOI10.1152/japplphysiol.00301.2020.

S3.4. TsDCS IN AMYOTROPHIC LATERAL SCLEROSIS – INTRINSIC EXCITABILITY AND SYNAPTIC EXCITATION

Marcin Bączyk

Department of Neurobiology, Poznan University of Physical Education, Poznań, Poland

Amyotrophic lateral sclerosis (ALS) is a progressive and lethal neurodegenerative disease, characterized by the brain stem and spinal motoneuron (MN) degeneration. Alterations in MN electrophysiological profile are one of the hallmarks of ALS pathophysiology and increasing MN excitability with chemogenetics proved effective in decreasing the disease markers in ALS mouse model. We show that trans-spinal direct current stimulation (tsDCS) significantly alters spinal MNs' electrophysiological profile. Anodal tsDCS increases the amplitudes of monosynaptic Ia EPSPs and facilitates MNs firing in ALS mice both during and after tsDCS application. The effects of cathodal tsDCS are weaker and not long-lasting. Importantly, no long-term effects of tsDCS are seen in WT MNs indicating that ALS cells are highly susceptible to this neuromodulation.

Supported by NCN SONATA 2017/26/D/NZ7/00728.

References: Bączyk M, Alami NO, Delestrée N, Martinot C, Tang L, Commisso B, Bayer D, Doisne N, Frankel W, Manuel M, Roselli F, Zytnicki D. Synaptic restoration by cAMP/PKA drives activity-dependent neuroprotection to motoneurons in ALS. J Exp Med. 2020 Aug 3;217(8): e20191734. doi: 10.1084/jem.20191734.

Jankowiak T, Cholewiński M, Bączyk M. Differential Effects of Invasive Anodal Trans-spinal Direct Current Stimulation on Monosynaptic Excitatory Postsynaptic Potentials, Ia Afferents Excitability, and Motoneuron Intrinsic Properties Between Superoxide Dismutase Type-1 Glycine to Alanine Substitution at Position 93 and Wildtype Mice. Neuroscience. 2022 Aug 21;498: 125-143. DOI: 10.1016/j.neuroscience.2022.06.035.

S4.1. AN ALTERED GENE FUNCTION IN AUTISM SPECTRUM DISORDERS

Claudia Bagni

Vice-Dean Research and Innovation, Faculty of Biology and Medicine, University of Lausanne, Switzerland & Department of Fundamental Neurosciences, Switzerland

Copy-number variants of the *CYFIP1* gene in humans have been linked to autism spectrum disorders (ASD) and schizophrenia (SCZ), two neuropsychiatric disorders characterized by defects in brain connectivity. We have shown that CYFIP1 plays an important role in brain functional connectivity and callosal functions, as well as in the motor coordination, sensorimotor gating and sensory perception, which are also known neuropsychiatric disorder-related symptoms. Furthermore, Drosophila mutants in the homolog of the human CYFIP1

exhibit mitochondrial hyperactivity and altered group behavior and we have identified the regulation of GABA availability by mitochondrial activity as a biologically relevant mechanism and demonstrate its contribution to social behavior. These results show that CYFIP1 deficits compromise brain connectivity and function, which might explain its genetic association to neuropsychiatric disorders.

References: Kanellopoulos AK, Mariano V, Spinazzi M, Woo YJ, McLean C, Pech U, Li KW, Armstrong JD, Giangrande A, Callaerts P, Smit AB, Abrahams BS, Fiala A, Achsel T, Bagni C. Aralar Sequesters GABA into Hyperactive Mitochondria, Causing Social Behavior Deficits. *Cell.* 180: 1178-1197, 2020.

Domínguez-Iturza N, Lo AC, Shah D, Armendáriz M, Vannelli A, Mercaldo V, Trusel M, Li KW, Gastaldo D, Santos AR, Callaerts-Vegh Z, D'Hooge R, Mameli M, Van der Linden A, Smit AB, Achsel T, Bagni C. The autism- and schizophrenia-associated protein CYFIP1 regulates bilateral brain connectivity and behavior. *Nat Commun.* 10: 3454, 2019.

S4.2. FEAR AND FRAGILE X SYNDROME

Sumantra Chattarji

Tata Institute of Fundamental Research, Bellary Road, Bangalore, Karnataka, India

Fragile X syndrome (FXS), a commonly inherited form of autism, is associated with emotional symptoms that implicate the amygdala. However, earlier studies focused on the hippocampus, where FXS defects have been corrected by inhibiting group I metabotropic glutamate receptors (mGluRs). This presentation will report that activation, rather than inhibition, of mGluRs in the amygdala reverses impairments in a rat model of FXS. FXS rats exhibit deficient conditioned fear, and deficient synaptic transmission and plasticity. Presynaptic mGluR5 in the amygdala, activation of which reverses deficient synaptic transmission and plasticity, restores normal fear learning in FXS rats. This highlights the importance of modifying the prevailing mGluR-based framework to include circuit-specific differences in FXS pathophysiology.

References: Fernandes G, Mishra PK, Nawaz MS, Donlin-Asp PG, Rahman MM, Hazra A, Kedia S, Kayenaat A, Songara D, Wyllie DJA, Schuman EM, Kind PC, Chattarji S. Correction of amygdalar dysfunction in a rat model of fragile X syndrome. *Cell Rep.* 37: 109805, 2021.

Yasmin F, Colangeli R, Morena M, Filipski S, van der Stelt M, Pittman QJ, Hillard CJ, Teskey GC, McEwen BS, Hill MN, Chattarji S. Stress-induced modulation of endocannabinoid signaling leads to delayed strengthening of synaptic connectivity in the amygdala. *Proc Natl Acad Sci USA.* 117: 650-655, 2020.

S4.3. THE ROLE OF MITOCHONDRIA IN THE PATHOMECHANISM OF AUTISM-ASSOCIATED NEURODEVELOPMENTAL DISORDER

Magdalena Dziembowska

Laboratory of Molecular Basis of Synaptic Plasticity, Centre of New Technologies, University of Warsaw, Poland

Autism is a neurodevelopmental disorder with a strong genetic background. In the last years, there is growing evidence of mitochondrial disturbance in the ASD. However, causative relations remained to be established. We identified heterozygous de novo Gln639Ter mutation in the *TRAP1* gene encoding mitochondrial chaperone of the HSP90 family in ASD patient whose identical twin brother was healthy. An additional survey of 176 unrelated ASD probands led to the identification of identical TRAP1 variant. To confirm the genotype-phenotype correlation we generated a knock-in TRAP1 p.Gln639Ter mouse which displayed behavioral abnormalities relevant for ASD, especially in males. Thus, TRAP1 Gln639Ter mutation is the first example of monogenic ASD in which disturbed mitochondrial protein homeostasis is causative.

References: Kuzniewska B, Cysewski D, Wasilewski M, Sakowska P, Milek J, Kulinski TM, Winiarski M, Kozielewicz P, Knapska E, Dadlez M, Chacinska A, Dziembowski A, Dziembowska M. Mitochondrial protein biogenesis in the synapse is supported by local translation. *EMBO Rep.* 21: e48882, 2020.

S4.4. TARGETED, SYMPTOM-SPECIFIC, AND MECHANISM-BASED STRATEGY TO REMEDY COGNITIVE DEFICITS IN Fmr1 KNOCK-OUT MOUSE MODEL OF AUTISM

Alicja Puścian

Nencki Institute, Polish Academy of Sciences, Center of Excellence for Neural Plasticity and Brain Disorders: BRAINCITY, a Nencki-EMBL Partnership, Warsaw, Poland

Breaking an impasse in finding mechanism-based therapies of neurodevelopmental disorders requires a strategic shift towards alleviating individual symptoms. We will present a symptom and circuit-specific approach to rescue deficits of learning in Fmr1 knockout mice, a model of Fragile X syndrome, the most common monogenetic cause of inherited mental disability and autism. We will show that central amygdala-targeted delivery of TIMP-1 designer nanoparticles reverses impaired cognition, while having no impact on social deficits, hence corroborating specificity of the proposed approach. Moreover, we will elucidate the underlying neural correlates, since the applied intervention restores functional synaptic plasticity and ultrastructure of neurons in the central amygdala.

References: Puścian A, Łęski S, Kasprowicz G, Winiarski M, Borowska J, Nikolaev T, Boguszewski PM, Lipp HP, Knapska E. Eco-HAB as a fully automated and ecologically relevant assessment of social impairments in mouse models of autism. *Elife*. 2016: e19532.

Puścian A, Winiarski M, Borowska J, Łęski S, Górkiewicz T, Chaturvedi M, Nowicka K, Wołyniak M, Chmielewska JJ, Nikolaev T, Meyza K, Dziembowska M, Kaczmarek L, Knapska E. Targeted therapy of cognitive deficits in fragile X syndrome. *Mol Psychiatry.* 2022 27: 2766-2776.

S5.1. CAN WE STIMULATE REMYELINATION *IN VIVO*? A GLANCE AT NOVEL THERAPEUTIC TARGETS

Aleksandra Rutkowska

Medical University of Gdańsk, Brain Diseases Center, Gdańsk, Poland

Remyelination in the central nervous system (CNS) is a complex process dependent on oligodendrocytes and their progenitors, microglia, astrocytes, neurons and peripheral immune cells. Demyelination has been observed in a range of CNS conditions including stroke, multiple sclerosis, dementia, infection and brain trauma, to name just a few. Irrespective of the cause of demyelination, remyelination begins almost immediately and follows the same steps. In multiple sclerosis, remyelination often fails for a number of factors, most of which are modulated by the glial cells. We identified a novel target for remyelination, which is expressed and highly functional in astrocytes, microglia and oligodendrocytes. Importantly, this target is a key immune modulator in the CNS and the peripheral immune system, an important aspect in the pathophysiology of multiple sclerosis.

S5.2. DePIEZing THE BRAIN: THE ROLE OF MECHANORECEPTOR Piezo1 IN CNS PATHOLOGICAL STATE

Maria Velasco-Estevez

H12O-CNIO Hematological Malignancies Group, Clinical Research Unit, Centro Nacional de Investigaciones Oncologicas (CNIO), Madrid, Spain

Astrocytes are important for information processing and the general maintenance of a healthy brain. Often overlooked are their important functions in mechanosensation. Glia can detect pathophysiological changes in the mechanical properties of injured or degenerating brain tissue. This is because glia in general, and astrocytes in particular, are highly mechanosensitive cells that sense this mismatch between brain stiffness *via* mechanosensitive channels. Piezo1 can translate mechanical to molecular signals through a process known as mechanotransduction. Here, we show the role of Piezo1 in different neurodegenerative and neuropathological states, such as neuroinflammation and glioma, and we find that the expression and function of Piezo1 have an important role in setting Piezo1 as both a novel biomarker and therapeutic target.

S5.3. MICROGLIA AND ASTROCYTES: THE BRAIN WHISPERERS AND KEEPERS

Ana Belen Lopez-Rodriguez

Molecular Neuroinflammation and Neuronal Plasticity Research Laboratory, Hospital Universitario Santa Cristina, Instituto de Investigación Sanitaria-Hospital Universitario de la Princesa, Madrid, Spain

Despite the numerous research studies on brain injury and neurodegenerative diseases, many pathophysiological mechanisms remain a mystery. Some experimental results clearly point to the beneficial effect of glia during the early phases of brain diseases whereas others are equally clear about the opposite effect. Brain injury and neurodegenerative diseases involve multiple factors and processes including hypoxia, haemorrhage, axonal injury, neuronal loss, protein accumulation, mitochondrial dysfunction, and many more but they share the neuroinflammatory process mediated largely by the glial cells. With this large repertoire of processes occurring, it is not surprising that glial cells play different and sometimes opposite roles in the central nervous system. I present here a summary of my results using animal models of traumatic brain injury, Alzheimer's disease and stroke.

S5.4. THE STIMULUS-SPECIFIC CHARACTER OF NEUROGLIAL RESPONSE TO CEREBRAL ISCHEMIA – A NEW PERSPECTIVE ON OLD PROBLEMS?

Przemysław Kowiański

Department of Anatomy and Neurobiology, Medical University of Gdańsk, Poland

Cerebral ischemia is a strong pathological stimulus triggering a complex reaction of neuroglia which results in its morphological and functional changes. The nature of this reaction is highly differentiated and depends on the intensity and duration of the stimulus, as well as the location of the stroke lesion. The important elements of neuroglial response include activation of proliferative potential, changes in the neuroglial phenotype, and direction of ischemia-induced differentiation. The character of the neuroglial response is also determined by interactions among its various subpopulations and interactions among all constituents of the neurovascular unit. Considering these factors, further research is needed on the stroke-induced morphological characteristics of neuroglia, its molecular profile, and the interactions of its various cell subpopulations.

S6.1. SENSITIVITY OF THE GAMMA-RANGE AUDITORY STEADY-STATE RESPONSES TO FLUCTUATIONS OF AWARENESS FOLLOWING SEVERE BRAIN INJURY AND DURING GENERAL ANAESTHESIA

Marek Binder & Róża Krycińska

Institute of Psychology, Jagiellonian University, Cracow, Poland

The issue of detecting awareness during the states of severely altered arousal such as coma or general anaesthesia remains a challenging task. EEG-based auditory steady-state responses induced by 40-Hz periodic acoustic stimulation appear as a marker of the changes in behavioral arousal. During our talk we will present the results of our recent studies on comatose states incurred by severe brain injury (such as vegetative state or minimally conscious state) and during propofol-remifentanil anaesthesia, showing that gamma-range responses to auditory stimulation become consistently attenuated during loss of consciousness.

References: Binder, M., Górska, U., Griskova-Bulanova, I., (2017). 40 Hz auditory steady-state responses in patients with disorders of consciousness: Correlation between phase-locking index and Coma Recovery Scale-Revised score. Clinical Neurophysiology 128(5), 799–806. doi: 10.1016/j.clinph.2017.02.012.

Binder, M., Górska, U., Pipinis, E., Voicikas, A., & Griskova-Bulanova, I. (2020). Auditory steady-state response to chirp-modulated tones: A pilot study in patients with disorders of consciousness. NeuroImage: Clinical, 27. doi: 10.1016/j.nicl.2020.102261.

S6.2. NEURAL SIGNATURES OF CONSCIOUS AND UNCONSCIOUS SEIZURES AS COMPARED TO NATURAL SLEEP

Urszula Górska-Klimowska

University of Wisconsin-Madison, USA

Loss of consciousness (LOC) is a hallmark of many epileptic seizures. Previous research associated LOC with increased slow-wave activity (SWA) in the brain during sleep, and sleep-like SWA was also observed during focal seizures. Another research suggested a local decrease in SWA in conscious (dreaming) as compared to unconscious (dreamless) sleep, while SWA during dream-like activities that accompany focal seizures was not yet evaluated. In this talk, I will introduce experiments involving intracranial EEG and accessing subjective reports from epileptic patients to directly contrast conscious and unconscious focal seizures as well as dreaming and dreamless sleep. I will present preliminary results showing differences in the involvement of the frontal *vs.* parietal cortex in focal seizures and sleep.

References: Juan, E., Górska, U., Kozma, C., Papantonatos, C., Bugnon, T., Denis, C., ... & Boly, M. (2023). Distinct signatures of loss of consciousness in focal impaired awareness *vs.* tonic-clonic seizures. Brain, 146(1), 109-123. doi: 10.1093/brain/awac291.

S6.3. PSILOCYBIN-MEDIATED CHANGES OF GAMMA-RANGE AUDITORY STEADY-STATE RESPONSES

Inga Griskova-Bulanova[1,2]

[1]Life Sciences Centre, Vilnius University, Vilnius, Lithuania, [2]National Institute of Mental Health, Klecany, Czechia

Due to the simplicity of the paradigm for human subjects and the ease of its translational aspects, gamma-range auditory steady-state responses are increasingly studied in both humans and animal models. We show that psilocybin acting as an agonist at serotonin 5-HT2A/C receptors changes subjective experiences and interferes with the ability to generate gamma-range activity. This knowledge is important for the correct interpretation of the findings and estimation of a better relationship to disorder-related alterations.

References: Viktorin, V., Griškova-Bulanova, I., Voicikas, A., Dojčánová, D., Zach, P., Bravermanová, A., Andrashko, V., Tylš, F., Korčák, J., Viktorinová, M., et al. Psilocybin—Mediated Attenuation of Gamma Band Auditory Steady-State Responses (ASSR) Is Driven by the Intensity of Cognitive and Emotional Domains of Psychedelic Experience. Journal of Personalized Medicine 2022, 12, 1004, doi: 10.3390/jpm12061004.

S6.4. PSILOCIN-INDUCED ALTERATIONS OF VISUAL PERCEPTION IN RATS EVALUATED BY VISUAL EVOKED POTENTIALS

Čestmír Vejmola[1,2]

[1]National Institute of Mental Health, Klecany, Czechia, [2]Third Faculty of Medicine, Charles University, Prague, Czechia

Visual hallucinations are a major hallmark of the effect of psychedelics. Despite increasing research interest, however, the phenomenon is poorly understood. Here, we studied the alteration of visual processing on visual evoked potentials in rats using three distinct visual stimuli. Each stimulus activates a set of different cell types, resulting in the recruitment of distinct neural pathways of visual processing the following stimulus parameters can be recently recommended: low luminance (<ca. 20 cd/m^2). The visual cortex response to each stimulus was tested after administration of a high and low dose of psilocin and psilocin in combination with MDL100907, a 5HT2A receptor antagonist. Psilocin disrupted most significantly the response to motion-onset evoked potential. Thus, psilocin appears to disrupt primarily higher-order visual processing.

References: M. Kuba, Z. Kubová, J. Kremláček, and J. Langrová, "Motion-onset VEPs: Characteristics, methods, and diagnostic use," *Vision Res.*, vol. 47, no. 2, pp. 189–202, 2007, doi: 10.1016/j.visres.2006.09.020.

S7.1. DECODING MITOCHONDRIAL STRUCTURE AND CALCIUM DYNAMICS IN ASTROCYTES

Amit Agarwal

The Chica and Heinz Schaller Research Group, Institute for Anatomy and Cell Biology, Heidelberg University, Germany

Little is known about the structure, dynamics and function of astrocytic mitochondria during cellular stress and neurodegeneration. We use mouse genetics tools, Ca2+ imaging, chronic *in vivo* multiphoton, 3D scanning electron and super-resolution (STED) microscopy techniques, and machine learning based computational analysis methods to elucidate the structure and function of mitochondria in astrocytes. Our new findings suggest that mitochondria in astrocytes are non-motile and form very stable densely networked structures. In response to cellular stress mitochondrial networks breakdown, but have an immense capacity to self-repair. Also, we have identified a novel marker to exclusively label astrocytic mitochondria and to study their structure *in vivo*.

References: Streich L, Boffi JC, Wang L, Alhalaseh K, Barbieri M, Rehm R, Deivasigamani S, Gross CT, Agarwal A, Prevedel R. *High-resolution structural and functional deep brain imaging using adaptive optics three-photon microscopy*. Nat Methods. 2021 Oct;18(10): 1253-1258.

S7.2. ASTROCYTIC NUTRIENT SIGNALING PATHWAYS AND ENTRAINMENT OF CIRCADIAN BEHAVIOR

Olga Barca-Mayo

Circadian and Glial Biology Lab, Physiology Department, Molecular Medicine and Chronic Diseases Research Centre (CiMUS), University of Santiago de Compostela, Santiago de Compostela, Spain

Endogenous circadian clocks respond to daily feeding and lighting cues, adjusting internal ~24 h rhythms to anticipate external cycles of day and night. The mechanism underlyingcircadian entrainment to feeding time is critical for understanding why mistimed feeding, as occurs during shift work, disrupts circadian physiology, a state associated with increased incidence of diseases such as type 2 diabetes. As astrocytes are at theinterface between vessels and neurons, they are in a privileged position to act as metabolic sensors of systemic cues. Here, we will discuss the role of nutrient signaling pathways in the entrainment of astrocyte clocks and their impact in regulating dailyrhythms on physiology and behavior.

References: Barca-Mayo O, López M. *Astrocyte Clocks and Glucose Homeostasis*. Front Endocrinol (Lausanne). 2021 Mar 18;12: 662017. doi: 10.3389/fendo.2021.662017.

S7.3. DYSREGULATION OF ASTROCYTIC GLUTAMINE TRANSPORT IN HYPERAMMONEMIC BRAIN EDEMA

Magdalena Zielińska

Department of Neurotoxicology, Mossakowski Medical Research Institute Polish Academy of Sciences, Warsaw, Poland

Ammonia is a potent neurotoxin, and its high systemic levels (i.e., hyperammonemia) are a major manifestation of hepatic encephalopathy, a neuropsychiatric disorder resulting from liver failure. Impaired ammonia clearance from blood gives rise to increased ammonia in the brain. Since brain glutamine synthesis is the only route of ammonia detoxification, hyperammonemia is as a rule associated with increased brain glutamine content which correlates with and contributes along with ammonia itself to brain edema, the frequently fatal complication associated with acute liver failure. Dysregulation of glutamine-transporting carriers located in the astrocytic membrane: Slc38a3 and Slc7a6, contributes in a vicious circle mode, to glutamine-driven astrocytic swelling and cytotoxic brain edema. Decreased functioning of the Slc38a3 transporter reduces glutamine efflux, augmenting its intra-astrocytic residence. The resulting glutamine surplus aggravates glutamine-induced osmotic (Slc38a3) and oxidative/nitrosative stress (Slc7a6), critical drivers of astrocytic swelling. Thus, both transporters may contribute to brain edema pathomechanism, representing a novel target to treat hyperammonemia-related conditions.

References: Zielińska M, Albrecht J, Popek M. *Dysregulation of Astrocytic Glutamine Transport in Acute Hyperammonemic Brain Edema*. Front Neurosci. 2022 Jun 6;16: 874750. PMID: 35733937.

S7.4. AGE-RELATED DECLINE IN MEMORY FORMATION IS ACCOMPANIED BY THE CHANGES IN PROTEOMIC AND METABOLIC PROFILE

Dominika Drulis-Fajdasz

Department of Molecular Physiology and Neurobiology, University of Wroclaw, Poland

Inhibition of glycogen degradation in brain of young animals has been shown to block memory formation. Unexpectedly, inhibition of glycogen phosphorylase (Pyg) activity, significantly improved the long term potentiation in hippocampal brain slices of old animals. Based on this we hypothesized that inhibition of Pyg activity may be used for the improvement of age-associated memory formation deficits. We tested behavior of young and old mice and we observed a significant improvement of memory formation in old animals treated with BAY U6751 (Pyg inhibitor). This observation is accompanied by changes of proteomic and metabolomic profiles. Our results reveal that inhibition of glycogen breakdown rejuvenates brains of old animals.

References: Drulis-Fajdasz D, Wójtowicz T, Wawrzyniak M, Wlodarczyk J, Mozrzymas JW, Rakus D. *Involvement of cellular metabolism in age-related LTP modifications in rat hippocampal slices*. Oncotarget. 2015 Jun 10;6(16): 14065-81.

S8.1. THE CIRCADIAN/VISUAL SYSTEM OF DIURNAL RODENTS – EXCITING TIMES AHEAD

Patrycja Orłowska-Feuer

University of Manchester, Manchester, United Kingdom

My comparative study between nocturnal and diurnal rodents investigating visual responses within the biological clock showed that in fact there is not much of a difference between these species at the level of the suprachiasmatic nucleus (SCN). Surprisingly however, diurnal *Rhabdomys pumilio* hypothalamus area is far more light-responsive than expected based on current knowledge acquired in nocturnal mice. In this brain region, called hereafter peri-SCN, not only significantly more neurons responded to light but also responses were biased towards fast, transient types. In fact, in contrast to SCN neurons which are specialised in coding ambient light irradiance, these neurons are not optimised to do that. This discovery raises several exciting questions. What is the function of light-responsive neurons outside the SCN in the diurnal *Rhabdomys pumilio*? Have diurnal rodents evolved visual pathways independent of classic vision and photoentrainment? Are these pathways also present in mice but masked by their nocturnally specialised vision? And finally, how does diurnality change the way we sense light for different physiological purposes?

S8.2. ULTRAFAST VOLUMETRIC IMAGING OF THE MOUSE RETINA FOR MONITORING HEMODYNAMIC CHANGES AND THE FUNCTIONAL RESPONSE TO LIGHT STIMULATION

Andrea Curatolo

International Centre for Translational Eye Research, Institute of Physical Chemistry PAS, Warsaw, Poland

We present a novel ultrafast imaging system using Spatio-Temporal Optical Coherence Tomography (STOC-T), capable of acquiring structural images of a mouse retina at a volumetric rate of 112 Hz. A calibrated fundus camera and white-light illumination aid the alignment of the mouse and help optimize the STOC-T image quality. We extract pulsatile blood flow frequency and other hemodynamic parameters from images of multiple retinal and choroidal vessels, and we perform optoretinography, i.e., we track the nanometric length change of retinal photoreceptors to light stimulation. Our work highlights the prospects of using STOC-T for mapping biomarkers of retinal function and health *in vivo*.

S8.3. RETINAL HOMEOSTATIC PLASTICITY

Henri Leinonen

University of Eastern Finland, Kuopio, Finland

We use the retina as a model tissue for plasticity, pharmacology, and drug discovery research for several reasons, such as amenability for noninvasive imaging due to eye's transparency, finely layered structure and well-characterized structure-function relationships, functional similarity to that of brain due to same neurodevelopmental origin. I detected retinal adaptability to sensory defect in year 2013 and our first paper related to this was published in 2020. Next, we aim to solve the molecular pathways enabling retinal homeostatic plasticity. This knowledge will help to find mechanisms how the central nervous system adapts to injury and malfunction and can guide pharmacotherapies. I will talk about the homeostatic plasticity concept and will present our latest results of retinal homeostatic plasticity mechanisms.

S8.4. VISUAL RESPONSES CHARACTERISTICS IN HEALTHY, DISEASED AND TREATED ANIMALS

Andrzej Foik

International Centre for Translational Eye Research, ICTER & Institute of Physical Chemistry PAS, Warsaw, Poland

Vision is not only the primary sense of humans, but also a great model to investigate broad aspects of neuroscientific research such as information coding and neuronal plasticity. Information is detected by the photoreceptor, processed by the inner retinal layer and sent to midbrain and thalamus *via* Retinal Ganglion cells, dividing processing into two main visual pathways. Any defects in those pathways can be detected in further parts of the visual system. During my talk I'll compare responses of the neurons in the superior colliculus and primary visual cortex, recorded in animals with retinal degeneration and after vision restoration treatment.

References: Suh, S., Choi, E. H., Leinonen, H., Foik, A. T., Newby, G. A., Yeh, W.-H., Dong, Z., Kiser, P. D., Lyon, D. C., Liu, D. R., & Palczewski, K. (2021). Restoration of visual function in adult mice with an inherited retinal disease *via* adenine base editing. *Nature Biomedical Engineering*, *5*(2), 169–178. https://doi.org/10.1038/s41551-020-00632-6.

Leinonen, H., Lyon, D. C., Palczewski, K., & Foik, A. T. (2022). Visual System Hyperexcitability and Compromised V1 Receptive Field Properties in Early-Stage Retinitis Pigmentosa in Mice. *Eneuro*, ENEURO.0107-22.2022. https://doi.org/10.1523/ENEURO.0107-22.2022.

S9.1. OPTICAL NEURAL NETWORKS

Andrzej Opala[1,2], Krzysztof Tyszka[1], Magda Furman[1], Rafał Mirek[1], Mateusz Król[1], Bartłomiej Seredyński[1], Jan Suffczyński[1], Wojciech Pacuski[1], Michał Matuszewski[2], Jacek Szczytko[1], Barbara Piętka[1]

[1]Institute of Experimental Physics, Faculty of Physics, University of Warsaw, Warsaw, Poland, [2]Institute of Physics, Polish Academy of Sciences, Warsaw, Poland

Over the last decade, artificial intelligence and artificial neural networks have become valuable tools in industry, research, and everyday life. This comes at the cost of high levels of energy consumption that are necessary to process large amounts of data. Unfortunately, the performance of standard computers based on the von Neumann architecture used to solve machine learning problems and process big data reaches its limit. For that reason, extensive research aims to develop novel systems characterized by high speed and high energy efficiency. Currently, the most promising way to further technological progress is to use optoelectronic systems in information processing. This presentation explains how an optoelectronic system can be a future for brain-inspired neuromorphic computing.

References: Phys. Rev. Applied 16, 024045 (2021).

Laser Photonics Rev, 2100660, (2022).

S9.2. USING MACHINE LEARNING TO DETECT MIND-WANDERING

Marieke van Vugt

University of Groningen, The Netherlands

Mind-wandering is a spontaneous process that happens to everyone and can be both helpful (for creativity and planning) and harmful (when it turns into depressive rumination). Since it is spontaneous, it by definitely cannot be controlled but only be measured. To help tracking mind-wandering continuously, we developed machine learning methods that can decode mind-wandering from the EEG signal. It turns out to the surprisingly hard to detect mind-wandering reliably. I will discuss the challenges in applying these machine learning methods, the ease with which you can overfit your data, and the fact that even fancy machine learning methods such as deep learning do not improve prediction much.

References: Jin, C.Y., Borst, J.P. & van Vugt, M.K. Predicting task-general mind-wandering with EEG. Cognitive, Affective, & Behavioral Neuroscience 19, 1059–1073 (2019).

Jin, C.Y., Borst, J.P., van Vugt, M.K. Distinguishing vigilance decrement and low task demands from mind-wandering: A machine learning analysis of EEG. European journal of neuroscience 52 (9), 4147-4164 (2020).

S9.3. AI-DRIVEN MODELLING FOR BRAIN-WIDE CREDIT ASSIGNMENT

Ellen Boven

Neural Dynamics Transition fellow, School of Physiology, Pharmacology & Neuroscience, University of Bristol, United Kingdom

The brain assigns credit to billions of synapses remarkably well. How the brain achieves this feat is one of the unsolved mysteries in neuroscience. Recently, we have developed a model of hierarchical credit assignment that captures a large number of biological features while approximating deep learning algorithms. Our model relies on long- and short-term synaptic plasticity, dendritic computations and excitatory-inhibitory cell-types to enable error propagation. However, credit assignment depends critically on behavioral feedback, which may not be always readily available. How the brain learns efficiently despite the sparse nature of feedback remains unclear. Inspired by recent deep learning algorithms we propose that a specialised brain region, the cerebellum, predicts feedback, thereby unlocking learning in cortical networks from future feedback. When trained in a range of motor and cognitive tasks the model shows faster learning and reduced dysmetria-like behaviors, in line with the widely observed functional role of the cerebellum. Overall, our work suggests that synaptic, sub-cellular, cellular and systems neuroscience features jointly underlie efficient credit assignment in the brain.

References: Greedy et al. NeurIPS 2022.

Boven et al. Nature Comms 2023.

S9.4. LATENT VARIABLES ESTIMATION FOR STUDYING COMPLEX BEHAVIORS IN MICE

Melisa Maidana Capitan[1,2]

[1]Neural Networks of Memory Lab, Donders Institute, Nijmegen, The Netherlands, [2]Laboratory of Sensory Perception Mechanisms, Center for Social and Affective Neuroscience, Linköping University, Sweden

The development of *in vivo* registration technologies has pushed systems neuroscience field growth by allowing the simultaneous recording of multiple data modalities in complex experimental setups. These modalities come as a set of time series signals from brain activity and behavioral readouts. We will discuss two examples where standard machine learning tools are used to extract relevant features to describe brain activity. At the same time, we will discuss why and how the development of specific models for these datasets could help to understand better the underlying process relating to behavior and brain activity. The first example consists of classifying electrophysiological recordings into different oscillatory types. The second relates to predicting freely moving behavior based on calcium imaging signals.

S10.1. EXPLORING NEURAL CORRELATES OF ROLE-PLAY USING HYPERSCANNING fNIRS

Mengyu Lim[1], Alessandro Carollo[2], Gianluca Esposito[2]
[1]Nanyang Technological University, Singapore, [2]University of Trento, Italy

Although role-play (RP) is incorporated into different interventions, the mechanism by which RP effects therapeutic change is unknown. Using the psychodramatic sociocognitive model of role reversal, this study explores neurological regions implicated during RP. A dyadic within-subjects paradigm was designed using hyperscanning fNIRS of the prefrontal cortex during 3 role-play scenarios: Natural conversation; Typical role-play; Role reversal. Participants aged between 18 and 35 from Singapore and Italy were recruited. Preliminary analysis on Singapore data showed four significant interaction effects between prior RP experience and condition. As data collection progresses, comparing Singaporean and Italian data may shed light on differential experiences of role-play between cultures.

S10.2. NEURAL SYNCHRONY WHEN EXECUTIVES PITCH EACH OTHER IDEAS: EFFECTS OF GROUP COMPOSITION AND PERCEPTIONS OF VALUE

Bear Goldstein, Ashley Binnquist, Matthew Lieberman
University of California, Los Angeles, USA

Psychology has long been interested in social behavior as it relates to communication. Nevertheless, the complex, adaptive, and dynamic nature of groups has made it difficult to study the neural mechanisms of real groups in real time. The present research aims to solve this tension by using fNIRS to study group communication in the field. We examined 20 groups of business executives as they engaged in naturalistic conversation. Neural activity in the temporoparietal junction (TPJ) and the medial prefrontal cortex (mPFC) was measured with fNIRS. Time courses of activity in these areas were correlated across group members to derive a group neural synchrony score for each part of the conversation. We found significant effects concerning how age and gender composition relate to a group's ability to synchronize in the brain and understand one another. We also found that group-level perceptions of how engaging a conversation leader is correlated with that leader's ability to synchronize the group, though leaders' self-perceptions do not. Additionally, the varying social demands of this naturalistic experiment allowed us to delineate functional differences between areas of the social brain, finding more mPFC synchrony during active discussion and more TPJ synchrony when one person is talking and others are passively listening. This study offers insights into the factors associated with a group's ability to achieve neural synchrony during communication as well as the extent to which people's experience of group dynamics align with these neural processes. Findings support social psychological theories surrounding group composition and evaluative self-reports, emphasizing the importance of diversity and group-level perspectives in effective group leadership. They also provide insight into the distinct roles of the TPJ and the mPFC in group interactions.

S10.3. SHALLOW OR DEEP CONVERSATIONS? INTERPERSONAL NEURAL SYNCHRONIZATION AS BIOLOGICAL MECHANISM FOR EMERGENCE OF GOOD SOCIAL RELATIONSHIPS

Grace Qiyuan Miao, Matthew Lieberman
University of California, Los Angeles, USA

Good social relationships have been identified as one of the strongest predictors of people's health and life satisfaction. However, the biological bases of meaningful social relationships, specifically shallow *vs.* deep ones, remain unknown (Kardas, Kumar & Epley, 2021). Performing hyperscanning using functional near infrared spectroscopy (fNIRS), this study investigates the neurobiological emergence of social connections initiated by shallow and deep questions. We expect to find different activations in the pre-frontal cortex and the temporoparietal junction in subject pairs through intersubject correlation analysis (Lieberman, 2022). Results will indicate unique brain-to-brain coupling specific to the emergence of good social relationships.

S10.4. THEORY OF MIND AND PARENTAL MENTAL-STATE TALK IN CHILDREN WITH COCHLEAR IMPLANTS

Agnieszka Pluta[1,2,3], Magdalena Krysztofiak[1], Małgorzata Zgoda[2], Joanna Wysocka[1], Karolina Golec[1], Katarzyna Gajos[1]

[1]University of Warsaw, Poland, [2]Bioimaging Research Center, Institute of Physiology and Pathology of Hearing, Warsaw, Poland, [3]University of California, Los Angeles, USA

Previous studies have suggested that parents may support the development of theory of mind (ToM) in their child during naturalistic interactions by talking about mental states (mental state talk; MST) (Bianco, et al., 2016). However, MST has not been sufficiently explored in deaf children with cochlear implants (CIs). This study investigated ToM and access to MST in deaf children with CIs (n=39) in comparison to their peers with typical hearing (TH; n=52). MST was measured during shared storybook reading. Parents' narratives were coded for cognitive, emotional, literal, and non-mental references. ToM was measured with a parental questionnaire. Children with CIs had lower ToM scores than their hearing peers and their parents used more literal references during storybook reading. Parental emotional references contributed positively to children's ToM scores only in the CI group. These results highlighted the role of MST in the development of ToM abilities in deaf children with CIs.

S11.1. POST-NATAL IMMUNE ACTIVATION IN A MOUSE MODEL OF TUBEROUS SCLEROSIS RESULTS IN SEXUAL DIMORPHIC MICROGLIA DEPENDENT SOCIAL MEMORY DEFICITS

Manuel F. López-Aranda

University of California, Department of Neurobiology, Gonda Neuroscience and Genetics Center Los Angeles (UCLA), USA

There is growing evidence that environmental factors, such as immune activation, contribute to the severity and range of cognitive phenotypes in neuropsychiatric disorders. We found, that early post-natal immune activation resulted in profound impairments in social behavior (deficits in social memory and communication), in adult male mice heterozygous for a gene responsible for tuberous sclerosis complex (*Tsc2+/-*), a genetic disorder with increased risk for ASD. We demonstrate that these memory deficits are caused by abnormal mammalian target of rapamycin (mTOR)-dependent interferon signaling and impairments in microglia function. Importantly, we also demonstrated that those phenotypes could be prevented or even permanently reversed with drugs that target mTOR and IFNβ signaling. These results open new therapeutical opportunities for neuropsychiatric disorders.

References: Manuel F. López-Aranda; et al. 2021. Postnatal immune activation causes social deficits in a mouse model of tuberous sclerosis: Role of microglia and clinical implications. Science Advances, DOI: 10.1126/sciadv.abf2073.

S11.2. CONTRIBUTION OF NUCLEAR mTOR ACTIVITIES TO NEURONAL PHYSIOLOGY AND mTORopathies

Jacek Jaworski

Laboratory of Molecular and Cellular Neurobiology, International Institute of Molecular and Cell Biology, Warsaw, Poland

The mechanistic/mammalian target of rapamycin (mTOR) is one of the major metabolic kinases that integrates extracellular instructions with the current metabolic status of the cells. mTOR is regulated by neuronal activity and is essential for neuronal development and plasticity. mTOR acts on many proteins changing their function but occurs mainly in the cytoplasm. However, more research, including our data, indicates that mTOR moves to the cell's nucleus, where it interacts with various proteins involved in epigenetic regulation and RNA metabolism. During the presentation, I will describe conditions needed for the nuclear translocation of mTOR in neurons, its nuclear proteome and the potential contribution of nuclear mTOR activities to neuronal physiology and mTOR-related disorders such as Tuberous Sclerosis Complex.

References: Tarkowski B, Kuchcinska K, Blazejczyk M, Jaworski J. Pathological mTOR mutations impact cortical development. Hum Mol Genet. 2019 Jul 1;28(13): 2107-2119. doi: 10.1093/hmg/ddz042.

S11.3. MANIPULATING RAPTOR AS A THERAPEUTIC STRATEGY FOR TUBEROUS SCLEROSIS COMPLEX

Helen Bateup

Department of Molecular & Cell Biology, University of California, Berkeley, USA

TSC is a neurodevelopmental disorder associated with an array of presentations that include focal cortical malformations, abnormal myelination, early-onset epilepsy, cognitive dysfunction and behavioral conditions such as autism spectrum disorder. Currently therapeutic strategies focus on mTOR inhibitors but these drugs are only partially effective and are associated with side-effects. We used mouse models to investigate whether mTORC1 suppression *via* reduction of the obligate protein Raptor, would be an effective therapeutic strategy for the neuropsychiatric presentations of TSC. We find that Raptor reduction, but not complete suppression, can improve multiple TSC-related phenotypes including cellular and brain anatomical abnormalities, neural network hyperactivity, and behavioral changes. Our results suggest that Raptor reduction could be a viable therapeutic strategy for TSC.

References: Kosillo P, Ahmed KM, Aisenberg EE, Karalis V, Roberts BM, Cragg SJ, Bateup HS. Dopamine neuron morphology and output are differentially controlled by mTORC1 and mTORC2. Elife. 2022 Jul 26;11: e75398. doi: 10.7554/eLife.75398.

Kosillo P, Doig NM, Ahmed KM, Agopyan-Miu AHCW, Wong CD, Conyers L, Threlfell S, Magill PJ, Bateup HS. Tsc1-mTORC1 signaling controls striatal dopamine release and cognitive flexibility. Nat Commun. 2019 Nov 28;10(1): 5426. doi: 10.1038/s41467-019-13396-8.

S11.4. mTOR AND EPILEPSY IN HUMANS: FROM PATHOLOGY TO TREATMENT OF SEIZURES AND PREVENTIVE STRATEGIES

Katarzyna Kotulska

Department of Neurology and Epileptology, The Children's Memorial Health Institute, Warsaw, Poland

Epilepsy affects about 1% of people of all ages, but most commonly seizures start in children. Despite an increasing number of available medical options, still about one third of individuals with epilepsy are refractory to existing therapies. In children, drug-resistant epilepsy is frequently associated with neuropsychiatric comorbidities, including intellectual disability and autistic features. A growing body of preclinical data has uncovered a role of mTOR pathway in many genetic and acquired epilepsy syndromes. mTOR is implicated in a number of cellular and molecular processes in the brain that directly affect neuronal excitability and seizures. Rapamycin and similar agents, like everolimus, inhibit mTORC1 and decrease seizures, delay seizure development, or even prevent epileptogenesis in many animal models of mTOR hyperactivation. In patients, the role of mTOR pathway in epilepsy is most clear in different types of cortical malformations, such as Tuberous Sclerosis Complex (TSC), focal cortical dysplasia and hemimegalencephaly, where somatic or germline mutations have been identified in upstream regulators of the mTOR pathway, such as TSC1/TSC2, DEPDC5, PI3K, PTEN, and mTOR itself. In TSC, epilepsy develops in about 80-85% of patients, usually before the age of 1 year, and is frequently drug-resistant. Everolimus was reported to alleviate seizures when added to standard antiepileptic drugs in TSC patients in the EXIST3 trial and now the drug is approved by EMA and FDA. Similar studies using rapamycin are ongoing. Given that the diagnosis of TSC is increasingly established before the onset of seizures, preventive strategies were proposed. Standard antiepileptic treatment with vigabatrin introduced after the onset of epileptiform discharges on EEG in TSC infants resulted in reduction of seizure risk and severity in the EPISTOP study. Currently, there are trials ongoing to determine the effect of mTOR inhibitors in prevention of seizures in TSC infants. There are also trials aimed to show the impact of mTOR inhibitors on neuropsychiatric comorbidities of epilepsy in TSC. Given the promising results of mTOR inhibition in TSC, rapamycin and other mTOR inhibitors are tested in other mTOR – dependent epilepsies in humans, including cortical dysplasia.

References: Pawlik B, Grabia S, Smyczyńska U, Fendler W, Dróżdż I, Liszewska E, Jaworski J, Kotulska K, Jóźwiak S, Młynarski W, Trelińska J. MicroRNA Expression Profile in TSC Cell Lines and the Impact of mTOR Inhibitor. Int J Mol Sci. 2022 Nov 21;23(22): 14493. doi: 10.3390/ijms232214493.

Kotulska K, Kwiatkowski DJ, Curatolo P, Weschke B, Riney K, Jansen F, Feucht M, Krsek P, Nabbout R, Jansen AC, Wojdan K, Sijko K, Głowacka-Walas J, Borkowska J, Sadowski K, Domańska-Pakieła D, Moavero R, Hertzberg C, Hulshof H, Scholl T, Benova B, Aronica E, de Ridder J, Lagae L, Jóźwiak S; EPISTOP Investigators. Prevention of Epilepsy in Infants with Tuberous Sclerosis Complex in the EPISTOP Trial. Ann Neurol. 2021 Feb;89(2): 304-314. doi: 10.1002/ana.25956. Epub 2020 Nov 27.

S12.1. CATEGORICAL CODING IN THE VENTRAL OCCIPITO-TEMPORAL CORTEX (VOTC) FOLLOWING TRANSIENT EARLY BLINDNESS

Stefania Mattioni, Mohamed Rezk, Xiaoqing Gao, Junghyun Nam, Zhong-Xu Liu, Terri Lewis, Daphne Maurer, Olivier Collignon

Department of Experimental Psychology, UGent, Center for Cognitive Neuroscience (CCN), UGent, Gent, Belgium

It has been suggested that a transient period of postnatal visual deprivation affects the development of object categorization in the visual system. We overturn this assumption by demonstrating typical categorical coding in VOTC despite early visual deprivation and pervasive alteration in the functional response in the early visual cortex (EVC). Using fMRI, we show that the encoding of low-level visual properties of our stimuli is impaired in EVC in cataract-reversal participants, while the categorical response in VOTC is preserved. These results challenge the classical view of a feedforward development of categorical selectivity in VOTC according to which the categorical organization of high-level regions depends on low-level visual protomaps.

References: Röder, B., Ley, P., Shenoy, B. H., Kekunnaya, R., & Bottari, D. (2013). Sensitive periods for the functional specialization of the neural system for human face processing. Proceedings of the National Academy of Sciences, 110(42), 16760-16765.

Arcaro, M. J., Schade, P. F., Vincent, J. L., Ponce, C. R., & Livingstone, M. S. (2017). Seeing faces is necessary for face-domain formation. Nature neuroscience, 20(10), 1404-1412.

S12.2. THE CORRELATION BETWEEN THE CORTICAL THICKNESS AND THE FUNCTIONAL ACTIVATION IN LANGUAGE TASKS IN THE OCCIPITAL CORTEX OF BLIND ADULTS

Maria Czarnecka[1], Anna Lena Stroch[1], Agata Wolna[1], Katarzyna Hryniewiecka[1], Gabriela Dzięgiel-Fivet[2], Joanna Plewko[2], Jyothirmayi Vadlamudi[3], Katarzyna Jednoróg[2], Olivier Collignon[3], Marcin Szwed[1]

[1]Institute of Psychology, Jagiellonian University, Cracow, Poland, [2]Laboratory of Language Biology, Polish Academy of Sciences, Warsaw, Poland, [3]Institute of Research in Psychology (IPSY) & Institute of Neuroscience (IoNS) – University of Louvain (UCL), Louvain, Belgium

Functional and structural reorganization in response to blindness is a well-documented phenomenon. However, it is still unknown how the functional reorganization relates to the observed structural changes. In the present study, 38 blind adults were tested on Braille reading and auditory tasks in the MRI scanner. They were presented with words, pseudowords, and a non-linguistic control conditions in both modalities. Whole-brain and ROI analyses of the activations in response to the stimuli were conducted and the average cortical thickness in occipital regions of interest was computed. Functional responses in the ROIs were correlated with the respective cortical thickness values. Increased activation was observed in the ventral occipito-temporal cortex in response to words *vs.* non-linguistic control in both modalities. In the next step we compared the cortical thickness with the functional activation. We were able to identify the regions where the cortical thickness corelates with the functional response to linguistic tasks. Those results suggest that regardless of the overall thicker occipital cortex in blindness, the functional reorganization of this area and neural recycling are associated with cortical thinning.

References: Beisteiner, R., Windischberger, Ch., Geissler, S., Gartus, A., Uhl, F., Moser, E., Deecke, L., & Lanzenberger, R. (2015). FMRI correlates of different components of Braille reading by the blind. Neurology Psychiatry and Brain Research, 21(4), 137-145.

Dehaene, S., Cohen, L., Morais, J., & Kolinsky, R. (2015). Illiterate to literate: behavioral and cerebral changes induced by reading acquisition. Nature reviews. Neuroscience, 16(4), 234-244.

S12.3. DECODING SPOKEN WORDS IN VISUAL CORTEX OF SIGHTED AND BLIND INDIVIDUALS

Łukasz Bola, Marta Urbaniak, Małgorzata Paczyńska, Marta Zbysińska, Maria Kossowska

Institute of Psychology, Polish Academy of Sciences, Warsaw, Poland

All over the world, language processing involves similar brain regions (Malik-Moraleda et al., 2022). Intriguingly, one population escapes this universal pattern – in blind individuals, linguistic stimuli, like spoken words, activate not only canonical language networks, but also "visual" areas (Bedny et al., 2011). Here, I will present the results of our studies that investigated what properties of spoken words are captured by the blind visual cortex. I will also show that certain spoken word properties are represented in visual areas even in sighted individuals. Based on

these findings, I will propose how activations for spoken words might emerge in the blind visual cortex.

References: Bedny, M., Pascual-Leone, A., Dodell-Feder, D., Fedorenko, E., & Saxe, R. (2011). Language processing in the occipital cortex of congenitally blind adults. Proceedings of the National Academy of Sciences, 108(11), 4429-4434.

Malik-Moraleda, S., Ayyash, D., Gallée, J., Affourtit, J., Hoffmann, M., Mineroff, Z., ... & Fedorenko, E. (2022). An investigation across 45 languages and 12 language families reveals a universal language network. *Nature Neuroscience*, *25*(8), 1014-1019.

S12.4. SENSORY-SPECIFIC COMPUTATIONS OF THE OCCIPITAL CORTEX DURING READING AND SPEECH PROCESSING IN CONGENITAL BLINDNESS

Jacek Matuszewski[1], Łukasz Bola[2], Olivier Collignon[1], Artur Marchewka[3]

[1]Institute for Research in Psychology (IPSY), Université Catholique de Louvain, Louvain-la-Neuve, Belgium, [2]Institute of Psychology, Polish Academy of Sciences, Warsaw, Poland, [3]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

The blind visual cortex responds to touch or sounds in a functionally specific fashion. However, the degree of retained cortical functionality is still debated (Amedi et al., 2017, Bedny, 2017). I will present a series of experiments investigating the roles of the "visual" cortex of early blind and sighted people with functional magnetic resonance imaging and chronometric transcranial magnetic stimulation. The results suggest that the computational preferences of the visual cortex during reading and speech processing may be retained to some extent, even without visual input during development. I will discuss the results in the context of currently evaluated theoretical frameworks.

References: Amedi, A., Hofstetter, S., Maidenbaum, S., & Heimler, B. (2017). Task selectivity as a comprehensive principle for brain organization. *Trends in cognitive sciences, 21(5)*, 307-310.

Bedny, M. (2017). Evidence from blindness for a cognitively pluripotent cortex. *Trends in cognitive sciences*, *21*(9), 637-648.

S13.1. NEURAL CIRCUITS FOR SOCIAL DECISION-MAKING

Diego Scheggia

Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy

Decisions that favor one's own interest *vs.* the interest of another individual depend on context and the relationships between individuals. The neurobiology underlying these decisions is not understood. We developed a social decision-making task in which mice can decide whether to share a reward with their conspecifics. Preference for altruistic choices was modulated by familiarity, sex, social contact, hunger, hierarchical status and emotional state matching. Basolateral amygdala (BLA) neurons are involved in the establishment of prosocial decisions. Moreover, BLA and prefrontal cortex (PFC) reciprocal connections mediated different facets of social decision-making. This provides a neurobiological model of altruistic and selfish choices with relevance to pathologies associated with dysfunctions in social decision-making.

References: De Waal, F. B. M. Putting the altruism back into altruism: the evolution of empathy. Annu. Rev. Psychol. 59, 279–300 (2008).

Rilling, J. K., King-Casas, B. & Sanfey, A. G. The neurobiology of social decision-making. Curr. Opin. Neurobiol. 18, 159–165 (2008).

S13.2. SOCIAL DECISION-MAKING IN FORAGING CONTEXTS

Cristina Marquez

DYNABrain ERA Chair holder Center for Neuroscience and Cell Biology, CNC-UC, Coimbra, Portugal

Prosocial behaviors are actions that benefit others. They are thought to be evolutionary conserved across different mammal species however, the behavioral and neural mechanisms that explain this type of actions are yet poorly understood. In this talk we will focus on how animals perceive rewarding states from others and incorporate these into social decision-making. Using novel behavioral paradigms that allow for deep analysis of social behavior, calcium imaging, closed-loop optogenetic experiments and computational modelling, we will explore how social hierarchy and the perception of the well-being of others guide the decision to help or not to help others.

References: Costa et al Scientific Reports Vol: 11: 14599 (2021).

Gachomba et al Current Biology, Vol 32: 15 (2022).

S13.3. SOCIAL REWARD CHANGES IN ADOLESCENCE

Zofia Harda

Department of Molecular Neuropharmacology, Maj Institute of Pharmacology of the PAS, Cracow, Poland

In humans, adolescence is a time of rapid psychological changes, for instance a decrease in affect associated with being in a family environment. However, it is not known if similar phenomenon occurs in animals. Using a social conditioned place preference task we found a decrease in rewarding effects of interactions with siblings in mid-adolescent mice. Next, we asked if the endogenous opioids regulate the observed changes in social reward. A selective mu-opioid receptor antagonist, cyprodime, restored the preference for social context in adolescent animals. Taken together, these data show clear similarities in the developmental changes of sensitivity to social reward in humans and mice and reveal the role of the mu-opioid receptor this phenomenon.

References: Harda et al Scientific Reports Vol 12: 11271 (2022).

Misiolek et al Scientific Reports Vol 13: 5583 (2023).

S13.4. MODELING SOCIAL EFFECTS IN MICE LEARNING IN INTELLIGENT CAGES

Daniel Wójcik

Laboratory of Neuroinformatics, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Intellicages are cages which allow for individualized behavioral protocols by controlling access to eight drinking bottles placed in four corners depending on animal identity for group-housed animals. If reward is presented in the same corner for every animal social cues may be helpful, otherwise they may be confounding. Here we propose a formal approach combining point processes with reinforcement learning which allows to estimate and model such behavior to better describe and differentiate phenotypes and identify individually and socially based learning strategies. The approach is illustrated with experiments using deterministic and probabilistic reward delivery. Our approach can easily generalize to other types of intelligent cages.

References: Kiryk et al Curr Alzheimer Res. 2011 8(8): 883-92.

Vouros et al Sci Rep. 2022 12(1): 12675.

S14.1. SLEEP/WAKE-DEPENDENT ASTROCYTIC PLASTICITY AT SYNAPSES TO OREXIN AND MCH NEURONS

Kazue Semba

Department of Medical Neuroscience, Dalhousie University, Halifax, Canada

Astrocytes regulate various behaviors by interacting with neurons within neural circuits, particularly at synapses. We have been investigating the role of astrocytes in regulating glutamatergic and GABAergic transmission to wake-promoting orexin (ORX) and sleep-promoting melanin-concentrating hormone (MCH) neurons in the lateral hypothalamus. We found that astrocytes associated with ORX and MCH neurons respond to acute sleep deprivation in a neuron type- and transporter-specific manner, and that astrocytes retract from synapses to ORX neurons in parallel with induction of presynaptic inhibition of glutamatergic inputs, which would favor transition to sleep. Structural remodeling of perisynaptic astrocytes may be a cellular mechanism for sleep homeostasis.

References: Deurveilher S, Antonchuk M, Saumure BSC, Baldin A, Semba K.(2021) No loss of orexin/hypocretin, melanin-concentrating hormone or locus coeruleus noradrenergic neurons in a rat model of chronic sleep restriction. Eur J Neurosci. 54: 6027-6043.

Hall S, Deurveilher S, Robertson GS, Semba K. (2020) Homeostatic state of microglia in a rat model of chronic sleep restriction. Sleep. 43: zsaa108.

S14.2. CIRCADIAN TIMEKEEPING IN GLIA IN BRAIN HEALTH AND DISEASE

Marco Brancaccio

Department of Brain Sciences, Imperial College, London, United Kingdom

Circadian timekeeping regulates daily patterns of behavior and physiology. We have previously shown that glia in the suprachiasmatic nucleus, the master circadian pacemaker in mammals, possess cell-autonomous circadian clocks distinct from neurons, and capable of restoring rest-activity patterns of behavior and intracellular neuronal calcium cycles in clock incompetent mice. The nature of the information released by astrocytes, as well as the mediators underpinning the neuron-astrocyte circadian interplay are however, poorly understood. Glia is deeply affected by neurodegenerative processes, including Alzheimer's disease (AD). Thus, the investigation of how this neuron-astrocyte interplay is mediated may also be critical for the understanding of the mechanisms underpinning disturbances of circadian timekeeping observed in early stages of AD. In this talk, I will focus on the nature of the temporal signals released by glia, their role as temporal synchronisers of neurons in circadian circuits in brain health, and their disturbance in models of early neurodegeneration.

References: Brancaccio M, Wolfes AC, Ness N. Astrocyte circadian timekeeping in brain health and neurodegeneration Circadian Clock in Brain Health and Disease, Advances in Experimental Medicine and Biology, Springer, 2021.

Brancaccio M, Edwards MD, Patton AP, Smyllie NJ, Chesham JE, Maywood ES, Hastings MH*: Cell-autonomous clock of astrocytes drives circadian behavior in mammals. Science, 2019.

S14.3. THE CLOCK GENE PERIOD IS REQUIRED FOR GENOME INTEGRITY IN NEURONAL PROGENITOR CELLS IN DROSOPHILA

Ezio Rosato

Department of Genetics, Leicester University, Leicester, United Kingdom

Although we have a mature understanding of the molecular mechanisms of the circadian clock in differentiated cells, our appreciation of the regulatory functions adopted by the clock in stem cells during development and later in life is patchy. In developing *Drosophila melanogaster* larvae, we have observed genotoxic stress in a null mutant of a key clock gene, *period* (*per*). In such *per0* mutants, larval neuroblasts (NBs, neuronal stem cells) show double-strand DNA breaks and chromosome aberrations. Our data indicate that the effect is largely non cell-autonomous but depending on cortex glia. We show that mis-regulation of the clock causes oxidative stress, a good candidate for explaining genotoxic effects.

References: Bradlaugh AA, Fedele G, Munro AL, Hansen CN, Patel S, Kyriacou CP, Jones AR, Rosato E*, Baines RA*. Essential elements of radical pair magnetosensitivity in *Drosophila*. Nature, *in press*.

Kyriacou CP, Rosato E. Genetic analysis of Cryptochrome in insect magnetosensitivity. Front Physiol., 13: 928416. doi: 10.3389/fphys.2022.928416. eCollection 2022.

S14.4. MULTICELLULAR REGULATION OF CIRCADIAN NEURONAL PLASTICITY

Milena Damulewicz

Department of Cell Biology and Imaging, Jagiellonian University, Cracow, Poland

Circadian neuronal plasticity was described in details in clock neurons of *Drosophila melanogaster*. Dorsal terminals of main pacemaker neurons, called small Lateral Neurons (sLNv), changes complexity and synaptic partners in daily manner. We showed that different cell types are involved in the regulation of this phenomenon, and in effect in rhythmic behavior of flies. We investigated different cell types housing peripheral oscillators, like glial cells and retinal photoreceptors and their connection with circadian plasticity. In this talk I will present the involvement of specific glia types in the maintaining of rhythmicity and amplitude of sLNv terminals changes, and effect of retinal clock disruption on central brain functioning.

References: Damulewicz M, Ispizua JI, Ceriani F, Pyza E. (2020) "Communication Among Photoreceptors and the Central Clock Affects Sleep Profile". *Front Physiol.* 11: 993.

Damulewicz M., Doktór B., Baster Z., Pyza E. (2022) „The role of glia clocks in the regulation of sleep in Drosophila melanogaster". *Journal of Neuroscience*, JN-RM-2340-21.

S15.1. EEG BRAIN MAPPING WITH INTERPRETABLE DEEP LEARNING

Maryna Kapitonova[1,2], Tonio Ball[1,2]

[1]Neuromedical AI Lab, Department of Neurosurgery, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany, [2]IMBIT//BrainLinks-BrainTools, Albert-Ludwigs-University, Freiburg, Germany

We introduce cross-class attributions (CroCA) for visualization of EEG decoding, in contrast to the conventional in-class gradients. We tested the hypothesis that cross-class gradients may reduce the noise in attribution maps, compared to traditional in-class maps. Additionally, we explored the usefulness of ensembling attribution maps across models as well as occlusion sensitivity mapping in temporal and frequency domains. Simulated EEG prototypes and real EEG data were analyzed. We showed that different networks had different preferred prototypes. The frequency of all types of errors was reduced in the CroCAs. CroCA as a novel variant of saliency mapping gave a clearer picture both for synthetic and real EEG data.

References: Schirrmeister, RT, Tibor R,...&, Ball T. (2017) Deep Learning with Convolutional Neural Networks for EEG Decoding and Visualization. *Human Brain Mapping* 38(11): 5391–5420.

S15.2. MACHINE LEARNING APPLICATION TO PROCESS EEG FOR MULTISENSORY REACTIVE BCI FOR CONTROL AND PASSIVE MODE FOR DEMENTIA NEURO-BIOMARKER ELUCIDATION

Tomasz M. Rutkowski[1,2]

[1]RIKEN AIP, Tokyo, Japan, The University of Tokyo, Tokyo, Japan, [2]Nicolaus Copernicus University in Toruń, Torun, Poland

Brain-computer interface (BCI) and efficient machine learning (ML) algorithms belonging to the so-called 'AI for social good' domain contribute to improvement of limited mobility and/or cognitive deficits in neurodegenerative disorders. The talk will review our recent results focusing on multisensory BCI for control and a dementia digital neuro-biomarker for early-onset prognosis of a possible cognitive decline utilizing end-to-end machine learning models for reactive BCI as well as for passive BCI using detrended fluctuation analysis features applied in supervised or unsupervised machine learning models.

References: Rutkowski TM, et al.(2022). Passive BCI Oddball Paradigm for Dementia Digital Neuro-biomarker Elucidation from Attended and Inhibited ERPs Utilizing Information Geometry Classification Approaches. In: 2022 IEEE International Conference on Systems, Man and Cybernetics (SMC). IEEE Systems, Man and Cybernetics. Prague, Czech Rep: IEEE Press.

S15.3. DECODING WORKING MEMORY-RELATED INFORMATION FROM REPEATED PSYCHOPHYSIOLOGICAL EEG EXPERIMENTS USING CONVOLUTIONAL AND CONTRASTIVE NEURAL NETWORKS

Jarosław Żygierewicz[2], Romuald A. Janik[1,4], Igor T. Podolak[1,3], Alan Drozd[1], Urszula Malinowska[1], Martyna Poziomska[2], Jakub Wojciechowski[1,6], Paweł Ogniewski[7], Paweł Niedbalski[7], Iwona Terczynska[5] and Jacek Rogala[6,8]

[1]Nencki Institute of Experimental Biology, Polish Academy of Science, Warsaw, Poland, [2]Faculty of Physics, University of Warsaw, Warsaw, Poland, [3]Faculty of Mathematics and Computer Science, Jagiellonian University, Cracow, Poland, [4]Institute of Theoretical Physics, Jagiellonian University, Cracow, Poland, [5]Institute of Mother and Child (IMC), Clinic of Paediatric Neurology, Warsaw, Poland, [6]Bioimaging Research Center, World Hearing Center, Institute of Physiology and Pathology of Hearing, Warsaw/Kajetany, Poland, [7]ELMIKO BIOSIGNALS LTD, Milanowek, Poland, [8]The Center for Systemic Risk Analysis, Faculty of 'Artes Liberales', University of Warsaw, Warsaw, Poland

The study evaluates a new approach to extract reliable information from EEG signal based on machine learning. We designed different neural network models to classify single experimental trials of a working memory task and test an accuracy of the models. We identified a subset of features common to all models that identified brain regions and frequency bands consistent with current neurophysiological knowledge about working memory. Our results indicate that explainable deep learning is a powerful tool for decoding information from EEG signals. It is crucial to train and analyze a range of models to identify stable and reliable features.

References: Żygierewicz J., ..., Rogala J. (2022). Decoding working memory-related information from repeated psychophysiological EEG experiments using convolutional and contrastive neural networks. Journal of Neural Engineering 19(4).

S15.4. ToFFi TOOLBOX FOR EEG/MEG-BASED BRAIN SPECTRAL FINGERPRINTING

Michał Konrad Komorowski[1,2,3], Krzysztof Rykaczewski[2], Tomasz Piotrowski[2,3], Katarzyna Jurewicz[4,5], Jakub Wojciechowski[4,6], Anne Keitel[7], Joanna Dreszer[8], Włodzisław Duch[2,3]

[1]Faculty of Philosophy and Social Sciences, Institute of Information and Communication Research, Nicolaus Copernicus University in Toruń, Poland, [2]Neurocognitive Laboratory, Centre for Modern Interdisciplinary Technologies, Nicolaus Copernicus University, Toruń, Poland, [3]Department of Informatics, Faculty of Physics, Astronomy, and Informatics, Nicolaus Copernicus University, Toruń, Poland, [4]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland, [5]Department of Physiology, Faculty of Medicine and Health Sciences, McGill University, Montreal, QC, Canada, [6]Bioimaging Research Center, Institute of Physiology and Pathology of Hearing, Kajetany, Poland, [7]Psychology, University of Dundee, Scrymgeour Building, Dundee, United Kingdom, [8]Faculty of Philosophy and Social Sciences, Institute of Psychology, Nicolaus Copernicus University in Toruń, Poland

Spectral fingerprints (SFs) are unique power spectra signatures of human brain regions of interest (ROIs, Keitel & Gross, 2016). SFs allow for accurate ROI identification and can serve as biomarkers of differences exhibited by non-neurotypical groups. We have created a modular, highly-configurable MATLAB Toolbox for Frequency-based Fingerprinting (ToFFi) which can transform EEG/MEG signals into unique spectral representations using ROIs provided by anatomical, functional or other custom volumetric brain parcellations. Investigating spectral representations of regional activity could help study cortical and subcortical activity modulation during cognitive processing in healthy and diseased brains, and facilitate construction of normative databases of cognition, valuable to researchers/clinicians.

References: Komorowski MK, ..., Duch W (2021). ToFFi-Toolbox for Frequency-based Fingerprinting of Brain Signals. arXiv preprint arXiv: 2110.09919.

Keitel A, Gross J (2016). Individual human brain areas can be identified from their characteristic spectral activation fingerprints. PLoS Biol 14 (6) e1002498.

POSTER SESSION 1

P1.1. IN UTERO ELECTROPORATION OF TBC1D5-GAP IMPAIRS MULTIPOLAR TO BIPOLAR TRANSITION IN MIGRATING NEURONS

Oliver Tkaczyk, Jacek Jaworski
International Institute of Molecular and Cell Biology, Poland

The proper formation and function of the complex six-layered cerebral cortex depend on the precise orchestration of neuron migration from the ventricular zone (VZ) through the intermediate zone (IZ) to the outermost layer of the cortical plate (CP). Migrating neurons in the IZ exhibit a multipolar morphology with multiple processes emanating from the cell body. However, as they approach the cortical plate, these neurons undergo a crucial morphological transition in which they adopt a bipolar morphology. The retromer accessory protein TBC1D5 is a GTP-activating protein (GAP) for Rab7 that catalyzes the hydrolysis of GTP to GDP and renders Rab7 inactive. Although Rab7 is known to play a role in neuronal migration, particularly in the terminal translocation of neurons, the contribution of TBC1D5 in this process is still unknown. To investigate the role of TBC1D5 in neuronal migration, we performed *in utero* electroporation of TBC1D5 into neuronal progenitor cells in the VZ of mouse fetal brain. Our results showed a 50% reduction in the proportion of neurons transitioning from a multipolar to a bipolar morphology compared with neurons electroporated with a control vector. Moreover, TBC1D5-expressing neurons that entered the cortical plate traveled a shorter distance. Interestingly, cells expressing a TBC1D5 mutant lacking GTPase activity behaved like control cells. Our findings suggest that TBC1D5 plays a critical role in regulating neuronal morphology through Rab7 regulation during cortical development. Specifically, TBC1D5 can functionally inhibit Rab7, affecting the transition from multipolar to bipolar cells. Furthermore, this study may lay the groundwork for understanding the underlying mechanisms of rare diseases associated with TBC1D5 mutations, which are characterized by developmental delay, infantile spasms, and progressive hearing loss.

Key words: migration, cortex , TBC1D5, Rab7, in utero electroporation

P1.2. MATERNAL, EMBRYONIC, AND PLACENTAL CONTRIBUTIONS TO NEURODEVELOPMENTAL PROGRAMMING IN THE BTBR MOUSE MODEL OF AUTISM: A MULTI-DEVELOPMENTAL STAGE STUDY

Silvestre Sampino, Maria Pia Viscomi, Joanna Czyrska, Dominika Żbikowska, Elżbeta Wenta-Muchalska, Agnieszka Bernat-Wójtowska, Karolina Król-Szmajda, Małgorzata Cybulska, Dawid Winiarczyk, Marta M. Ziętek
Institute of Genetics and Animal Biotechnology PAS, Department of Experimental Embryology, Jastrzębiec, Poland

The BTBR mouse strain recapitulates multiple behavioral phenotypes relevant to the core diagnostic symptoms of autism spectrum disorders, thus it is considered as a model of human idiopathic autism. The etiological factors leading to the occurrence of the BTBR phenotype are not fully known, and early windows of fetal development have been understudied in this strain. Here, we report a series of studies aimed to explore the maternal, embryonic, and placental factors that may contribute to the developmental programming of the BTBR autism-like phenotype. Our results show that the behavioral phenotype of BTBR mice is already established at preimplantation stages, as BTBR blastocysts transferred to B6 control mothers still display strain-specific autism-like behaviors after birth. BTBR preimplantation embryos display a lower level of lipid drops compared to other strains and required specific metabolic conditions for *in vitro* culture. The placental and fetal brain expression profiles of genes involved in metabolic pathways were strain-specific, indicating a peculiar energy metabolism in the BTBR placenta as compared to other strains. The BTBR placenta was also characterized by specific histological features, including an enlarged labyrinth area, which is involved in nutrients exchange. These results indicate that the BTBR placenta display a peculiar metabolic phenotype, which may in turn affect neurodevelopment and contribute to developmental programming of BTBR behavioral features and brain peculiarities. To address this hypothesis, we are currently working on establishing a mouse model in which the placenta and the fetus belong from two different strains, in our case BTBR and B6. Placenta-Fetus BTBR-B6 chimeras may be useful to provide a valid proof of the involvement of the placenta in the developmental programming of the BTBR postnatal brain and behavioral phenotypes.

This research was financed by the National Science Center, Poland, grant nr. 2020/39/B/NZ4/02105.

Key words: BTBR mouse, autism, placenta, pregnancy, etiology, embryos

P1.3. NEURAL CORRELATES OF CHANGES IN THE REWARDING PROPERTIES OF SOCIAL INTERACTIONS OCCURRING DURING ADOLESCENCE

Karolina Przyborowicz, Klaudia Misiołek, Marta Klimczak, Łukasz Szumiec, Magdalena Chrószcz, Maria Kaczmarczyk-Jarosz, Barbara Ziółkowska, Julia Netczuk, Rafał Ryguła, Jan Rodriguez Parkitna, Zofia Harda

Maj Institute of Pharmacology Polish Academy of Sciences, Poland

In humans, adolescence is a time of rapid behavioral, including a temporary decline in affect associated with being among family members. In our study, we have described similar changes in the rewarding effects of interaction with siblings in adolescent male and female mice.

Adolescence is also a time of dynamic neural changes, especially in the prefrontal GABAergic system. Hence, we asked whether the development of the prefrontal inhibitory cells corresponds to the observed behavioral changes. We focused on the two areas of the prefrontal cortex that control social behavior, the orbitofrontal and dorsomedial cortex.

Male and female mice of the C57BL/6 strain were used. Four developmental time points were examined: pre (around post natal day 33 [P33]), early (P36), middle (P39) and late adolescence (P42). We studied the rewarding effects of cohousing with siblings using the social conditioned place preference test. We also examined age related changes in the prefrontal GABAergic system using immunofluorescent staining for parvalbumin and calretinin on a separate cohort of mice.

The rewarding effects of interactions with siblings in adolescent male mice followed a similar pattern to humans: high levels during pre-adolescence, a decline in mid-adolescence and a return to initial levels in late adolescence. No statistically significant age related changes in social reward were observed in female mice. The analysis of immunofluorescent staining results is in progress. These data show clear similarities in the developmental changes of sensitivity to social reward in humans and mice. Hence, we conclude that mice are a suitable model to study developmental changes in social interactions in normal and pathological conditions.

Key words: adolescence, social reward, prefrontal cortex, GABAergic system, parvalbumin, calretinin

P1.4. QUALITY OF DYADIC INTERACTION AND THETA POWER DISTRIBUTION IN OCCIPITAL AND FRONTAL AREAS OF INFANT BRAIN CAN BE USED AS EARLY INDICATORS OF AUTISM OUTCOMES AT 3 YEARS OF AGE AT AN ELEVATED LIKELIHOOD FOR ASD

Tanaya Batabyal[1], Rianne Haartsen[2], Eirini Papageorgiou[2], Ming Wei Wan[3], Greg Pasco[4], Tony Charman[4], Przemysław Tomalski[5], Anna Anzulewicz[1], Kalinka Timmer[1], Mark H. Johnson[6], Emily J.H. Jones[2]

[1]University of Warsaw, Poland, [2]Birkbeck, University of London, United Kingdom, [3]The University of Manchester, United Kingdom, [4]King's College London, United Kingdom, [5]Institute of Psychology, Polish Academy of Sciences, Warsaw, Poland, [6]University of Cambridge, United Kingdom

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social behavior disruption and uncontrolled motor behavior in the early stages of development. Genetic susceptibility to ASD and early dyadic experiences plays a crucial role in shaping up developmental outcomes in symptoms profile.

We investigated, whether younger infant siblings born to elder siblings with a history of typical likelihood (TL-ASD) (n=41) and elevated likelihood (EL-ASD) (n=91) to ASD, have a differential association between Dyadic Mutuality (DM) at 6 months, Power spectral density differences in theta ($\theta^{Occipital}$, $\theta^{Frontal}$) and alpha ($\alpha^{Occipital}$, $\alpha^{Frontal}$) at 12 months and behavioral outcomes measured by ADOS total (T), social affect (SA) and Restricted and Repetitive Behaviors (RRB) scores at 36 months.

Mixed method longitudinal analysis to check for correlational associations and linear regression to check for predictability.

Only EL-ASD showed a predictive negative association between DM and ADOS (T) (ß=-.228, R^2=.052, F(1,89)=4.882, p=.030) and SA (ß=-.226, R^2=.051, F(1,89)=4.811, p=.031). $\theta^{Occipital}$ predicted positive association with T (ß=.214, R^2=.046, F(1,89)=4.253, p=.042) and SA (ß=.268, R^2=.072, F(1,89)=6.873, p=.010), while $\theta^{Frontal}$ partially predicted positive association with SA (ß=.221, R^2=.049, F(1,89)=4.561, p=.035). Additive effect of using DM as a predictor along with $\theta^{Occipital}$, improved the predictability of T (ß=.306, R^2=.093, F(2,88)=4.529, p=.013) and SA (ß=.343, R^2=.118, F(2,88)=5.867, p=.004). DM as a predictor along with $\theta^{Frontal}$ improved the predictability of SA (ß=.313, R^2=.098, F(2,88)=4.789, p=.11).

Overall, these results suggest that early dyadic interaction quality and neural oscillatory features in the theta band can serve as early indicators of ASD outcomes in infants with a family history of the condition.

Key words: dyadic interaction, infants, autism, social deficits, theta power

P1.5. SERUM RESPONSE FACTOR IS ESSENTIAL FOR DEVELOPMENTAL SYNAPTIC MATURATION IN THE HIPPOCAMPUS

Matylda Roszkowska[1], Anna Krysiak[1], Anna Beroun[2], Karolina Nader[1], Martyna Pekala[1], Jacek Jaworski[3], Tomasz Wojtowicz[4], Ludwika Kondrakiewicz[5], Alicja Puścian[5], Ewelina Knapska[5], Leszek Kaczmarek[1], Katarzyna Kalita[1]

[1]Nencki institute of Experimental Biology, Warsaw/ Laboratory of Neurobiology. Braincity, Poland, [2]Nencki institute of Experimental Biology, Warsaw/ Laboratory of Neuronal Plasticity. Braincity, Poland, [3]International Institute of Molecular and Cell Biology, Warsaw, Poland/ Laboratory of Molecular and Cellular Neurobiology, Poland, [4]Nencki Institute of Experimental Biology, Warsaw, Poland/ Laboratory of Cell Biophysics, Poland, [5]Nencki institute of Experimental Biology, Warsaw/ Laboratory of Emotions Neurobiology, Braincity, Poland

Disturbances of gene expression patterns during brain development can severely affect the signal transmission, connectivity, and plasticity—key features underlying brain memory formation and storage. Abnormalities at the molecular level can manifest as changes in the structural and functional plasticity of dendritic spines that harbor excitatory synapses, leading to developmental neuropsychiatric conditions such as autism spectrum disorder, intellectual disability, and schizophrenia. In the present study, we investigated the role of the major transcriptional regulator – serum response factor (SRF) in postnatal synapse maturation and its impact on animal behavior. Using *in vitro* and *in vivo* models of early postnatal SRF deletion, we studied its influence on key morphological and physiological hallmarks of excitatory synapse development. The early postnatal elimination of SRF in hippocampal CA1 excitatory neurons caused spine immaturity *in vivo*, accompanied by a specific social deficit frequently observed in autism spectrum disorders. Additionally, the elimination of SRF in developing neurons *in vitro* similarly resulted in a phenotype of immature dendritic spines and impairments in excitatory transmission. Moreover, using a combination of molecular and imaging techniques, we showed that SRF-depleted neurons exhibited a lower level of specific glutamate receptor mRNAs and decreased surface expression. Altogether, our data suggest that the regulation of structural and functional dendritic spine maturation begins at the stage of gene transcription, which underpins the crucial role of such transcription factors as SRF in synapse development after birth. Moreover, disturbances of the postnatal expression of SRF translate to behavioral changes in adult animals.

Key words: SRF, dendritic spines, social behavior, developmental disorders

P2.1. KIF3A, KIF3C AND KIF21B ARE INVOLVED IN TUBEROUS SCLEROSIS COMPLEX ABNORMAL NEURONAL PHENOTYPE

Jan Węsławski[1], Joanna Lipka[2], Jacek Jaworski[1]

[1]International Institute of Molecular and Cell Biology in Warsaw, Poland, [2]Utrecht University, The Netherlands

Tuberous sclerosis complex (TSC) is a genetic, multi-systemic disease, resulting from mutations in the *TSC1* or *TSC2* genes, which lead to hyperactivity of mTOR kinase. This in turn, disrupts neuronal growth regulation, triggering abnormal increase in neuronal cell body size, and dendritic tree arborization. Neurons, with their unique architecture of long axons and dendrites, rely heavily on intracellular transport for their normal function and development. Thus, motor proteins, such as kinesins, involved in moving cargos along the neuron's microtubule tracks, may play a crucial role in hyperactive mTOR rapid and excessive neuronal growth. This study aimed to identify key kinesins involved in this pathological process. Initial screening of 38 kinesins was conducted using a rat primary neuronal culture model with a constitutively active form of PI3-kinase as a strong mTOR pathway activator. Kinesin expression was silenced with shRNA, and changes in cell body size and dendritic tree arborization were analyzed. This step aimed to identify kinesins, silencing of which mitigated neuronal growth towards control levels. The second phase focused on 10 kinesins that substantially influenced neuronal growth. The secondary screening study utilized shRNA against TSC2, providing a closer disease model. This phase identified KIF3A, KIF3C, and KIF21B as potentially crucial in pathological neuronal growth. Finally, functions of these kinesins that could be connected to phenotype of mTOR hyperstimulation were explored. Including both selected cargo transport, and unconventional functions. For KIF3A and KIF3C (kinesin-2 family), this was primary cilia development, and for KIF21B (kinesin-4 family), microtubule dynamics. The study suggests that specific kinesins, especially KIF3A, KIF3C, and KIF21B, may significantly contribute to abnormal neuronal growth in TSC, justifying further in-depth research.

This work was supported by Polish National Science Centre grant 2016/21/B/NZ3/03639.

Key words: mTOR, TSC, kinesin, KIF, primary neuron culture, motor protein, disease

P3.1. DO THEY TALK? NOVEL APPROACH TO STUDY NEURONAL MATURATION IN BRAIN ORGANOIDS

Bogna Badyra[1], Matylda Roszkowska[1], Karolina Protokowicz[1], Dominika Kurpiewska[1], Marcin Barański[1], Ewa Liszewska[2], Jacek Jaworski[2], Leszek Kaczmarek[1]

[1]Laboratory of Neurobiology, BRAINCITY, Nencki Institute of Experimental Biology of the Polish Academy of Sciences, Warsaw, Poland, [2]Laboratory of Molecular and Cellular Neurobiology, International Institute of Molecular and Cell Biology, Warsaw, Poland

Brain organoids provide a great tool to decipher human brain diseases at the molecular and physiological levels. The organoids are of great value in understanding neurodevelopmental diseases, as they can reflect changes occurring even in the prenatal period. Those diseases are often accompanied by aberrant changes in the formation of dendritic spines harboring excitatory synapses. Yet, none of the studies focused on detailed characterization of dendritic spines in organoids. Herein, we present the novel protocol to visualize and characterize single dendritic spines in matured organoids.

Human induced pluripotent stem cells were differentiated to cortical spheroids. On subsequent stages of development organoids were evaluated by whole organoids' imaging and western blot analysis. Till day 200 the organoids were evaluated for proper differentiation: rosettes formation, cortex layering and glial/neuronal differentiation. After day 200 organoids were evaluated for their maturation properties. Live calcium imaging was performed to analyze spontaneous activity of cells. Next, organoids older than one year were evaluated for dendritic spines formation. Spines were characterized using biolistic delivery of lipophilic dye combined together with subsequent immunolabeling of pre- and postsynaptic markers.

We show that organoids' maturation can be manifested by spontaneous activity of neurons with visible synchronization. This maturation is accompanied by changes in expression of repertoire of synaptic-related proteins (glutamate receptors, postsynaptic scaffolding proteins). Importantly, we were able to optimize protocol of DiI staining to successfully visualize dendritic spines in neurons within organoids. Furthermore, we were able to immunolabel dendritic spines with antibodies directed to proteins forming either pre- or postsynaptic compartments. This method enables a more detailed characterization of complex dendritic spine structure and function in both health and disease.

Key words: brain organoids, dendritic spines

P3.2. IMPAIRED MODULATION OF MOVEMENT-RELATED EEG BETA OSCILLATIONS IS ASSOCIATED WITH DOPAMINE DEFICIENCY IN THE POSTERIOR PUTAMEN AND WITH DECLINED MANUAL DEXTERITY IN PARKINSON'S DISEASE

Karolina Lorek[1], Joanna Mączewska[2], Leszek Królicki[2], Małgorzata Chalimoniuk[3], Józef Langfort[4], Magdalena Siemiatycka[5], Katarzyna Kisiel-Sajewicz[5], Jarosław Marusiak[5]

[1]Department of Kinesiology, Wroclaw University of Health and Sport Science, Wroclaw, Poland, [2]Nuclear Medicine Department, Medical University of Warsaw, Warsaw, Poland, [3]Department of Physical Education and Health in Biala Podlaska, Jozef Pilsudski University of Physical Education in Warsaw, Biala Podlaska, Poland, [4]Institut of Sport Sciences, Jerzy Kukuczka Academy of Physical Education in Katowice, Katowice, Poland, [5]Department of Kinesiology, Wroclaw University of Health and Sport Science, Wroclaw, Poland

The role and mechanisms of pathological movement-related electroencephalographic (EEG) beta oscillations in Parkinson's disease (PD) have not been elucidated. Hence, our study aimed to compare between healthy subjects (HCO) and mildly affected PD patients: (i) the values of beta band event-related desynchronization (ERD), (ii) striatal dopaminergic function, (iii) brain-derived neurotrophic factor (BDNF) level and (iv) manual dexterity. Our secondary aim was to evaluate associations between the above-mentioned outcomes in PD patients.

The study involved fifteen HCO subjects and thirthy patients with mild PD. All subjects were assessed by: (i) EEG recorded during bimanual anti-phase index finger movement from which we calculated the beta band ERD; (ii) positron emission computed tomography with an estimation of striatal [18F]Fluorodopa uptake ratio ([18F]FDOPA PET/CT) to evaluate dopaminergic function; (iii) blood measure of BDNF level, and (iv) the Purdue Pegboard Test (PPT) to evaluate one-hand and bimanual dexterity.

PD patients, compared to HCO subjects, exhibited significantly lower values of the beta band ERD, [18F] FDOPA PET/CT uptake ratio in the posterior and anterior putamen as well as in the caudate nucleus, BDNF blood level, and worse one-hand and bimanual dexterity. Pearson's correlation estimates showed in PD patients a significant positive correlation between lowered values of the beta band ERD and decreased [18F] FDOPA PET/CT uptake in the posterior putamen, as well

as a worsened one-hand manual dexterity. Furthermore, the decreased [18F]FDOPA PET/CT uptake in the caudate nucleus significantly positively correlated with worsened bimanual dexterity.

Our findings demonstrated that in Parkinson's disease, the impaired modulation of movement-related EEG beta oscillations was associated with dopamine deficiency in the posterior putamen and with a decline in one-hand manual dexterity.

The work was supported by the National Science Centre, Poland, under research project no 2017/25/B/NZ7/02795, entitled „Effect of high intensity interval training on mechanisms of neuroplasticity and psychomotor behaviors in Parkinson's disease patients: a randomized study with 1-year follow up", awarded to Jaroslaw Marusiak.

Key words: motor impairment, beta oscillations, [18F]FDOPA PET/CT, Parkinson's disease

P3.3. UNVEILING THE *IN VIVO* ANTIDEPRESSANT PROPERTIES OF GYROPHORIC ACID, A LICHEN SECONDARY METABOLITE

Nicol Urbanska, Patrik Simko, Rastislav Jendzelovsky, Zuzana Jendzelovska, Terezia Kiskova

Pavol Jozef Šafárik University in Košice, Faculty of Science, Košice, Slovakia

Gyrophoric acid (GA) belongs to lichen secondary metabolites. The aim of our study was to investigate the neurobehavioral and potential antidepressant effects of GA. Two independent experiments were carried out. The first experiment with healthy animals, the second with the rats with immobilisation-stress induced depression. GA (10 mg/kg body weight) was administered an 10% ethanol solution daily for 30 days (60^{th}-90^{th} postnatal days). Our preliminary results show that due to its polyphenolic structure, GA is an antioxidant, as it significantly reduced the levels of reactive oxygen species in lymphocytes compared to the control groups. In healthy animals, in the OFT test, we observed a significantly elevated rearing activity compared to untreated animals. After GA, in the EPM test, we also observed significantly increased rearing in compared to the untreated groups, indicating the potential of GA in depression. Concomitantly, GA increased the number of Ki-67 positive proliferating cells in the hilus and subgranular zone (SGZ) of the hippocampus ($P<0.05$) showing its neurogenic activity. Thus, the second experiment led to reveal the antidepressant potential of GA. During depression-like states, we observed an increase in time spent in open arms in EPM compared to the untreated groups, which indicates a potential effect of GA in anxiety or depression. Moreover, GA increased the number of Ki-67 positive proliferating cells in the hilus region of the hippocampus and, importantly, the number of mature NeuN positive neurons in the CA1 region of the hippocampus compared to the untreated depressive groups of animals. Our results demonstrate for the first time the effects of GA in a living organism (healthy and depressive), focusing on its neurologic potential.

The work was financially supported by the scientific grant agency APVV (APVV-21-0321), VEGA (1/0658/20) and the internal scientific grant system of PF UPJŠ (VVGS-PF-2022-2136 and VVGS-PF-2023-2161).

Key words: gyrophoric acid, antidepressant, hippocampus, depressive-like states

P3.4. UTILIZING A NOVEL BIOORTHOGONAL PROBE TO STUDY THE DYNAMICS OF CERTAIN POST-TRANSLATIONAL MODIFICATION IN HIPPOCAMPAL SUBREGIONS IN RESPONSE TO EXCITOTOXIC STIMULI

Aleksandra Owczarek[1], Remigiusz Serwa[2], Michał Węgrzynowicz[1]

[1]Mossakowski Medical Research Institute PAS, Laboratory of Molecular Basis of Neurodegeneration, Poland, [2]The International Institute of Molecular Mechanisms and Machines PAS, Proteomic Core Facility, Poland

Hippocampal pyramidal neurons, especially in the subregion CA1, are particularly sensitive to a variety of neurotoxic stimuli, especially those involving excitotoxicity. CA1 neuronal injury and death is observed in neuropathologies like ischemia, epilepsy or traumatic brain injury. There is, however, a distinct heterogeneity across the hippocampal CA region in the neuronal response to pathology, as CA3 neurons are certainly less sensitive, and CA2 neurons – virtually resistant to excitotoxicity.

The molecular basis of these differences are not well known, but regional differences in protein post-translational modifications (PTMs) may be a possible mechanism potentially contributing to this heterogeneity. PTMS plays a crucial at every level of neuronal functioning, and can determine specific phenotypes of individual populations of the cells. The availability of the tools to study the dynamics of PTMs in the brain, in response to specified neurotoxic stimuli, in spatial and temporal

manner is low, therefore the need for new solutions and protocols is great.

Here, we employed acute sections of mouse hippocampus as an *ex vivo* model to analyze the subregion-specific dynamics of one of PTMs (named here PTM1) in experimentally induced excitotoxicity with the use of a novel bioorthogonal probe (named here P1). After entering the cell, P1 is utilized by endogenous enzyme to modify cellular proteins in the pattern reflecting the original profile of PTM1 in given conditions. Then, we labeled modified proteins *in situ* by attaching a fluorochrome to the probe in a specific reaction. Moreover, we show that labeling the slices with P1 can be combined with immunofluorescence, allowing precise regional, cellular and subcellular localization of P1-labeled proteins. These results show that the P1 probe may be an invaluable tool that will allow to understand better the crucial aspects of yet poorly studied PTM1 in physiology and pathology in individual cells, regions, and tissue types.

Key words: staining methods, post-translational modification, hippocampus, CA1, CA2

P4.1. THE EFFECT OF PHENCYCLIDINE ADMINISTRATION IN THE EARLY POSTNATAL PERIOD ON THE LEVELS OF GLUTATHIONE AND SULFUR AMINO ACIDS IN THE RAT BRAIN AS A POTENTIAL CAUSATIVE FACTOR UNDERLYING SCHIZOPHRENIA-LIKE BEHAVIOR IN ADULTHOOD

Zofia Rogóż[1], Kinga Kamińska[1], Magdalena Górny[2], Małgorzata Iciek[2], Elżbieta Lorenc-Koci[1]

[1]Maj Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland, [2]The Chair of Medical Biochemistry, Jagiellonian University Medical College, Kraków, Poland

Phencyclidine, an NMDA receptor antagonist, is frequently used to model behavioral and neurochemical changes of the schizophrenic type in laboratory animals. The aim of our study was to evaluate the effects of repeated administration of phencyclidine during early postnatal development on glutathione and sulfur-containing amino acids levels, as well as on enzymatic activity of antioxidant enzymes in the brain of 12-day-old rats and on schizophrenia-like symptoms in adulthood.

The male Sprague-Dawley pups were treated subcutaneously on the postnatal day p2, p6, p9 and p12 with either phencyclidine (10 mg/kg) or saline. In 12-day-old pups, 4 hours after the administration of the last dose of phencyclidine, the levels of glutathione, cysteine, methionine and homocysteine were determined, as well as the enzymatic activity of superoxidase dismutase (SOD), glutathione peroxidase (GPx) and glutathione reductase (GR) in the frontal cortex, hippocampus and striatum. Schizophrenia-like behaviors were assessed in 70-72-day-old rats treated with phencyclidine using the social interaction test, the novel object recognition test and open field test.

In 12-day-old pups treated with phencyclidine, significant decreases in glutathione and cysteine levels were found in all brain structures examined, but methionine was reduced only in the striatum and homocysteine in both the frontal cortex and the striatum. GR activity was increased in the frontal cortex while SOD activity was decreased in the hippocampus. In adult rats perinatal phencyclidine induced social and cognitive deficits.

The present study suggests that perinatal administration of phencyclidine induces long-term deficits observed in adult rats in behavioral tests used for evaluation of some negative and cognitive symptoms of schizophrenia.

This study was financially supported by statutory funds of the Maj Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland.

Key words: phencyclidine in early postnatal development, glutathione deficiency, social and cognitive deficits, neurodevelopmental model of schizophrenia

P4.2. COMING TOGETHER – THE NEURAL DYNAMICS OF TRANSITION FROM OUT-GROUP RESERVE TO IN-GROUP FELLOWSHIP

Anjaly Yadav, Mateusz Rycerz, Fahmida Haque, Anna Bryksa, Alicja Puścian

Laboratory of Emotions Neurobiology, BRAINCITY – Centre of Excellence for Neural Plasticity and Brain Disorders, Nencki Institute, Polish Academy of Sciences, Warsaw, Poland

Identifying conspecifics as belonging to an in-group, or the social cohort one belongs to, is a quick and unconscious process. In social species, diverse attitudes toward in-group and out-group individuals are reflected in the well-conserved neuronal background. Understanding those brain mechanisms may be facilitated by the behavioral protocols allowing to elicit naturalistic social behavior.

To investigate the emergence of social bonds between two unfamiliar groups, we used mice, a species of a highly social nature. Each of the groups, though of the same C57BL6/J strain, came from a different colony. Animals were tested in Eco-HAB, a computer-controlled system mimicking natural murine habitats. The Eco-HAB territory was divided into two equivalent parts – one for each group – which were subsequently merged. From that moment the animals from both groups could freely interact.

We show that immediately after the merger animals prefer following in-group conspecifics rather than the out-group ones. Notably, this tendency changes over the following hours. After overcoming initial hesitancy mice start to follow unfamiliar conspecifics with higher frequency than the familiar individuals. Further, in the initial phase after merger animals tend to spend more time with in-group conspecifics. However, to a varying degree, depending on both, the particular group and the individual. In the following hours, the social structure starts shifting, with some mice sticking to their previous social preferences, while others form close relationships with strangers.

In summary, we present the data illustrating the process of consolidation of the two previously unfamiliar groups. The presented discoveries form a foundation for further studies of the brain mechanisms underlying novel social bonds.

Key words: Systems Neuroscience, Social Interaction and Behavior, In-cohort Sociability

P4.3. IS THE TRIPLE NETWORK DYNAMICS A FRAME ASSOCIATED TO THE DISTURBANCE OF TEMPORAL EXPERIENCE IN SCHIZOPHRENIA? A KINAESTHESIA BASED PHENOMENOLOGICAL HYPOTHESIS

Camilo Sanchez[1], Marcin Moskalewicz[2], Drozdstoj Stojanov[3]

[1]Poznan University of Medical Sciences/Doctoral School/ Department of Humanities and the Social Sciences, Poland, [2]Poznan University of Medical Sciences/ Department of Humanities and the Social Sciences, Poland, [3]Plovdiv University of Medical Sciences, Bulgaria

POSTER WITHDRAWN

P4.4. MMP-9 MEDIATES BEHAVIORAL ALTERATIONS AFTER BACTERIA-LIKE INFLAMMATION IN EARLY LIFE

Karolina Protokowicz, Leszek Kaczmarek

BRAINCITY, Laboratory of Neurobiology, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Neurodevelopmental disorders (NDDs) that are characterized by altered social behavior such as autism spectrum disorders or schizophrenia are considered to have complex etiology. In a growing number of studies, neuroinflammation emerges as one of the potential causes. In our studies, we investigate the role of matrix metalloproteinase-9 (MMP-9) an extracellular protease, a well-known mediator of inflammatory responses, in behavioral consequences of early postnatal, LPS-driven, inflammation.

In the present study, we challenged the immune system of 7-day-old mice with a single injection of lipopolysaccharide (LPS; 0.05 mg/kg b.w.) to mimic bacterial infection or physiological saline as a control. To evaluate acute response to LPS, 2 and 6 hours after injection we measured serum levels of several inflammation agents using Luminex multiplexing assay. We observed elevated serum levels of TNF-α ($p<0.0001$), IL-6 ($p<0.0001$), IFN-γ ($p=0.16$), CCL-5 ($p<0.0001$), IL-10 ($p<0.0001$), and TIMP-1($p<0.0001$) in both sexes in comparison to saline-treated control 2 hours post-injection. Additionally, in males (but not females) treated with LPS, elevated levels of MMP-9 were observed ($p=0.0005$).

To further study the role of MMP-9, we conducted a behavioral assessment of adult wild-type animals (MMP-9 WT) and littermates lacking MMP-9 (MMP-9 KO) after LPS injection in P7, employing automated Eco-HAB® (EH) system and Three Chamber test (3Ch), both to assess sociability. WT males after the immune challenge were less interested in social odor from unknown animals (EH $p=0.0019$; 3Ch $p=0.0027$) while females were more interested in the unknown social object (EH $p<0.0001$; 3Ch ns). Interestingly this effect was not observed in MMP-9 KO animals.

In aggregate, the presented results suggest, that MMP-9 is involved in behavioral deficits after immune activation during the critical stage of neurodevelopment.

Key words: inflammation, development, sociability, MMP-9

P4.5. IMPACT OF REGULAR CYCLING TRAINING ON COGNITIVE CONTROL: A PRELIMINARY DATA FROM A LONGITUDINAL RANDOMIZED CONTROLLED TRIAL

Gabriela Rajtar, Michał Marzec-Remiszewiski, Tomasz S. Ligęza
Psychophysiology Laboratory, Institute of Psychology, Jagiellonian University, Poland

The relationship between exercise and cognitive function has been recently investigated, revealing promising effects on cognition, particularly inhibition. Inhibition is a core component of cognitive control and is essential for suppressing irrelevant information and maintaining focus on task-relevant stimuli. This preliminary study aimed to investigate the impact of regular cycling training on behavioral indices of inhibition in a flanker task. A total of 28 sedentary, young adults participants were randomly assigned to either the experimental group (n=14) or the control group (n=14). The experimental group (EG) underwent a supervised cycling training program for six weeks, with three training sessions per week. At the same time, the control group (CG) was instructed to stick to their usual habits. Before and after the intervention, all participants completed a Flanker task concurrently with EEG recordings. The task involved identifying the direction of a central target arrow while ignoring the surrounding distractor arrows. The task included trials with congruent (distractors point in the same direction as the target) and incongruent (distractors point in the opposite direction, demanding more inhibition) stimuli. Both reaction time (RT) and accuracy were recorded for each participant.

Comparing pre- to post-intervention, EG but not CG showed a significant improvement in RT in incongruent ($p<0.01$). None of the other effects of intervention (accuracy, RT in response to congruent trials) were significant. This suggests that regular cycling training boosted specifically inhibition. Overall, the findings support the hypothesis that regular cycling training can enhance cognitive control abilities, specifically related to response inhibition. Further analysis is planned to confirm the observed effects at the neuroelectrical level.

Key words: regular exercise, cognitive control, flanker task, inhibition

P4.6. EFFECTS OF ATRANORIN ON BEHAVIORAL PATTERNS IN EXPERIMENTAL ANIMALS: INVESTIGATING THE PHARMACOLOGICAL PROPERTIES AND POTENTIAL ANTIDEPRESSANT APPLICATIONS

Patrik Simko, Simona Mattova, Nicol Urbanska, Terezia Kiskova
Institute of Biology and Ecology, Faculty of Science, Pavol Jozef Safarik University in Kosice, Slovakia

Atranorin (ATR) is a secondary metabolite commonly found in lichens, exhibiting a diverse range of biological activities. Recent evidence suggests that ATR holds also potential neuroprotective properties. Thus, the aim of our study was to establish the neurobehavioral effects of ATR. Our research involved two distinct experiments: one with control groups consisting of healthy individuals (males and females handled independently) and an experiment with depressive-like groups (DEP) of laboratory Sprague-Dawley rats. Throughout both experiments, ATR was orally administered to the animals from 60th-90th postnatal days using a 10% ethanol solution at

a dosage of 10 mg/kg body weight. Subsequently, behavioral tests were conducted to observe and document the physiological effects of ATR on the laboratory animals, specifically the Open Field Test (OFT) and Elevated Plus Maze (EPM). In healthy rats treated with ATR, a significant increase in rearing behavior and defecation compared to the control untreated groups was revealed in OFT. Moreover, EPM test showed a significant increase in crossings through the center of the maze, and time spent in open arms. These clues led to the idea of testing the effects of ATR during depression-like states. In the DEP groups, we observed a significant increase in peripheral movement speed and distance traveled along the periphery in OFT. Additionally, in the DEP groups treated with ATR, there was an increase in the number of rearing events and time spent in open arms compared to untreated animals with depression. These findings lead to the conclusion that ATR exhibits a high potential as an antidepressant, highlighting the need for further research in this area.

The work was financially supported by the scientific grant agency APVV (APVV-21-0321), VEGA (1/0658/20) and the internal scientific grant system of PF UPJŠ (VVGS-PF-2022-2136 and VVGS-PF-2023-2161).

Key words: atranorin, behavior, behavioral tests, laboratory rats

P4.7. PEER INFLUENCE ON REWARD LEARNING OF MICE IN INTELLICAGES ALLOWS TO RECOVER THEIR SOCIAL STRUCTURE

Michał Lenarczyk[1], Bartosz Jura[1], Zofia Harda[2], Magalena Ziemiańska[2], Łukasz Szumiec[2], Jan Rodriguez Parkitna[2], Daniel Wójcik[3]

[1]Jagiellonian University, Faculty of Management and Social Communication, Kraków, Poland, [2]Maj Institute of Pharmacology of the Polish Academy of Sciences, Department of Molecular Neuropharmacology, Kraków, Poland, [3]Jagiellonian University, Faculty of Management and Social Communication, Kraków, Poland and Nencki Institute of Experimental Biology, Warsaw, Poland

Social influence in groups of freely interacting animals was shown to constitute a significant factor determining their behavior in many studies, but there is no universally accepted approach to describe inter-individual influences in quantitative terms. Here we propose a model-based approach to describe learning in a social context in mice. Our strategy extends reinforcement learning principles to encompass reward experience-based and social influence-based learning. We introduce a hierarchic Q-learning model which accounts for influences between each pair of animals in the group. We propose a heuristic procedure for the efficient fitting of model parameters to data and for pruning the model to retain only significant influences. The fitted model gives novel insight into the social structure of the group and constitutes a platform for exploration by simulation. Using the model and data from an Intellicage-based experiment in which a group of mice was taking part in a reversal learning task with saccharin as the reward, we discover that individual influences can be both positive or negative (attraction to or avoidance of visited corner), learning in some animals is driven primarily by social influence rather than by reward experience, and self influence (tendency to repeat or avoid repeating visits in the same corner) is always among the strongest predictors of choice.

Supported by the Foundation for Polish Science (grant no POIR.04.04.00-00-14DE/18-00) carried out within the Team-Net program co-financed by the European Union under the European Regional Development Fund, by grant OPUS 2019/35/B/NZ7/03477 from the National Science Centre Poland, and by the statutory funds of the Maj Institute of Pharmacology of the Polish Academy of Sciences.

Key words: reversal learning, social influence, social structure, model

P4.8. LEXICAL SEARCH BASED ON LETTER CUES IS MORE DEMANDING THAN BASED ON CATEGORY CUES: EVIDENCE FROM FMRI

Piotr Górniak, Agata Wolna, Zofia Wodniecka

Language and Bilingualism Lab, Institute of Psychology, Jagiellonian University, Kraków, Poland

Verbal fluency (VF) is a task widely used in research on cognitive control and language processing. There are two versions of the task. In both, participants are asked to produce as many words as possible following a given cue, be it a semantic category in a semantic fluency task (SF) or a letter in a phonological fluency task (PF). The goal of the analyses was to explore the brain basis of mechanisms engaged in the VF task and to compare outcomes with that of previous investigations.

41 participants performed SF and PF tasks during the fMRI scanning. For each task, 12 cues were used. By increasing the number of cues, we should increase their

generalizability. For each cue, participants were given 10 s to produce as many words as they could.

On a behavioral level, we found that the participants produced more words in the SF task than in the PF. On a neural level, both VF tasks were linked to a significant increase in activation in a network of left-lateralized structures including the middle frontal gyrus, inferior frontal gyrus, paracingulate gyrus, and fusiform cortex. These structures were previously shown to be important for both language processing as well as cognitive control.

Contrasts between the two different versions of the task show that the SF involves stronger activations in middle temporal gyrus, precentral gyrus, lingual gyrus, and cerebellum, while the PF is linked to increased activity in inferior frontal gyrus and posterior cingulate gyrus. What is more, PF showed stronger left-lateralization than SF.

Our study confirms previous behavioral findings indicating that word retrieval based on phonological cues is more difficult than based on semantic cues. The fMRI results indicate that PF sets higher demands on cognitive control, while SF performance has stronger connections to semantic memory.

Key words: verbal fluency, fMRI, semantic fluency, phonological fluency, cognitive demand

P4.9. ERP SIMILARITIES AND DIFFERENCES BETWEEN SIMON, FLANKER AND MULTI-SOURCE CONFLICTS: THE SAME SEQUENCE BUT CONFLICT-SPECIFIC INTENSITY OF COGNITIVE PROCESSES

Ingrida Antonova[1], Katarzyna Paluch[1], Patrycja Dzianok[1], Jan Nikadon[2], Jakub Wojciechowski[3], Katarzyna Jurewicz[4], Ewa Kublik[1]

[1]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland, [2]Centre for Modern Interdisciplinary Technologies, Nicolaus Copernicus University, Toruń, Poland, [3]Bioimaging Research Center, Institute of Physiology and Pathology of Hearing, Warsaw, Poland, [4]Faculty of Medicine and Health Sciences, McGill University, Montreal, Canada

Brain's cognitive control helps to select task-relevant information and suppress erroneous behaviors. Its consecutive processes: monitoring, suppression, and resolution of a conflict may be represented by the N2, N450 and SP (slow potential) waves of event related potentials (ERP) [1].

To monitor these processes in Simon (S0) and flanker (F0) conflict types, we recorded EEG in young adults performing extended Multi-Source Interference Task [2]. We used ERP-microstate (MS) and source analyses, and correlated differences in MS dynamics with behavioral performance [3].

Performance worsened from no-conflict, to S0, F0 and multi-source (FS) condition. Superadditively more errors were made for combined (FS) than separate conflicts.

MS analysis revealed the same consecutive mental processes in all conditions. Conflict suppression (MS5; MS6 related to N450/P3b waves) and resolution (MS7 related to SP) showed significant effects for both S0 and F0 trials. MS6; MS7 had lower amplitudes for conflicts presented together (FS) than separately. The flanker effect was found also for the selective attention (MS3) involved in flanker conflict monitoring.

Longer MS5 correlated with lower accuracy in F0 trials, while weaker MS7 correlated with longer RTs for F0 and FS. For the Simon effect, slower responses were associated with weaker MS6. Source analysis showed that MS5 represented activation of intraparietal sulci, MS6 – posterior cingulate cortex, and MS7 – frontal eye fields, anterior cingulate cortex and left motor cortex.

DAN activity during conflict suppression and resolution was crucial for F0 and FS conflict processing and behavioral outcome, while default mode network (DMN) activation during suppression phase was more important for fast processing of S0 conflict.

1. Heidlmayr et al. 2020, 10.1016/j.bandc.2020.105637, 2. Sheth et al. 2012, 10.1038/nature11239, 3. Schiller et al. 2016, 10.1073/pnas.1515828113.

Key words: cognitive control, event-related potential, microstate

P4.10. SYNAPTIC PLASTICITY IMPAIRMENT RESCUE IN AN IDIOPATHIC MODEL OF AUTISM SPECTRUM DISORDER

Ksenia Meyza[1], Tomasz Nikolaev[1], Tomasz Górkiewicz[1], Klaudia Nowicka[2], Maciej Winiarski[1], Maria Wołyniak[1], Małgorzata Śliwińska[3], Joanna Jędrzejewska-Szmek[4], Ewelina Knapska[1]

[1]Laboratory of Emotions Neurobiology, BRAINCITY – Center of Excellence for Neural Plasticity and Brain Disorders, Nencki Institute of Experimental Biology, Poland, [2]Laboratory of Neurobiology, BRAINCITY – Center of Excellence for Neural Plasticity and Brain Disorders, Nencki Institute of Experimental Biology, Poland, [3]Laboratory of Imaging Tissue Structure and Function, Nencki Institute of Experimental Biology, Poland, [4]Laboratory of Neuroinformatics, Nencki Institute of Experimental Biology, Poland

Autism spectrum disorder (ASD) is characterized by, among other indicators, low social approach, and high cognitive rigidity. These deficits belong to Systems for Social Processes and Cognitive Systems Domains of the Research Domain and Criteria framework. To study neuronal mechanisms underlying these deficits in an idiopathic mouse model of ASD (the BTBR $T^{+}Itpr3^{tf}$/J strain) we employed automated behavioral protocols based on voluntary exploration and preference for alimentary reward. To make these tests ethologically accurate and devoid of human bias we utilized a home-cage approach and tested their social preference in the Eco-HAB system and their ability to discriminate between 10% sucrose and water in the IntelliCage system (TSE). We found that BTBR mice displayed prolonged interest in (lack of habituation to) social stimuli and impaired discrimination learning skills. This was accompanied with an aberrant synaptic plasticity profile (instability of long-term potentiation and an immature dendritic spine morphology) within the central nucleus of the amygdala, CeA, a structure crucial for reward learning. Seeing as both of these measures are reliant on extracellular matrix metalloproteinase activity (e.g., MMP-9) we tested the hypothesis that aberrant MMP-9 could be responsible for the synaptic phenotype of the BTBR model. We found an overabundance of this enzyme in the CeA, which could be readily lowered with a local supplementation of tissue inhibitor of metalloproteinases-1 (TIMP-1). The TIMP-1 releasing nanoparticles proved effective at rescuing the morphological and functional synaptic plasticity in the CeA of BTBR mice but proved less effective in altering behavior. The lack of the effect in the social deficit domain recapitulates our finding in the monogenic ASD model, the FXKO mouse. The modest improvement of discriminative learning however raises new questions as to the mechanism of BTBR reward learning disfunction.

The study was funded by Polish National Science Centre grants 2015/18/E/NZ4/00600 to KM and 2017/27/B/NZ4/02025 to EK.

Key words: autism, synaptic plasticity, BTBR, MMP-9

P4.11. CHEMOGENETIC INHIBITION OF THE VTA-ACC PATHWAY DECREASES MOTIVATION FOR SOCIAL INTERACTION IN C57BL/6 MICE

Marcin Lipiec[1], Asia Macaione[2], Mohammad Abdelfattah[2], Anju Cyriac[2], Ewelina Knapska[2]

[1]Nencki Institute of Experimental Biology, Laboratory of Emotions Neurobiology, Warsaw, Poland, [2]Nencki Institute of Experimental Biology, Laboratory of Emotions Neurobiology, Warsaw, Poland

Our research focuses on cellular and neural mechanisms that underlie emotions and motivation for social interactions. Prior research from our laboratory suggests that the drive for social interaction in mammals may be influenced by the circuit between the anterior cingulate cortex (ACC) and the ventral tegmental area (VTA). To investigate this, we used inhibitory DREADD receptors, expressed specifically in the VTA neurons that project to the ACC in C57BL/6 mice, to chemogenetically inhibit the activity within the pathway in question.

First, we evaluated the propensity for social engagement between the DREADD-expressing animals and their wild-type partners in a social interaction test after a saline or DREADD agonist Compound 21 (C21) injection. Then, we housed a mixed population of both DREADD-expressing and wild-type animals in Eco-HAB – an RFID-based cage system for automated measurement and analysis of social preference. We assessed changes in their in-cohort sociability, social hierarchy, and individual approach to social stimuli before and after C21 injections. We found that inhibition of the VTA-ACC projections changes socially relevant actions, indicating that this pathway is at least partially responsible for the motivation for social contacts.

Key words: DREADD receptors, Chemogenetic inhibition, Social interaction test, Eco-HAB, Motivation for social contacts

P4.12. CHANGES IN APPETITIVE ASSOCIATIVE LEARNING IN COMPULSIVE SEXUAL BEHAVIOR DISORDER – fMRI STUDY

Jakub Wojciechowski[1], Małgorzata Draps[2], Ewa Kublik[3], Tomasz Wolak[4], Mateusz Gola[5]

[1]Institute of Physiology and Pathology of Hearing, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland, [2]Institute of Psychology of PAS, Poland, [3]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland, [4]Institute of Physiology and Pathology of Hearing, Poland, [5]Institute for Neuronal Computation of University of California San Diego, Institute of Psychology of PAS, Poland

The Compulsive Sexual Behavior Disorder (CSBD) is experienced by 3-6% of the population and is characterized by repeated failure to resist an impulse or urge to engage in different kinds of sexual behaviors. Those behaviors, initially rewarding, turn into harmful and impair important areas of living. Only recently WHO officially recognized CSBD (2021) under impulse control disorder, although there is consensus among scientists that currently the evidence to conclusively determine whether CSBD is impulse-control, compulsivity-related or addictive disorder is insufficient. In our study we aimed to answer this call and fill the knowledge gap on appetitive conditioning and extinction processes in CSBD in key regions of interest (ROI) processing motivation and reward – Ventral Striatum and Orbitofrontal Cortex (OFC). Brain activity was measured using fMRI, during which subjects were tasked with processing of erotic and monetary events.

Age-matched CSBD patients and healthy-control subjects (n=32 in each group) participated in the study. In addition to measuring fMRI brain activity and reaction times (RT) in tasks, subjects also rated their arousal and valence toward abstract cues paired with rewards before and after conditioning. Statistical analysis of RT, arousal and valence and ROI were conducted using 3-way ANOVA: (2)Group *(2)Condition *(2)Task Phase.

The results suggest that associative learning is altered in CSBD patients on both behavioral and functional level. CSBD subjects showed increased value attribution and motivation for both rewarding cues on declarative and behavioral, suggesting general alteration of rewarding actions learning. Striatal activity showed hypoactivation in CSBD subjects for both rewarding cues. At the same time, mirroring this activity, OFC showed hyperactivity for both rewarding cues. These findings are partially in line with previous studies on addictions.

Supported by NCN-Grant-2016/21/N/HS6/02635.

Key words: Compulsive Sexual Behavior Disorder, conditioning, fMRI, reward system

P4.13. SOCIAL BOX AS A TOOL TO STUDY COMPLEX SOCIAL BEHAVIOR IN MICE

Bartosz Zglinicki[1], Patrycja Ziuzia[1], Mathias Schmidt[2], Michal Slezak[1]

[1]Lukasiewicz Research Network – PORT Polish Center for Technology Development, Poland, [2]Max Planck Institute of Psychiatry, Germany

Validation of any biological intervention developed for tackling the root or symptoms of neuropsychiatric disorders requires the proper tools. Disturbances of social behavior is a hallmark of many psychiatric conditions, such as depression, anxiety and schizophrenia. Capturing and quantifying broad range of social behavior simultaneously within a single tool is therefore essential, as it would allow for registration and clustering of groups of behavior specific for particular disorders. Such method would be of great advantage for better translational studies.

Currently available setups for quaintifying social behavior suffer from various factors, which influence reliability and reproducibility. Automatization of the process can overcome limitations such as experimentator bias, data collection and data analysis, including the exploitation of AI for big data volume. The emergence of tools based on machine learning in recent years allows to standardize behavioral studies and produce high quality data sets and results.

Same-NeuroID project is a multicenter collaboration aiming to unify tools for translational research. In particular, we implemented a pipeline for efficient characterization of complex social behavior in mice, in a simple, scalable, affordable, validated and "future-proof" way.

In the experimental setup, animals are housed together in semi-naturalistic environment with proper bedding, food and water, under 12h/12h light/dark cycle. Animals are recorded for long hours to ensure capturing of diverse behavior, specific to both active and non-active phases. DeepLabCut software is used subsequently for pose estimation of recorded animals and extracted coordinates are processed by deepOF software to create set of features. These features are then used to "feed" models of both supervised and unsupervised learning for complex behavior classification.

This work was supported by the HE Twinning project 'SAME-NeuroID' and a grant OPUS UMO-2021/41/B/NZ3/04099.

Key words: Social Box, social behavior, automatization, machine learning, deep learning, DeepLabCut, DeepOF, psychiatric conditions

P4.14. EFFECT OF CHRONOTYPE ON SLEEP DEPRIVATION TOLERANCE

Karolina Warzecha[1], Halszka Kontrymowicz-Ogińska[2]

[1]Institute of Zoology and Biomedical Research, Jagiellonian University, Cracow, Poland, [2]Institute of Applied Psychology, Jagiellonian University, Cracow, Poland

Human cyclic functioning is based on three clocks: the social clock, which determines the hours of social action; the sundial, which hinges on day and night; and our internal biological clock, which hinges on biological processes at both the cellular and behavioral levels. Genetic and environmental differences have made the molecular structure of the biological clock an individual matter, affecting an individual's specific fit with the external schedule. These differences have been described as the chronotype (morning, intermediate and evening type). It determines the time of day when an individual achieves the highest activity and the ability to fit into the external schedule. We investigated whether chronotype affects the tolerance of sleep deprivation. We determined the chronotype using the ChQ questionnaire and then subjected them to chronic sleep deprivation (n= 29; 5 days/5h each night) and acute sleep deprivation (n=28; sleepless night). After each condition, subjective feelings experienced after sleep deprivation were checked with the CHICa questionnaire. It was shown that subjective phase (ME scale, morning-evening orientation) didn't differentiate significantly the severity of sleep loss effects. In contrast, subjective amplitude (AM scale, distinctness of the rhythm, the ability to modulate physiological states as defined by ChQ) played an important role. The higher score on the AM scale, the higher the CHICa score, thus the lower the tolerance to sleep deprivation in both chronic and acute deprivation conditions ($r=0.41$, $p<0.03$ and $r=0.40$, $p<0.03$, respectively). Given that the evening chronotype is associated with the higher risk of health disorders, an in-depth understanding of this phenomenon is important in order to tailor individual strategies and therapies and take appropriate steps to minimize the negative effects of the evening chronotype.

Funding: Polish National Science Centre Nr 2018/29/B/HS6/01934.

Key words: chronotype, sleep deprivation, chronic sleep deprivation

P5.1. FROM GENES TO BRAIN FUNCTION: UNVEILING THE IMPACT OF ALZHEIMER'S DISEASE RISK-GENES ON RESTING-STATE EEG/fMRI FEATURES IN NON-DEMENTED MIDDLE-AGED INDIVIDUALS

Patrycja Dzianok[1], Jakub Wojciechowski[1], Tomasz Wolak[2], Ewa Kublik[1]

[1]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Poland, [2]Bioimaging Research Center, Institute of Physiology and Pathology of Hearing, Poland

The etiology of late-onset Alzheimer's disease (LOAD) is influenced by genetic risk. The apolipoprotein E (*APOE*) gene is the major susceptibility gene for LOAD and the gene encoding the phosphatidylinositol-binding clathrin assembly protein (*PICALM*) has been shown to interact with *APOE* increasing the risk. It is well known that LOAD affects EEG rhythms by reducing signal complexity and shifting signal strength to lower frequencies (so-called "EEG slowing"). Functional connectivity is also disrupted in AD patients, particularly within the default mode network (DMN). Research on presymptomatic at-risk individuals is needed to understand how genetic risk affects the brain function and early progression to dementia.

We used electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) during the resting protocol to test healthy middle-aged participants (N=~78) with different genetic burden of LOAD. We analyzed the EEG signal using spectral analysis (relative power) and complexity analysis (Higuchi's algorithm). In addition, a connectivity analysis using group-level independent component analysis (group ICA) was performed to estimate temporally consistent networks from the fMRI data.

Healthy, presymptomatic LOAD risk carriers were characterized by reduced EEG complexity and slight EEG slowing. The effects of *APOE/PICALM* genotypes on functional connectivity in fMRI were complex and showed subtle differences between healthy risk carriers and non-risk carriers within the DMN and in the anterior cingulate cortex (ACC). This finding is interesting because ACC is linked to higher-level cognitive processes and plays a crucial role in executive functions that are disrupted in late-onset Alzheimer's disease.

Key words: Alzheimer's disease, APOE, PICALM, risk-genes, biomarkers, EEG, fMRI

P5.2. THE RELATIONSHIP BETWEEN GENERAL COGNITIVE FUNCTIONING, NUMEROSITY COMPARISON ABILITY AND COGNITIVE STRATEGIES IN ELDERLY PEOPLE

Jakub Słupczewski[1], Małgorzata Gut[2], Jacek Matulewski[3], Adam Tarnowski[2]

[1]Doctoral School of Social Sciences, Nicolaus Copernicus University in Torun, Poland, [2]Institute of Psychology, Faculty of Philosophy and Social Sciences, Nicolaus Copernicus University in Torun, Poland, [3]Department of Informatics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Torun, Poland

Literature has shown age-related differences in numerical competences, e.g., decline in the level of numerosity comparison ability is visible at age of 30. Some studies point out individual differences in the cognitive strategies used during this task performance and that they are also related to age. The aim of our study was to determine the relationships between numerosity comparison ability, cognitive strategies used in the performance of such task and the general cognitive functioning in older people.

Forty-seven elderly people without neurological or psychiatric problems (mean age=70,45, SD=4,63) participated in the study. General cognitive functioning was examined with the use of MMSE and MoCA scales. During the measurement of the numerosity comparison level, in the various difficulty variants, the reaction time and correctness was recorded. Cognitive strategies were reported by participants during the interview.

The obtained results showed that level of performance in the attention and executive function processing is positively related with the correctness of numerosity comparison. Moreover, greater level of long-term memory resources and the level of visuospatial skills correlated with shorter reaction time during numerical task performance. Regression analyses showed that both the level of general cognitive functioning (e.g., attention or visuospatial abilities) and the cognitive strategies used by participants in numerosity comparison test explain 9 to 21 percent of the variance in the obtained results.

Based on the results, it can be concluded that there are positive relationships between cognitive functioning and proficiency in numerosity comparison. Furthermore, cognitive resources are reflected in the strategies used by older people. Therefore, it seems that the study of the cognitive strategies used during numerosity comparison may have applications in the planning and development of new methods useful for diagnosing cognitive deficits.

Key words: aging, numerical cognition, cognitive strategies, attention, memory, executive functions

P5.3. ALTERED GAIT PARAMETERS UNDER SPATIAL NAVIGATION TASK IN OLDER ADULTS WITH SUBJECTIVE COGNITIVE COMPLAINTS AND MEDIAL TEMPORAL ATROPHY

Natalia Anna Pawlaczyk[1], Rafał Milner[1], Magdalena Szmytke[2], Bartłomiej Kiljanek[1], Bibianna Bałaj[1], Monika Lewandowska[1]

[1]Institute of Psychology, Faculty of Philosophy and Social Sciences, Nicolaus Copernicus University in Torun, Torun, Poland, [2]Faculty of Psychology, University of Warsaw, Warsaw, Poland

Self-reported subjective cognitive complaints (SCC) are considered an objective indicator of cognitive decline. Patients with SCC may already have discrete lesions in the brain that do not yet affect standard neuropsychological tests performance. The aim of this study is to verify whether the gait parameters, measured while navigating, could differentiate between the seniors reporting cognitive complaints with and without medial temporal lobe atrophy. In our study, older adults (≥60 years of age; n=45) with SCC performed the ecological navigation task with simultaneous recording of gait parameters and underwent neuropsychological assessment. The compared groups were not significantly different in neuropsychological test scores; however, differences in some gait parameters (propulsion index, gait speed, step length, stance, and symmetry) were found in certain phases of the navigation task. Additionally, the propulsion index best classified the participants into groups with and without medial temporal lobe lesions (80% of correct classifications). These findings suggest that selected gait parameters in the navigation task are sensitive enough to detect even subtle medial temporal atrophy in older adults with cognitive complaints and subtle medial temporal atrophy.

The research was supported by the grant: "Through the foot to the brain" in the Excellence Initiative – Debuts II Competition (2020) at the Nicolaus Copernicus University in Torun.

Key words: older adults, subjective cognitive complaints, spatial navigation, gait parameters

P5.4. ELECTROPHYSIOLOGICAL ASSESSMENT OF BIO-BEHAVIORAL PERSONALITY SYSTEMS? REVISED REINFORCEMENT SENSITIVITY THEORY AND FEEDBACK RELATED NEGATIVITY

Julia Zaborowska, Sławomir Duda, Krzysztof Tołpa, Joanna Dreszer, Rafał Milner

Institute of Psychology, Faculty of Philosophy and Social Sciences, Nicolaus Copernicus University in Torun, Poland

The Reinforcement Sensitivity Theory (RST) is classified as personality theory, although some researchers associate it with the neuropsychological theory of emotions, motivation, and learning. Studies attempt to embed it within specific brain structures and mechanisms. One of the proposed electrophysiological indices for underlying mechanisms of reinforcement learning is Feedback Related Negativity (FRN).

The aim of our study was to verify if individual differences in the personality traits, measured by the Revised Reinforcement Sensitivity Theory-Personality Questionnaire (RST-PQ), would be reflected in changes of the Feedback Related Negativity (FRN).

Forty-nine subjects participated in the study. The RST-PQ consisted of several subscales assessing different aspects of biologically-rooted bio-behavioral systems: the Behavioral Inhibition System (BIS), the Fight-Flight-Freeze System (FFFS) and the Behavioral Approach System (BAS). A 64-channel EEG system was used to record FRN in response to rewarding and punishing stimuli during the Monetary Incentive Delay task.

The study employed repeated measures analysis of FRN latency, with the within-subject factors: the location (frontal, central, parietal), condition (reward *vs.* punish *vs.* control), and response correctness (correct *vs.* incorrect) and the between-subjects factor: the intensity level of the bio-behavioral systems.

The analysis showed a significant main effect of the BAS-RI level. The low-BAS RI individuals showed higher latencies. In addition, for the FFFS as between-subjects factor two significant interaction effects were observed: with condition and with correctness. Specifically, subjects with high FFFS scores exhibited higher latencies, for the reward condition and correct responses respectively.

Further analysis should enable better understanding of the mechanisms underlying personality biological systems.

This study was supported by a grant of the programme Research University Excellence Initiative at NCU, no. 90-SIDUB.6102.69.2021.G4NCUS2.

Key words: EEG, Feedback Related Negativity, RST, Reinforcements, Personality

P5.5. BOLD CORRELATES OF SIMON AND FLANKER CONFLICTS AND TIME-ON-TASK EFFECTS IN EXTENDED MULTI-SOURCE INTERFERENCE TASK

Jakub Wojciechowski[1], Katarzyna Jurewicz[2], Patrycja Dzianok[3], Ingrida Antonova[3], Katarzyna Paluch[4], Tomasz Wolak[5], Ewa Kublik[3]

[1]Nencki Institute of Experimental Biology, Warsaw, Poland, Bioimaging Research Center, Institute of Physiology and Pathology of Hearing, Warsaw, Poland,
[2]Nencki Institute of Experimental Biology, Warsaw, Poland, Faculty of Medicine and Health Sciences, McGill University, Montreal, Canada,
[3]Nencki Institute of Experimental Biology, Warsaw, Poland, [4]BRAINCITY, Nencki Institute of Experimental Biology, Warsaw, Poland, [5]Bioimaging Research Center, Institute of Physiology and Pathology of Hearing, Warsaw, Poland

Adequate cognitive control brain mechanisms are essential to identify and resolve conflicts between standard and alternative behaviors, to properly navigate in interfering information streams. Specific mechanisms may be dedicated to particular interference types or the same mechanism may serve to control any effortful task, even one devoid of conflict component. The latter hypothesis is supported by reports attributing activity observed in the presence of conflict to longer time spent on the task (i.e., time-on-task effects).

We used functional magnetic resonance imaging (fMRI) to determine shared and conflict-specific mechanisms of conflict resolution and their separability from the time-on-task effects. Forty healthy young adults (24.6±4.2 years old) performed Multi-Source Interference Task (MSIT [1,2]) in an extended version, which uses stimuli with Simon and flanker type interference alone or in combination. Conflict conditions were contrasted with no-conflict neutral trials and time-on-task effects in Simon, flanker, and multi-source conflicts were estimated on the basis of their mean reaction time (RT) and GLM parametric modulation model parameters obtained for no-conflict condition.

We found [3] common and conflict-specific activity patterns: increases of activity in the dorsal attention network (DAN) and decreases of activity in the default mode network (DMN) were largely shared across the tasks. These DMN and DAN (de)activations followed increases in reaction time. On the other hand, activity in the sensory and sensorimotor cortices, as well as in the posterior medial frontal cortex (pMFC) – a key region implicated in conflict processing – could not be fully explained by the time-on-task effects.

[1] Bush et al. 2003 DOI: 10.1038/sj.mp.4001217, [2] Sheth et al. 2012 DOI: 10.1038/nature11239, [3] Wojciechowski, Jurewicz et al. preprint DOI: 10.1101/2023.05.19.541457.

This work was funded by the Polish National Science Centre (NCN) grant no. 2016/20/W/NZ4/00354.

Key words: cognitive control, time-on-task, response conflict, fMRI, mPFC

P5.6. EFFECTIVENESS OF THE COGNITIVE TRAINING WITH THE USE OF THE MATHEMATICAL COMPUTER GAME IN CHILDREN WITH DYSCALCULIA RISK

Małgorzata Gut[1], Katarzyna Mańkowska[2], Jakub Słupczewski[2], Jacek Matulewski[3]

[1]Institute of Psychology, Faculty of Philosophy and Social Sciences, Nicolaus Copernicus University in Torun, Poland, [2]Doctoral School of Social Sciences, Nicolaus Copernicus University in Torun, Poland, [3]Department of Informatics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Torun, Poland

The beneficial effect of cognitive training using computer games on the level of mathematical skills has been widely proven, and it is used in education and therapy, e.g., in dyscalculia. However, some methodological limitations (no control game or no passive and healthy control groups) make it difficult to compare the results obtained in studies and to make clear conclusions.

Sixty eight children (8-11 years old) with the risk of dyscalculia participated in the study and they were divided into 3 groups: 21 children undergoing cognitive training with the computer game Kalkulilo (based on numerical-spatial relationship); 23 playing with the control game (using non-numeric symbols); and 19 with no training. They performed two (pre- and post-test) computer tasks measuring the level of basic numerical skills: number comparison, Numerical Stroop, numerosity estimation, number line estimation (0-100 and 0-1000 range). The cognitive training lasted 5 hours and was divided into 8-10 sessions of 30-45 min each.

The results showed the shorter reaction times in Numerical Stroop and the greater precision of 0-1000 number line estimation after the training with the Kalkulilo game.

Although the effect of both Kalkulilo and the control game showed in individual participants in the results of several tasks, there were no clear differences at the group level. The probably reason is the great heterogeneity of the sample, observed even at the pre-test (children differ in the level of dominant deficit symptoms, which reflects the existence of several types of dyscalculia) and at the post-test (individual participants showed improvement, but in the level of various skills – e.g. only in numerosity estimation or in number line estimation).

These results are consistent with the discussion concerning, on the one hand, difficulties in diagnosing dyscalculia, as well as developing and demonstrating the effectiveness of cognitive training and the transfer of trained to non-trained skills.

This study was supported by the National Science Centre, SONATA BIS grant, number 2017/26/E/HS6/00033.

Key words: mathematical cognition, computer games, mental number line, dyscalculia

P5.7. NEURODYNAMICS OF DIVERGENT THINKING: AN EEG MICROSTATE ANALYSIS

Ewa Ratajczak, Martyna Olszewska

Nicolaus Copernicus University, Institute of Psychology, Poland

Neural correlates of creativity have been investigated in several ways, including EEG microstate analysis. However, the microstate neurodynamics of the most basic component of the creative process – divergent thinking – has not been analysed up to date. The EEG signal was collected from young healthy participants upon inventing alternative uses for five objects of everyday use (umbrella, shoe, soap, pen, and brick). Creative performance was assessed as fluency (the number of valid alternative uses generated) and average idea originality (idea uniqueness in the analysed sample). EEG microstate analysis revealed 8 microstate classes. 3 parameters were calculated for each class: occurrence (the number of times a given class is dominant per second), duration (the average time lapse a given class is dominant), and coverage (the percent of total recording time a given class is dominant). The influence of fluency and originality on microstate parameters was analysed with a two-factor ANOVA. The results revealed that higher fluency was possibly related to decreased phonological/abstract and visual processing, and enhanced mind wandering and internally directed attention. Enhanced average originality was feasibly represented by diminished phonological/abstract processing, and increased

abstract thinking. Significant interaction effects between fluency and average originality were observed. Generally, more creative individuals seem to engage cognitive control and focus their attention internally. At the same time, they are characterized by more imaginative, rather than semantic or sensory processing of the object and the surrounding.

Key words: creativity, divergent thinking, microstate neurodynamics

P6.1. INDUCED mTOR PATHWAY HYPERACTIVITY IN DENTATE GRANULE CELLS LEADS TO THE IMPAIRMENT OF PATTERN SEPARATION IN MICE

Farzad Khanipour, Karol Sadowski, Adam Gorlewicz

Nencki Institute of Experimental Biology, Neurobiology of Emotions Lab, Poland

Temporal lobe epilepsy (TLE) is the most common form of focal epilepsy in humans. In addition to seizures, TLE is often linked to cognitive impairments, with episodic memory being a major deficit in this condition. Nevertheless, the neurobiological mechanisms behind the common etiology of TLE and episodic memory dysfunction are poorly understood. The hippocampus, a focal point for seizure propagation in the temporal lobe and a hub for episodic memory formation, plays the main role in the pathophysiology of TLE. In hippocampus, the axons of dentate gyrus (DG) granule cells, namely mossy fibers, innervate CA3 pyramidal neurons *via* presynaptic terminal expansions known as giant mossy fiber boutons. This physiological synaptic pattern, when impaired, might lead to the destabilization of tuned transmission between DG and CA3 cells contributing to cognitive dysfunctions. In the presented research, we explore dispersion of giant mossy fiber boutons as an underrecognized phenomenon that seems to be associated with a spectrum of epileptiform neuropsychiatric dysfunctions in different mouse models. Using functional and structural imaging in conjunction with behavioral studies, we demonstrate that hyperactivation of mTOR in DG granule cells may lead to dispersion of mossy fiber boutons with severe implications for pattern separation during episodic memory formation. We hypothesize that dispersion of mossy fiber boutons might link temporal lobe seizures with deficits in hippocampus-dependent cognition.

P6.2. THE ROLE OF Brg1 IN THE DEVELOPMENT OF SEIZURE-LIKE BEHAVIOR IN ZEBRAFISH LARVAE

Roberto Pagano, Justyna Zmorzyńska, Jacek Jaworski

Laboratory of Molecular and Cellular Neurobiology, International Institute of Molecular and Cell Biology, Warsaw, Poland

The Brahma-related gene 1 (Brg1) encodes the catalytic subunit of the SWItch/Sucrose Non-Fermentable (SWI/SNF) chromatin remodeling complex, which regulates gene expression by relaxing chromatin structure and allowing greater access to transcription factors and repressors. Although many SWI/SNF-regulated genes have been linked to autism spectrum disorder and epilepsy, the role of Brg1 in epilepsy has not been well characterized. In this study, we investigated the effects of a Brg1 inhibitor on zebrafish larvae to analyze the role of Brg1 in the development of seizures. Our results show that 1 day-post fertilization (dpf) larvae treated with the Brg1 inhibitor exhibited more double body coils, indicating seizure-like behavior controlled by the glutamatergic system. Then 5 dpf larvae were tested for locomotor behavior. After 48 hours of treatment, inhibition of Brg1 resulted in reduced fish locomotion accompanied by increased levels of inflammatory markers associated with human temporal lobe epilepsy and neuronal death. In contrast, after 24 hours of treatment, zebrafish exhibited increased burst level and fast swimming, representing seizure-like behavior, which was rescued by N-methyl-D-aspartate receptor antagonist treatment. This behavior was also accompanied by an initial proinflammatory response but no neuronal death. Furthermore, we found that Brg1 inhibition led to lower levels of GAD65+67 in the optic tectum and cerebellum but not in the pallium after 24 hours of treatment.

In conclusion, our results suggest that Brg1 is involved in the development of seizure-like behavior by affecting the glutamatergic system and may be a potential therapeutic target for epilepsy.

The research was financed under the NCN MAESTRO grant 2020/38/A/NZ3/00447 project.

Key words: Brg1, Zebrafish, Epilepsy, Seizure

P6.3. COMPARATIVE TRANSCRIPTOMIC ANALYSIS OF MATURE RAT NEURON MODELS OF INDUCED INSTABILITY OF THE DENDRITIC ARBORS

Juan Zeng, Magdalena Mlostek, Katarzyna Misztal, Malgorzata Urbanska, Jacek Jaworski

International Institute of Molecular and Cell Biology in Warsaw, Poland

Neuronal dendritic arbors are essential elements of neuronal networks. Once established during development, mature dendritic arbors remain relatively stable. Yet, the loss of dendrite stability has been associated with mental disorders, including major depressive disorder. The molecular mechanisms accountable for the dendritic arbor stability remain largely unknown, and they are the subject of our research. To reveal them, we first developed *in vitro* models of mature dendritic arbors' destabilization using cultured neurons and stimuli often linked with depression (e.g., changed neuronal activity or inflammatory cytokines). Next, we compared transcriptomes of control mature neurons, mature neurons with unstable dendrites, and young neurons with naturally dynamic dendritic arbor. From the transcriptome profiling, 77 differentially expressed genes were selected for further functional analysis to verify their role in dendrite dynamics. As a result, we identified 14 genes previously unknown to have a role in mature dendritic arbor dynamics. The new genes were significantly enriched in KEGG terms such as the calcium signaling pathway and long-term depression suggesting their importance in dendritic arbor stabilization.

This work was financed by the TEAM grant from the Foundation for Polish Science (POIR.04.04.00-00-5CBE/17-00).

Key words: dendritic arbor, stability, transcriptome, mechanism

P6.4. ANXIOLYTIC AND ANTIDEPRESSANT ACTIVITY OF NEW PYRROLIDINE DERIVATIVE WITH 5-HT1A RECEPTOR INTERACTION IN MICE

Jolanta Orzelska-Górka[1], Claudia Sorbi[2], Silvia Franchini[3], Marta Kruk-Słomka[1], Ewa Kędzierska[1], Grażyna Biała[1]

[1]Department of Pharmacology and Pharmacodynamics, Medical University of Lublin, Poland, [2]Dipartimento di Scienze della Vita, Università degli Studi di Modena e Reggio Emilia, Italy, [3]Università degli Studi di Modena e Reggio Emilia, Italy

Depression is a serious neuropsychiatric problem. About half of all major depressive disorder patients do not respond to first line treatment, and more than 65% do not achieve complete remission. Hence, there is a clear need to develop more effective and safer drugs. The aim of the present experiments was to evaluate the potential central activity of a new heterocyclic compound – pyrrolidine derivative (TB62). It is known that it is a ligand for the 5-HT_{1A} receptor.

The experiments were performed on male albino Swiss mice. The forced swimming test (FST) was used to evaluate the antidepressant-like activity; the elvated plus maze test (EPM) to evaluate the anxiolytic activity of TB62. (±)-8-hydroxy-2-dipropylaminotetralin hydrobromide (8-OH-DPAT, a 5-HT_{1A} receptor agonist) was used as a reference drug. WAY100635 (a 5-HT_{1A} receptor antagonist) was used to ascertain the observed effects of TB62 were specifically mediated by its 5-HT_{1A} receptor agonist properties.

The administration of TB62 at the doses, 3.75, 7.5 and 15 mg/kg was able to significantly increase the time spent in the open arms and the number of open arm entries by animals during the observation period in the EPM. Similarly, the results obtained indicate that TB62 (3.75, 7.5 and 15 mg/kg) revealed antidepressant-like properties, shortening the immobility time of mice in the FST. These effects were comparable to 8-OH-DPAT (1 mg/kg). The anxiolytic and antidepressant effects of TB62 administration were shown to be attributable to an interaction on 5-HT_{1A} receptors, because they were antagonized by WAY100635 (0.1 mg/kg).

To sum up, the compound TB62 revealed significant anxiolytic and antidepressant properties. The obtained data further emphasize the 5-HT_{1A} receptor affinity of TB62 as its effects were entirely WAY100635-sensitive.

The study was partially supported by statutable funds provided by the Polish Ministry of Science and Higher Education for the Medical University of Lublin, Poland (G. Biała) and patrially by the project funded by the National Science Centre (NCN, Poland, 2020/04/X/NZ7/00565).

Key words: depression, anxiety, pyrrolidine derivative, mice

P6.5. SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF SOME NOVEL ARYLPIPERAZINE DERIVATIVES

Ewa Kędzierska[1], Jolanta Orzelska-Górka[1], Marta Kruk-Słomka[1], Jolanta Kotlińska[1]
Department of Pharmacology and Pharmacodynamics, Medical University of Lublin, Poland

Preclinical and clinical studies point to the 5-HT1A and 5-HT2C receptors as a therapeutic target in the search for new, more effective psychotropic drugs used in the treatment of depression, anxiety and schizophrenia. In addition, drugs that act through 5-HT1A receptors have a better safety profile because they modulate rather than directly mediate neurotransmission in brain regions involved in the development of depressive and anxiety disorders: they do not cause sedation, memory disorders, do not interact with alcohol, and have no addictive potential. Examples of such drugs are clinically effective buspirone, vortioxetine and vilasodon (the derivatives of arylpiperazine). Thus, the search for new drugs among substances targeting serotoninergic transmission, in particular among ligands of 5-HT1A and 5-HT2C receptors, is still a very promising direction for the development of modern and safer psychotropic drugs that could be used in the treatment of depression and anxiety (also co-occurring with other diseases, such as schizophrenia).

The aim of this work was to examine potential central activity of the four new compounds from the group of arylpiperazine derivatives with the with affinity to serotonin 5-HT1A and/or 5-HT2C receptors. Compounds were studied in panel of behavioral tests used to predict a potential influence on the central nervous system in mice (e.g., motility, coordination tests, after their *i.p.* or *s.c.* administration) with particular emphasis on the antidepressant-, anxiolytic-like and antipsychotic action. Obtained results of the conducted pharmacological studies confirmed such activity, providing the basis for further, extended research.

Key words: arylpiperazine derivatives, behavioral studies, depression, anxiety

P6.6. CHANGES IN BRAIN OREXIN SYSTEM IN A RAT MODEL OF DEPRESSION INDUCED BY PRENATAL ADMINISTRATION OF DEXAMETHASONE

Katarzyna Głombik, Magdalena Kukla-Bartoszek, Katarzyna Curzytek, Agnieszka Basta-Kaim
Maj Institute of Pharmacology, Polish Academy of Sciences, Department of Experimental Neuroendocrinology, Kraków, Poland

Neuropeptides orexin A and orexin B are involved in various processes that range from the control of autonomic functions (i.a., food intake and sleep/wake states) and modulation of response to physical activity, as well as higher cognitive functions, including attention, cognition, and mood regulation. It is known that orexins may increase hedonic behaviors and orexin signaling impairment may underlie anhedonia, such as that observed in depression. Our goal was to investigate whether there are changes in the level of orexins: A and B and their receptors in two brain structures particularly involved in the pathomechanisms of depression. The studies were performed in a rat model of depression based on prenatal administration of dexamethasone (DEX) in the third trimester of pregnancy (0.1 mg/kg, days 14 -21). Behavioral verification showed depression-like behavior measured in a forced-swim test in adult male rats treated with DEX. Two hours before being sacrificed, subgroups of the DEX-treated and control rats were additionally subjected to acute immobilization stress. A biochemical study revealed that orexin A was decreased in the frontal cortex of DEX-treated animals (with and without additional stress in adulthood). Orexin B in this brain structure was diminished by DEX and also by the stress in the control group. In the hippocampus, DEX administration resulted in a decline in the orexin B protein level. Furthermore, additional stress led to a reduction in orexin A in the DEX group compared to the same-treated control group. No changes have been detected in the levels of receptors: type 1 and type 2 in both studied brain areas. Our study showed that DEX treatment in the prenatal period is associated with orexin system dysregulation in the adult brain but further studies are required to establish functional changes that follow this process.

Supported by grant 2020/39/D/NZ7/01610 from the National Science Centre, Poland.

Key words: depression, dexamethasone, orexins

P6.7. REGION SPECIFIC ALTERATION AND ACTIVATION OF PROTEIN TYROSINE KINASE 2 BETA IN TEMPORAL LOBE EPILEPSY

Ozasvi R Shanker[1], Sonali Kumar[1], Jyotirmoy Banerjee[2], Manjari Tripathi[3], P Sarat Chandra[4], Aparna Banerjee Dixit[1]

[1]University of Delhi, Dr. B. R. Ambedkar Centre for Biomedical Research, Delhi, India, [2]All India Institute of Medical Sciences, Department of Biophysics, New Delhi, India, [3]All India Institute of Medical Sciences, Department of Neurology, New Delhi, India, [4]All India Institute of Medical Sciences, Department of Neurosurgery, New Delhi, India

POSTER WITHDRAWN

P6.8. SEARCHING FOR EPILEPTOGENESIS/EPILEPSY BIOMARKERS – CIRCULATING microRNA LEVELS CHANGES IN THE RAT MODEL OF TEMPORAL LOBE EPILEPSY

Kinga Szydłowska, Anna Bot, Karolina Nizińska, Maciej Olszewski, Katarzyna Łukasiuk

Laboratory of Epileptogenesis, Nencki Institute of Experimental Biology, Poland

Epilepsy frequently develops as a result of brain insult, e.g., brain injury or stroke, however currently there are no tools allowing us to predict which patients suffering from trauma will eventually develop epilepsy. microRNAs are interesting candidates for biomarkers, as several of them were described changing their levels in the brain of epileptic subjects. There is evidence suggesting that microRNAs levels are altered also in the plasma during epilepsy. This study was conducted to evaluate the usefulness of plasma miRNAs as epileptogenesis/epilepsy biomarkers.

In our studies we used the rat model of temporal lobe epilepsy. An epileptogenic insult was status epilepticus evoked by the stimulation of the left lateral nucleus of amygdala. Next, animals were continuously video and EEG monitored for 3 months. Blood was collected at 14, 30, 60, and 90 days after stimulation from the tail vein. Blood plasma was separated and processed using Affymetrix miRNA 4.1 array strip microarrays.

We have compared miRNA levels between sham operated (n=12) and stimulated animals (n=15). We have detected 14 miRNA differentiating between sham operated and stimulated animals at 14 days, 6 at 30 d, 16 at 60 d, and 11 at 90 days. We have also compared the miRNAs levels between animals with high and low number of seizures. We found differences in levels of 11 miRNAs at 14 d, 7 at 30 d, 11 at 60 d and 8 at 90 d (at $p<0.01$).

We propose three miRNAs which could be potential biomarkers of different stages of epileptogenesis: miR-671, miR-9a-3p and miR-7a-5p. According to us, miR-206-5p is a potential biomarker of epileptogenesis, and miR-221-3p as a potential biomarker of epilepsy severity, characterized by the number of seizures. We also think that these five miRNAs can be considered in the future as potential treatment targets.

This work was supported by the FP7-HEALTH project 602102 (EPITARGET) and Polish Ministry of Science and Education grant W19/7.PR/2014.

Key words: epileptogenesis, epilepsy, miRNA, biomarker, plasma

P6.9. A NEW PATHOGENIC MECHANISM FOR A RARE GENETIC FORM OF HEREDITARY SPASTIC PARAPLEGIA (AKA SINO SYNDROME): MUTATED Kidins220 ACCUMULATES IN CELLS AND DISRUPTS INTRACELLULAR INTERACTIONS *VIA* LIQUID-LIQUID PHASE SEPARATION

Alicja Krawczun-Rygmaczewska[1], Martina Albini[2], Fabio Benfenati[2], Fabrizia Cesca[1]

[1]University of Trieste, Department of Life Sciences, Trieste, Italy, [2]Fondazione Istituto Italiano di Tecnologia, Center for Synaptic Neuroscience and Technology, Genova, Italy

SINO is a newly described syndrome whose main manifestation is Spastic paraplegia, often accompanied by Intellectual Disability, Nystagmus and Obesity. SINO is caused by heterozygous mutations in the *KIDINS220* gene. KIDINS220 (kinase D interacting substrate of 220kDa) is a multi-functional scaffold protein abundantly expressed across the nervous system. Some KIDINS220 pathogenic mutations result in truncated proteins resembling the isoforms naturally expressed during adulthood. This work examines the molecular effects of KIDINS220 mutations on protein expression and on cell homeostasis in HEK293T and primary neurons. Immunocytochemistry revealed that truncating mutations form aggregates and colocalise with p62 and calnexin. Investigation of mitochondrial membrane potential revealed adverse effects of the mutant proteins on mitochondrial health. Protein extraction of both soluble and insoluble fractions and western blot analysis confirmed that the mutated protein aggregates, unlike the WT, accumulate in the insoluble fraction suggesting impaired liquid-liquid phase separation (LLPS) mechanism which was further assessed by 1,6-hexanediol treatment. In conclusion, we show that mutated KIDINS220 aggregates in cells potentially trapping other proteins and disrupting the intracellular interactions. We hypothesise that LLPS could be the main mechanism behind aggregate formation and a potential druggable target for treatment of KIDINS220-related movement disorders.

Key words: Hereditary Spastic Paraplegia, KIDINS220, SINO, Liquid-liquid phase separation

P6.10. ALTERED HISTONE DEACETYLASE 4 (HDAC4) LEVELS AND DYSREGULATED INTERACTION WITH A NON-HISTONE SUBSTRATE IN TEMPORAL LOBE EPILEPSY

Sonali Kumar[1], Ozasvi R Shanker[1], Jyotirmoy Banerjee[2], Manjari Tripathi[3], P Sarat Chandra[4], Aparna Banerjee Dixit[1]

[1]University of Delhi, Dr. B. R. Ambedkar Centre for Biomedical Research, Delhi, India, [2]All India Institute of Medical Sciences, Department of Biophysics, New Delhi, India, [3]All India Institute of Medical Sciences, Department of Neurology, New Delhi, India, [4]All India Institute of Medical Sciences, Department of Neurosurgery, New Delhi, India

POSTER WITHDRAWN

P6.11. THE LIPOPOLYSACCHARIDE-EVOKED SYSTEMIC INFLAMMATORY RESPONSE ENHANCES THE TRANSCRIPTION OF CD33 IN THE MOUSE HIPPOCAMPUS; THE ROLE OF THE BET PROTEINS

Grzegorz Czapski, Marta Matuszewska, Magdalena Cieślik, Joanna Strosznajder

Mossakowski Medical Research Institute Polish Academy of Sciences, Department of Cellular Signalling, Warsaw, Poland

The bacterial endotoxin, lipopolysaccharide (LPS), was suggested to trigger or/and accelerate neuropathological alterations in Alzheimer's disease (AD). LPS-induced activation of the innate immune system involves changes in gene expression patterns, therefore controlling LPS-evoked changes may be potentially an efficient strategy to attenuate the progression of AD. Genome-wide association studies demonstrated that among several AD-related genetic risk factors (AD-GRF) the majority is connected to the function of the immune system. Therefore, the aim of our study was to identify AD-GRF affected in the brain by LPS-evoked systemic inflammatory response (SIR). Moreover, we analysed the role of bromodomain and extraterminal (BET) proteins, the readers of acetylation code, in controlling selected AD-GRF genes in the brain during neuroinflammation.

In our study, we used lipopolysaccharide (LPS; 1.5×10^7 U/kg; i.p.) to induce SIR in mice, brain tissue was analysed 3 and 12 h after administration of LPS. Moreover, mice were treated with an inhibitor of BET proteins, JQ1 (50 mg/kg; i.p.). The level of mRNA in the hippocampus was analysed using microarray and qPCR.

Our data demonstrated that among the established and investigated AD-GRF, only expression of CD33 was significantly increased during SIR. An inhibitor of BET proteins, JQ1, efficiently prevented an LPS-evoked increase in CD33 expression in the hippocampus.

Our study suggests that LPS-evoked SIR may increase CD33 expression in the brain which may potentially affect the pathomechanism of AD. We also propose that the upregulation of CD33, which occurs in the progression of AD, may be efficiently inhibited by using inhibitors of BET proteins.

Key words: endotoxin, lipopolysaccharide, CD33, neuroinflammation, Alzheimer's disease, bromodomain and extraterminal domain proteins

P6.12. BIOELECTRICAL BRAIN ACTIVITY DIFFERENCES IN PATIENTS WITH PSYCHOSOMATIC DISEASES DURING RESTING-STATE PARADIGM

Łukasz Grabowski[1], Marek Chełstowski[1], Marta Nowacka[1], Maja Hiszpańska[1], Krzysztof Tołpa[1], Monika Lewandowska[1], Rafał Milner[1], Jakub Kopowski[2]

[1]Nicolaus Copernicus University in Toruń, Poland, [2]Kazimierz Wielki University in Bydgoszcz, Poland

Psychosomatic diseases (PD) are defined as medically unexplained symptoms affecting one or more organ systems (e.g., gastrointestinal, musculo-skeletal, cardiovascular and others). The exact causes as well as the pathophysiological brain mechanisms that underlie these disorders are still not fully explained. There is also a lack of methods (e.g., electrophysiological techniques) that enable an objective diagnosis of psychosomatic disorders.

The study aimed to identify a distinctive pattern of brain bioelectrical activity that differentiates patients with PD from healthy individuals. Detecting potential differences among the subjects could be treated as bioelectrical markers of disorders and be useful in designing neurotherapeutic protocols.

Forty-nine people participated in the study (age range 18-43): 30 PD subjects and 19 healthy volunteers.

The study was conducted using a 21-channel system (Mitsar, St. L.o.). The EEG signal was recorded during 7-minute blocks with eyes open (EO) and eyes closed (EC) in a resting-state paradigm, and were quantitatively analyzed using the Neuroguide software. Multiple Analysis of Variance (MANOVA) was used to detect statistical differences in quantitative EEG parameters between the studied groups.

Significant differences between the patient and control groups were obtained in the Absolute Power (AP) of Alpha rhythm (8-12 Hz) in frontal electrodes (F3, F4, Fz) in EO condition. AP of Alfa rhythm was significantly low in patients compared to controls. Moreover, patients were characterized by significantly lower AP of the Delta rhythm (1-4 Hz) in the right frontal region (F4 electrode) in EC condition.

The results of our study indicate that psychosomatic patients exhibit a distinct pattern of brain bioelectrical activity compared to healthy individuals. The differences were observed in both EO and EC conditions, involved low-frequency bioelectrical activity and were evident in the frontal regions of the brain.

Key words: psychosomatic disorders, electroencephalography

P6.13. ENERGY METABOLISM DISRUPTION ACCOMPANIES BRAIN CANCER PROGRESSION IN SPRAGUE-DAWLEY RATS

Terezia Kiskova[1], Andrea Leskanicova[1], Zuzana Porvazova[1], Nicol Urbanska[1], Patrik Simko[1], Nela Zidekova[2], Martin Kertys[2]

[1]Pavol Jozef Šafárik University in Košice, Faculty of Science, Košice, Slovakia, [2]Biomedical Center Martin (BioMed), Jessenius Faculty of Medicine in Martin, Martin, Slovakia

The metabolomics is used for identification of biomarkers and altered metabolic pathways in cancer. The direct molecular data of cell status that display a meaningful physiological phenotype are ultimately represented by the levels of metabolites. The aim of this research was to follow the changes of selected metabolites in the blood of laboratory rats and to identify the most important metabolites with the focus on amino acids, biogenic amines and acylcarnitines during chemically-induced brain cancer in Sprague-Dawley rats (n=6 males/group; n=6 females/group). Using statistical multivariate methods, the metabolites were evaluated both sex-dependently and independently. Sex independently, the acylcarnitines with short (C0, C3-C5, C5-OH, C3-DC) or medium long chains (C6, C18: 2, C14: 2) were found to be depressed during cancer. Biogenic amines such as dopamine, spermidine or carnosine and methionine sulfoxide were shown to be significantly changed during cancer. Most of the metabolites were common for females and males evaluated separately. However, in females, among others, methionine-sulfoxide (Met-SO), spermidine and ornithine were found to be significantly changed. On the other hand, kynurenine and arginine have been found to be depressed in males. In conclusion, energy metabolism plays an important role during brain cancer progression. Defining the panel of significant metabolites may lead to early diagnosis possibilities.

Key words: metabolomics, brain cancer, laboratory rats

P6.14. KETOGENIC DIET PREVENTS NEURONAL LOSS IN CONTRALATERAL HIPPOCAMPUS BUT DOES NOT CHANGE GLIOSIS AROUND LESION SITE AFTER TRAUMATIC BRAIN INJURY

Zuzanna Rauk, Gabriela Hatala, Zuzanna Setkowicz-Janeczko

Jagiellonian University, Institute of Zoology and Biomedical Research, Laboratory of Experimental Neuropathology, Krakow, Poland

Traumatic brain injury (TBI) is a frequent cause of disability and a risk factor for the development of neurodegenerative diseases, as a result of a global tissue response to insult, including contralateral reaction – pathological changes in non-injured hemisphere. Ketogenic diet (KD) is considered a potential therapy due to its neuroprotective and ani-inflammatory properties. The aim of this project was to evaluate KD influence on neuronal loss and glial scar formation after TBI.

Penetrating cortical brain injury was induced on postnatal day 30 (P30) in rats obtaining standard diet (SD) or KD. Animals were perfused on P60. Brain tissue was sectioned with vibratome and stained immunohistochemically against glial fibrillary acidic protein (GFAP, astrocyte marker) and NPY (neuropeptide Y, neuronal marker). The number of NPY neurons was counted in medial, central and lateral part of the hippocampus, and GFAP-positive area was counted around the lesion site in the cortex.

NPY neurons decline was observed in medial hippocampus of injured hemisphere of male rats on SD and males and females on KD, compared to control (non-injured) rats. However, in non-injured hemisphere, NPY neurons decline was observed only in males on SD, which let us conclude that KD prevents this aspect of contralateral reaction. The analysis of area covered by astrocytes creating the scar around the lesion did not reveal any differences between diets. GFAP-positive area in the region corresponding to lesion site in non-injured hemisphere was also similar in all groups.

To conclude, KD attenuates global tissue reaction to TBI, preventing neuronal loss in the hippocampus of non-injured hemisphere, but does not change the area covered by astrocytes around the lesion. Further analyses will include the morphological analysis of cortical astrocytes creating glial scar, gliosis assessment in hippocampus and comparing the results with the data derived from animals sacrificed at the early stage after TBI.

The project was funded by "The Excellence Initiative – Research University" programme of Jagiellonian University in Krakow.

Key words: traumatic brain injury, ketogenic diet, gliosis, neuronal loss

P6.15. ARE INTEROCEPTION PROCESSES ALTERED AMONG PATIENTS SUFFERING FROM PSYCHOSOMATIC DISORDERS? – A HEART EVOKED POTENTIALS STUDY

Marek Chełstowski[1], Łukasz Grabowski[1], Marta Nowacka[1], Maja Hiszpańska[1], Krzysztof Tołpa[1], Monika Lewandowska[2], Rafał Milner[2]

[1]Institue of Psychology, Nicolaus Copernicus University, Poland, [2]Department of Clinical Psychology and Neuropsychology,Institue of Psychology, Nicolaus Copernicus University, Poland

Psychosomatic disorders (PD) are characterized by physical symptoms not fully explained by general medical conditions, affecting many organ systems and significantly impairing patient`s quality of life (Kirmayer et al., 2004). Actual causes of PD have been hypothesized in various theories, with some suggesting misinterpretation of signals from the body's periphery (interoception processes) could be the source of disorders (Henningsen et al., 2018). Our comprehension of how the brain interprets internal signals remains unclear. Studies using heart-evoked potentials (HEP) – considered as a bioelectrical marker of the interception (Al et al., 2020) might be reliable and useful tool for investigating this process in various clinical patient populations.

The aim of the study was to verify whether the interoception (HEP parameters) was altered in PD patients compared to a healthy control group.

Sixteen PD patients and eleven healthy volunteers participated in the study. HEPs were recorded using a 19-channel EEG system (Mitsar, St. L.o.) along with ECG activity. The experimental conditions included internal attention (IA), when subjects were asked to count their heartbeats and external attention (EA), when subjects were performing a visual oddball paradigm. HEPs were derived from averaging EEG epochs relative to the R peak markers in ECG signal.

Results indicated smaller differences in HEP amplitude in both IA and EA conditions in the PD patients compared to the healthy control. This effect was most pronounced in frontal and temporo-parietal brain regions, especially the right hemisphere. Within the 150-350 ms latency range across frontal, parietal and temporo-occipital brain regions, only the PD patients showed altered HEP amplitude in EA compared to IA conditions.

The results suggest disrupted interoception PD patients, particularly during the external stimuli processing. However, these findings require further confirmation, thereby designating this study as a pilot one.

Key words: Psychosomatic disorders, Interoception, Heart Evoked Potentials

P7.1. HuR SILENCING PROMOTES RETINAL GANGLION CELLS DEGENERATION AND ALLEVIATES THE ACTIVITY OF EXOGENOUS NEUROPROTECTION IN GLAUCOMA

Anna Pacwa[1], Joanna Machowicz[1], Piotr Rodak[1], Bartosz Machna[1], Klaudia Bugara[1], Saeed Akhtar[2], Marialaura Amadio[3], Joanna Lewin-Kowalik[1], Adrian Smedowski[1]

[1]Department of Physiology, Faculty of Medical Sciences in Katowice, Medical University of Silesia in Katowice, Poland, [2]Department of Optometry, College of Applied Medical Sciences, Inaya Medical College, Riyadh, Kingdom of Saudi Arabia, [3]Department of Drug Sciences, Section of Pharmacology, University of Pavia, Pavia, Italy

To evaluate the impact of HuR gene silencing on the ratio of age-related degeneration of Retinal Ganglion Cells (RGC), which potentially describes the efficiency of endogenous neuroprotection mechanisms, as well as to assess the exogenous neuroprotection capacity of HuR-silenced RGC in rat glaucoma model treated with metallothionein.

Thirty-five eight-week-old Long Evans rats were divided into two groups: experimental and control. Experimental group received intravitreal injection of AAV-shRNA-HuR. Control group received AAV-shRNA-control. Animals were sacrificed in 3 different time points. Healthy and treated retinas were collected and processed for immunostainings and RGC count. During the experiment electroretinography tests (ERG) were performed. For the second trial, 8 weeks after AAV injection, unilateral episcleral vein cauterization was performed to induce glaucoma model. Half of animals received metallothionein (MT). During the experiment IOP was monitored and ERG tests were performed. Retinas were collected for immunostainings and RGC count.

RGC count was 310±31, 296±25, 189±41 in experimental group and 399±51, 395±49, 390±23 in control respectively for 2, 4 and 6 months after injection (Kaplan-Mayer trend rank $p<0.0001$). Loss of RGC in central retina was 33.7% in animals from shRNA-HuR MT-treated glaucoma and 11.4% in shRNA-control, MT-treated glaucoma ($p<0.05$). In peripheral part of the retina the loss was 37.4% in animals from shRNA-MT-treated glaucoma and 11.5% in shRNA-control-MT-treated glaucoma ($p<0.01$).

Key words: HuR protein, Retinal Ganglion Cells, Glaucoma, Electroretinography, Neuroprotection

P7.2. INTRASTRIATAL INJECTION OF α-SYNUCLEIN OLIGOMERS INTO MICE TRIGGERS A DECREASE IN PARKIN LEVEL AND EVOKES AN INFLAMMATORY RESPONSE IN THE STRIATUM AND SUBSTANTIA NIGRA PARS COMPACTA

Anna Wilkaniec[1], Eva Ruiz-Ortega[1], Gabriela Olech-Kochańczyk[1], Grzegorz A. Czapski[1], Elżbieta Gawinek[1], Carsten Culmsee[2], Agata Adamczyk[1]

[1]Mossakowski Medical Research Institute, Polish Academy of Sciences, Department of Cellular Signalling, Warsaw, Poland, [2]Institute of Pharmacology and Clinical Pharmacy, Philipps-University Marburg, Marburg, Germany

Parkinson's disease (PD) is characterized by a progressive loss of dopaminergic neurons. Deposition of α-synuclein (α-syn) in Lewy bodies, parkin impairment and neuroinflammation are key features of PD pathology. The underlying pathogenesis, however, is largely unclear and causal treatment strategies are still missing. Since our previous *in vitro* results implicated α-syn–induced oxidative/nitrosative stress in parkin degradation, we evaluated the effects of α-syn administration on parkin pathology *in vivo*. C57BL/6 mice received bilateral intrastriatal injections of oligomeric murine α-syn and were euthanized at 3 hours, 7, 14, 30, 90 or 180 days post-injection. We demonstrated that α-syn pathology causes time-dependent neuroinflammation, dopaminergic neurodegeneration and behavioral deficits. A significant decrease in striatal dopamine and DOPAC levels were observed as early as 14 days after injection. Also in the striatum and substantia nigra pars compacta (SNpc) a significant increase in mRNA levels of proinflammatory cytokines, TNF-α, IL-1β, and IL-6 as well as the progressive development of astrogliosis was observed following the administration of α-syn oligomers. Moreover, activation of nitric oxide synthase in the striatum and SNpc followed by a significant decrease in parkin protein level was observed throughout the investigated time-points. Taken together, our findings demonstrate that α-syn oligomers induce changes in inflammatory response, and parkin the nigrostriatal pathway indicative of early Parkinson's disease.

Funding: Narodowe Centrum Nauki, grant 2020/39/I/NZ4/01031.

Key words: alpha-synuclein, parkin, inflammation, Parkinson's disease

P7.3. ON THE WAY TO A NEW MODEL OF NEURODEGENERATION? FIRST EVIDENCE OF THE EXPRESSION OF GATA1 IN THE BRAIN

Martyna Podgajna[1], Aleksandra Kaczyńska[2], Francesco Bellomi[3], Claudia Caturano[3], Paola Verachi[4], Michał Węgrzynowicz[5], Maria Zingariello[3], Mario Falchi[6], Anna Rita Franco Migliaccio[3], Giorgio Vivacqua[3]

[1]Microscopic and Ultrastructural Anatomy Laboratory, Campus Bio-medico University of Rome, Rome, Italy, Laboratory of Molecular Basis of Neurodegeneration, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland, [2]Microscopic and Ultrastructural Anatomy Laboratory, Campus Bio-medico University of Rome, Italy, Laboratory of Molecular Basis of Neurodegeneration, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland, [3]Microscopic and Ultrastructural Anatomy Laboratory, Campus Bio-medico University of Rome, Italy, [4]Laboratory of Confocal Microscopy, Italian National Institute of Health (ISS), Rome, Italy, [5]Laboratory of Molecular Basis of Neurodegeneration, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland, [6]Microscopic and Ultrastructural Anatomy Laboratory, Campus Bio-medico University of Rome, Rome, Italy, Laboratory of Confocal Microscopy, Italian National Institute of Health (ISS), Rome, Italy

GATA1 is a transcription factor belonging to GATA family and involved in the development and the maturation of the hematopoietic cells. At present, there are no clear evidences about the expression of GATA1 in neuronal lineage, in contrast to the widely-described expression of GATA2. Previously, a potential role for GATA1 in neurodegenerative diseases has been reported. Moreover, studies conducted on red-blood cells have shown that GATA1 regulates the expression of SNCA gene (encoding for Alpha-synuclein). Here, we aimed at determining the detailed GATA1 expression in the brain.

The study was performed using control mice with CD1 background and genetic model of GATA1 knock down mice (STOCK GATA1tm2Sho/J). Immunohistochemistry was employed to scan the brain for the expression of GATA1 and Co-immunofluorescence for GATA1 and different markers was performed to determine specific neuronal localization. Dates were visualized and quantified in ImageJ software. TEM was used to compare the ultrastructure of GATA1 positive neurons in CD1 and GATA1 low mice. Neuronal expression of GATA1 was confirmed by RNAscope.

GATA1 is expressed in discrete brain regions. Olfactory bulbs are distinguished by an staining in peri-glomerular neurons expressing Tyrosine Hydroxylase and calbindin D28 kDa. Differential expression of GATA1 has been detected at different ages and ultrastructural analysis revealed the expression of GATA1 in vesicles-like structures in the cytoplasm and at peri-nuclear level. As expected, expression of GATA1 was reduced in GATA1low mice, where GATA1 expressing neurons appear shrinker and morphologically altered.

Our results prove, for the first time, that GATA1 is expressed in the brain and particularly in the glomerular layer of the Olfactory bulbs. Regulation of SNCA gene and modulation of neuronal stem cells niche, represent key biological functions of GATA1, which request detailed exploration to link GATA1 to neurodegeneration.

Key words: olfactory bulb, GATA1 binding factor, neurodegeneration, SNCA, neuronal stem

P7.4. EFFECTS OF SWIM TRAINING ON THE SKELETAL MUSCLES OF ALS MODEL MICE

Anbarieh Saadat[1], Emilia Białobrodzka[2], Ewa Rodziewicz-Flis[2], Damian Flis[2], Wiesław Ziółkowski[2], Elżbieta Pyza[1]

[1]Department of Cell Biology and Imaging, Jagiellonian University, Kraków, Poland, [2]Department of Pharmaceutical Pathophysiology, Medical University of Gdańsk, Poland

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder that affects nerve cells in the brain and spinal cord. It specifically affects motor neurons that provide voluntary movement and muscle control which results in the loss of patients' ability to speak, eat, move, and breathe. Since there is no cure for this disease, it is important to manage it with gentle, low-impact aerobic exercise such as walking, and swimming to strengthen the unaffected muscles with the range of motion and stretching exercises. Previous studies showed the protective effects of different physical training in the animal model of ALS[1]. However, the positive effects of training were observed when training was started before the appearance of the first symptoms of the disease in mice. The main aim of our study was to determine the molecular mechanism of the protective effect of swim training applied after the onset of disease on skeletal muscle atrophy and the progression of ALS, and whether it will limit destructive changes in the skeletal muscles and prolong the life span. Mice were divided into three groups: the early stage of ALS, terminal untrained ALS, and terminal swimming-trained ALS. Muscles were prepared for Transmission Electron Microscopy. Additionally, Tibialis Anterior muscle (TA) samples were dissected at 4°C at the end of the study and weighed to determine muscle atrophy. Analysis of electrographs showed morphological changes in the skeletal muscles such as; sarcomere misaligned, enlarged mitochondria with vacuolization, irregular shapes and disintegrated membranes. The obtained results showed that swim training started after the onset of disease symptoms prolongs the life of mice by 12%. The body mass showed significant decline between early stage and both terminal trained and untrained ALS mice. The ratio of TA mass to the body mass showed significant increase from early stage to terminal untrained but declined from untrained to trained mice.

1. C. Desseille, et al., Specific Physical Exercise Improves Energetic Metabolism in the Skeletal Muscle of Amyotrophic-Lateral-Sclerosis Mice, Front Mol Neurosci 10 (2017) 332.

Funding: NCN OPUS 20 nr UMO-2020/39/B/NZ7/03366 to WZ and EP.

Key words: Tibialis Anterior muscle, Body mass, Mitochondria, TEM

P7.5. GHRELIN RECEPTOR AGONIST MK-0677 RESCUES MOTOR IMPAIRMENTS AND PROTECTS SUBSTANTIA NIGRA DOPAMINE NEURONS IN MOUSE α-SYNUCLEIN AGGREGATION MODEL

Katarzyna Maziarz[1], Monika Jankowska-Kiełtyka[1], Justyna Barut[1], Gabriela Burda[1], Małgorzata Figiel[2], Piotr Chmielarz[1]

[1]Maj Institute of Pharmacology, Polish Academy of Sciences, Department of Brain Biochemistry, Kraków, Poland, [2]Jagiellonian University, Department of Physical Biochemistry, Faculty of Biochemistry, Biophysics and Biotechnology, Kraków, Poland

Parkinson's disease (PD) is neurodegenerative disorder which motor symptoms are connected with progressive loss of dopamine neurons. Another sign of PD is Lewy Pathology which formation and transmission is linked with alpha-synuclein's (α-syn) prion properties. Using a-syn preformed fibrils (PFFs), we and others have shown Akt and Src signaling pathways have ability to reduce accumulation of a-syn in dopaminergic cells. This pathways are also activated by Ghrelin Receptor (GHS-R). Our goal was to determine a dosage of MK-0677 which protects dopaminergic neurons in mice injected with α-syn PFFs. We received PFFs from monomeric recombinant a-syn into self-templating, infectious amyloid form a-syn preformed fibrils (PFFs). PFFs or monomers of a-syn were injected bilateral into the striatum of 8 week old mice. Mice were treated with saline (SAL) or MK-0677 at doses 0.2mg/kg, 1mg/kg, 5mg/kg i.p. and 2mg/kg p.o. for 30 days. Subsequently, we performed behavioral tests, scarified mice and extracted theirs brains, and stained for Thyrosine Hydroxilase (TH) and phosphor-S129-a-syn. In multiple static rods test, PFF+SAL mice exhibited increased rotation time as compared to SHAM+SAL group, MK-0677 at 1mg/kg i.p. and 2mg/kg p.o. rescued motor behavior. Travel time was

longer for PFF+SAL mice compared to control but the effect was alleviated by MK-0677 at 1mg/kg and 2mg/kg. PFF+SAL group had decreased number of TH+ neurons in substantia nigra which was rescued by MK-0677 at 0.2mg/kg, 1mg/kg and 2mg/kg. Number of a-syn aggregates in TH+ cells increased in 0.2mg/kg dose, while it decreased in 2mg/kg. We have however not observed changes in striatal TH fiber density between groups. Our results strongly support further investigations of GHS-R agonist for treatment of PD at early stages.

This research was funded by National Science Centre, Poland, grant number 2019/35/D/NZ7/03200 (Sonata 15).

Key words: neurodegenerative, Parkinson`s disease, Lewy Pathology, Ghrelin Receptor

P7.6. GRAPHENE QUANTUM DOTS (GQDs) AS A NOVEL APPROACH IN PREVENTING α-SYN AGGREGATIONS IN α SYNUCLEINOPATHY MODEL OF PARKINSON'S DISEASE

Anna Alwani[1], Katarzyna Maziarz[1], Małgorzata Figiel[2], Małgorzata Kujawska[3], Piotr Chmielarz[1]

[1]Maj Institute of Pharmacology, Polish Academy of Sciences, Department of Brain Biochemistry, Kraków, Poland, [2]Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Department of Physical Biochemistry, Kraków, Poland, [3]Poznan University of Medical Sciences, Department of Toxicology, Poznań, Poland

Parkinson's disease (PD) is the second leading, slowly progressing, neurodegenerative disorder which features both motor and non-motor dysfunctions. The neuropathology of this disease is correlated with the presence of Lewy Bodies (LBs) inclusions as a result of α-synuclein (α-syn) aggregation progress/development, which are mostly associated with the degeneration of dopaminergic (DA) neurons. Nanomaterials such as Graphene Quantum Dots (GQDs) due to their low cytotoxicity and high biocompatibility are proposed a novel strategy against α-syn development pathology in α-synucleinopathy model of PD.All experiments were conducted on primary hippocampal, cortical and dopaminergic neuronal cultures treated with GQD1 and GQD2 (0.2, 1, 5, 10 ug/ml) and preformed fibrils (2,5 ug/ml) of recombinant mice α-syn monomer at DIV7 and incubated until DIV14. Fixed (4% PFA) cells and α-syn fibrils were stained with fluorescent NeuN and alpha-Synuclein Antibodies, visualized in fluorescent microscopy and obtained images were analyzed in Cell Profiler Software.

Our research revealed a significant decrease (approximately 50%) in the mean percentage of primary hippocampal and cortical neuronal cells exhibiting intracellular a-syn aggregations. This reduction was observed in groups treated with a dose of 10 ug/ml of GQD1 in combination with α-syn fibrils, compared to the positive control group (treated with α-syn fibrils) (p=0,05). Additionally, the mean neuronal viability remained stable in all treated groups compared to the control group, signifying the non-toxic properties of GQDs on neuronal cells.

Our findings suggest that GQDs emerge as potent inhibitors of α-syn fibril aggregation, offering a potential breakthrough in preventing neuronal degeneration in primary neuronal cultures.

Key words: Parkinson's disease, Graphene Quantum Dots, α-synuclein preformed fibrils, primary cultures

P7.7. EVALUATION OF NEURITE OUTGROWTH INDUCED BY LOW-BASICITY 5-HT7 AGONISTS IN HUMAN NEUROBLASTOMA SH-SY5Y CELLS

Klaudia Jakubowska[1], Sławomir Gołda[2], Adam Hogendorf[3], Danuta Jantas[1]

[1]Department of Experimental Neuroendocrinology, Maj Institute of Pharmacology of the Polish Academy of Sciences, Krakow, Poland, [2]Department of Molecular Neuropharmacology, Maj Institute of Pharmacology of the Polish Academy of Sciences, Krakow, Poland, [3]Department of Medicinal Chemistry, Maj Institute of Pharmacology of the Polish Academy of Sciences, Krakow, Poland

Serotonin (5-hydroxytryptamine, 5-HT) is a monoamine that serves as a tissue hormone and neurotransmitter, regulating various physiological functions *via* activation of several subtypes of 5-HT receptors. 5-HT7R is the lately discovered receptor belonging to 5-HTRs family, thus its role is not fully understood. It is widely distributed in the brain and among various activities its impact on neurite outgrowth is quite well-evidenced. In this study, we compared the effects of three new low-basicity 5-HT7 agonists (AH-494, AGH-238, and AGH-194) with the one mediated by commercially available 5-HT7 agonist, 5-CT (5-carboxamidotryptamine) on neurite outgrowth in human neuroblastoma SH-SY5Y cells. We demonstrated that 24 hrs treatment with AH-494 (0.01 and 0.1 uM) and AGH-194 (0.1 and 1 uM), but not with 5-CT or AGH-238, evoked significant neurite elongation when compared to the control group and this effect was similar to the one mediated by retinoic acid

(RA, 10 uM). However, after 48 hrs we did not observe any additional increase in neurite outgrowth by tested 5-HT7 agonists. Additionally, we investigated the expression of 5-HT7R mRNA under various experimental conditions. We were able to demonstrate the differential expression of 5-HT7R between undifferentiated and RA-differentiated SH-SY5Y cells. Similar observation was made when we used two different experimental cell culture medium (DMEM+1% FBS *vs.* Neurobasal+B27). We observed higher expression of 5-HT7R in cells cultured in DMEM+1%FBS when compared to Neurobasal+B27 medium and the level of 5-HT7R mRNA was higher in RA-differentiated cells when compared to undifferentiated ones. Our data showed higher potency of AH-494 and AGH-194 in stimulation of neurite outgrowth when compared to the effect of the commercially available 5-CT. Moreover, expression of 5-HT7R could be regulated by various experimental factors which could hamper the investigation of the role of 5-HT7R under physiological and pathological conditions.

Key words: 5-hydroxytryptamine, 5-HT7R, SH-SY5Y cells; neurite outgrowth

P7.8. SPERMIDINE RESTORES THE NUMBER OF PERIPHERAL BLOOD LEUKOCYTES AND THEIR SUBSETS IN RAT MODEL OF PARKINSON'S DISEASE

Beata Grembecka[1], Joanna Dunacka[1], Oliwia Harackiewicz[1], Daria Korewo-Labelle[2], Irena Majkutewicz[1], Danuta Wrona[1]

[1]Department of Animal and Human Physiology, Faculty of Biology, University of Gdańsk, Poland, [2]Deparment of Physiology, Faculty of Medicine, Medical University of Gdańsk, Poland

Parkinson's disease (PD) is characterized by progressive loss of the neurons in the substantia nigra pars compacta (SNpc) and its input to the striatum (CPu). Although the etiology of PD is not fully elucidated, neuroinflammation and peripheral immune cell infiltration are believed to be one of the mechanisms contributing to the PD pathology [1]. Spermidine (SPER), a natural polyamine, possesses anti-oxidant, anti-aging properties and its anti-inflammatory potential still being assessed [2].

The aim of this study was to test the potential effects of SPER long term treatment on peripheral blood leukocytes number changes in progressive neurodegeneration in rat model of PD.

Male Wistar rats (n=34) received infusion of 6-hydroxydopamine (6-OHDA, 24 µg dissolved in 4 µl 0.02% ascorbic acid solution) or *vehiculum* (VEH) into dorsal and ventral CPU in right hemisphere. One day after, rats were treated with 10 mg/kg SPER or placebo (PL) oral supplementation for next 30 days. Blood samples were collected from the tail vein before PD model induction (baseline) and 30 days after. The samples were analyzed using ABX Micros 60 Hematology Analyzer. Kruskal-Wallis tests were used to analyze obtained data (SPPS v.21).

We found that the number of peripheral blood leukocytes, lymphocytes and monocytes decreased in rats with PD model compare with baseline ($p \leq 0,05$; $p \leq 0,05$; $p \leq 0,01$) and VEH ($p \leq 0,05$; $p \leq 0,05$; $p \leq 0,01$). Long-term SPER treatment in rats with PD elevated blood leukocytes, lymphocytes and monocytes number compares to 6-OHDA group ($p \leq 0,05$; $p \leq 0,01$; $p \leq 0,001$).

Spermidine treatment has beneficial effects on peripheral blood leukocytes number in the progressive rat model of PD.[1] doi: 10.3389/fneur.2019.00232[2] doi: 10.1126/science.aan2788

Key words: spermidine, rat model of Parkinson's disease, leukocytes

P7.9. INVESTIGATING THE CHIP/STUB1 PATHWAY AND ITS IMPACT ON NEURODEGENERATION

Dominika Bedran[1], Erisa Nita[2], Ailish Tynan[2], Artur Piróg[1], Jakub Faktor[1], Georges Bedran[1], Sachin Rote[1], Kathryn Ball[2], Ted Hupp[2]

[1]International Centre for Cancer Vaccine Science, University of Gdansk, Poland, [2]Edinburgh Cancer Research Centre at the Institute of Genetics and Molecular Medicine, Edinburgh University, United Kingdom

Neurodegenerative diseases have a widespread impact, affecting millions of individuals globally and leading to progressive motor and cognitive impairments. Currently, available treatments focus on managing symptoms and relieving pain, without offering effective disease-modifying medications. Consequently, researchers are investigating alternative therapeutic approaches, including the examination of CHIP protein as a potential protective agent for neuronal cells. Previous studies have indicated that CHIP plays a crucial role in regulating cellular membrane integrity under acute stress conditions, acting as a sensor for maintaining protein stability. Given that protein misfolding, aggregation, and oxidative stress contribute to the pathophysiology of neurodegenerative diseases, CHIP's ability to protect neurons and central nervous system

cells from oxidative stress suggests its involvement in proteostasis and native protein function regulation.

This study proposes a comprehensive evaluation of CHIP's impact on neurodegeneration by adopting a "network level" perspective on signaling in SH-SY5Y cell models of Parkinson's disease. By investigating protein homeostasis in wild-type (WT) and CHIP knockout (KO) SH-SY5Y cell models, we observed an overexpression of key neuromodulatory peptides in the absence of CHIP. These findings underscore the potential significance of CHIP in neurodegeneration. Future investigations will further explore CHIP's role in the development of neuronal cell processes and the maintenance of membrane repair integrity, aiming to unravel its mode of action and protective mechanisms against neuronal cell damage. The insights gained from this research may pave the way for the development of more effective therapeutic strategies for neurodegenerative diseases.

Key words: neurodegeneration, ubiquitin ligase, neurogenesis

P7.10. OVEREXPRESSION OF MYRISTOYLATED Akt PROTECT NEURONS FROM ALPHA-SYNUCLEIN AGGREGATION INDEPENDENTLY OF ITS KINASE ACTIVITY

Piotr Chmielarz[1], Gabriela Burda[1], Katarzyna Maziarz[1], Małgorzata Figiel[2]

[1]Maj Institute of Pharmacology, Department of Brain Biochemistry, Krakow, Poland, [2]Jagiellonian University, Department of Physical Biochemistry, Faculty of Biochemistry, Biophysics and Biotechnology, Krakow, Poland

Parkinson's disease is a progressive age-related neurodegenerative disorder with unclear etiology, and there are no treatments available to slow its progression. The pathogenesis of Parkinson's disease is thought to involve a combination of multiple risk factors, including age, genetic predisposition, and environmental exposures. Recent findings, however, indicate that in addition to these risk factors, prion-like spreading of pathologically misfolded alpha-synuclein plays a critical, if not indispensable, role in Parkinson's disease.

Our recent work demonstrated that activation of RET tyrosine kinase, potentially *via* the Akt pathway, protects neurons from accumulating misfolded alpha-synuclein. We have also observed similar protective effects with the overexpression of constitutively active Akt.

In this study, we investigated the downstream protective mechanisms associated with overexpression of constitutively active Akt. We employed *in vitro* formed alpha-synuclein fibrils to aggregation in hippocampal neuronal cultures. These cells were concurrently transduced with a lentiviral vector expressing either constitutively active, myristoylated Akt kinase or GFP, and treated with AZD5356, a specific Akt kinase activity inhibitor, or rapamycin, an inhibitor of the Akt downstream target, mTOR. After seven days of treatment, the cells were fixed, stained, and the quantity of cells harboring aggregates was determined.

We found that while AZD5356 and rapamycin significantly increased the number of cells with aggregates, neither inhibitor negated the protective effects of mAkt, which consistently reduced aggregate quantity across all treatment groups.

Our data suggest that the Akt/mTOR pathway is integral to the development of alpha-synuclein pathology, while myristoylated Akt can protect neurons through an unidentified mechanism, independent of its kinase activity.

Key words: Parkinson's disease, alpha-synuclein, Akt

P8.1. PRO-TUMORIGENIC PROPERTIES OF MICROGLIA DURING GLIOBLASTOMA PROGRESSION ARE PROMOTED BY SorLA

Paulina Kaminska[1], Peter L. Ovesen[2], Mateusz Jakiel[3], Magda Bakun[4], Tomasz Obrebski[5], Michal Draminski[3], Vanessa Schmidt[2], Bozena Kaminska[6], Michal Dadlez[4], Thomas E. Willnow[2], Anna R. Malik[5]

[1]Cellular Neurobiology Research Group, Faculty of Biology, University of Warsaw, Poland / Laboratory of Molecular Neurobiology, Nencki Institute of Experimental Biology, Warsaw, Poland, [2]Max-Delbrueck Center for Molecular Medicine, Berlin, Germany, [3]Laboratory of Computational Biology, Institute of Computer Science, Warsaw, Poland, [4]Laboratory of Mass Spectrometry, Institute of Biochemistry and Biophysics, Warsaw, Poland, [5]Cellular Neurobiology Research Group, Faculty of Biology, University of Warsaw, Poland, [6]Laboratory of Molecular Neurobiology, Nencki Institute of Experimental Biology, Warsaw, Poland

SorLA (*SORL1* gene) is known for its functions in neurons, where it directs protein cargo to destined subcellular compartments. Recent reports suggest that SorLA may be also expressed in microglia, where its level is dependent on the pathophysiological context. During glioblastoma progression, microglia and macrophages are re-programmed by the tumor to support its growth and suppress immune responses. These cells, collectively called glioma associated microglia and macrophages (GAMs), account for up to 30% of the tumor mass.

To explore how SorLA contributes to tumor-supportive properties of GAMs and thereby to glioma progression.

We performed bioinformatical analysis of published RNA-seq datasets to characterize *SORL1* expression in subpopulations of human GAMs. Using *in vitro* models, we verified if the level of microglial *SORL1* transcript is regulated by external stimuli and we identified SorLA protein targets using proteomic approaches. The impact of SorLA on tumor growth was assessed in murine GL261 gliomas implanted intracranially to wild-type and SorLA-deficient mice.

Our bioinformatical analysis and *in vitro* experiments indicated that low and high level of *SORL1* expression is linked to pro- or anti-inflammatory activation of GAMs, respectively. Proteomic studies revealed protein targets of SorLA in microglia, crucial for immune response. Tumor growth in SorLA-depleted mice was reduced, which coincided with infiltration of neutrophils, intensified necroptosis and changes in microglia morphology.

SorLA affects activation state of microglia by regulating secretion of various biologically active factors. Its depletion unlocks anti-tumor response *in vivo*.

Studies were supported by the National Science Center, Poland (2020/37/B/NZ3/00761), the Foundation for Polish Science co–financed by the EU (POIR.04.04.00 00 5CEF/18 00) and the Excellence Initiative – Research University Programme at the University of Warsaw.

Key words: glioblastoma, microglia, intracellular sorting

P8.2. ROLE OF GLIAL PITUICYTES IN NEUROHYPOPHYSEAL SYNAPTIC MORPHOGENESIS

Naveen Nedunchezhian

Adam Mickiewicz University, Poland

Neurohypophysis (posterior pituitary) is a major neuroendocrine interface in the brain through which water homeostasis is maintained. Neurohypophysis majorly consists of glial pituicytes, neuropeptides oxytocin- and vasopressin-loaded synapses, and permeable capillaries. We recently identified that pituicyte-derived secreted factors can regulate neurohypophyseal neurovascular morphogenesis. However, the role of other secreted factors expressed in the neurohypophysis in neurovascular morphogenesis is unknown. Towards this goal, we have been employing pharmacological and genetic perturbations to explore the roles of candidate molecules that could regulate neurohypophyseal synapse morphogenesis. Our studies of the glial pituicytes is expected to reveal novel players in the development of a key neuroendocrine interface conserved in vertebrates.

References: 1. Anbalagan, S. et al. Pituicyte Cues Regulate the Development of Permeable Neuro-Vascular Interfaces. Dev Cell 47, 711-726 e715, doi: 10.1016/j.devcel.2018.10.017 (2018). 2. Gutnick, A. et al. The hypothalamic neuropeptide oxytocin is required for formation of the neurovascular interface of the pituitary. Dev Cell 21, 642-654, doi: 10.1016/j.devcel.2011.09.004 (2011). 3. Anbalagan, S. et al. Robo2 regulates synaptic oxytocin content by affecting actin dynamics. Elife 8,doi: 10.7554/eLife.45650 (2019).

Key words: Glial Pituicytes, Neurohypophysis, Oxytocin, Synapses, Synaptic Morphogenesis

P8.3. MODULATION OF HIF1-α SIGNALING PATHWAY AFFECTS OLIGODENDROCYTE MATURATION IN THE *IN VITRO* MODEL OF PERINATAL ASPHYXIA

Justyna Janowska, Joanna Sypecka

Mossakowski Medical Research Institute Polish Academy of Sciences, Poland

Perinatal asphyxia is a frequent complication during labor. In preterm-born babies it can lead to hypoxic-ischemic encephalopathy, which means a reduction in the volume of white matter. It can be caused by impaired maturation of oligodendrocytes and process of myelination as well as oligodendrocyte lineage cell death. Temporal hypoxia is one of the key factors in the pathophysiology of injury; therefore, we wanted to answer the question of whether HIF-1 signaling is involved in the altered oligodendrocyte growth under this condition.

The aim of our study was to evaluate the effect of modulation of the HIF1-1 pathway after *in vitro* mimicked hypoxic-ischemic injury. Procedure was performed on neonatal rat oligodendrocyte progenitor cells and it relied on exposing cell cultures to oxygen and glucose deprivation (OGD) lasting 50 min. After the insult, we induced chemical inhibition (KC7F2) or enhanced activation ($CoCl_2$) of HIF-1α and analyzed the expression of myelin proteins and cell viability.

The OGD procedure does not cause massive cell loss in culture, but inhibition of HIF-1α translation with

KC7F2 resulted in decreased cell viability. However, HIF-1α inhibition promoted cell maturation, because the number of cells with an expression of myelin proteins significantly increased. It also caused inhibition in proliferation, with 33% less Ki67-positive cells compared to OGD-treated cultures. Further stimulation of hypoxia with $CoCl_2$ did not have a significant effect on oligodendrocyte growth after OGD.

The results obtained suggest an important contribution of HIF-1 signaling to oligodendrocyte proliferation and maturation. Further studies will indicate the target for pathway involved directly in cell growth and hopefully, help to define new target for therapy of hypoxic-ischemic encephalopathy.

Key words: oligodendrocytes, asphyxia, white matter, HIF-1

P8.4. INDUCTION OF CLOCK GENES BY GR STIMULATION OF ASTROCYTES *IN VITRO*

Tansu Göver[1, 2], Paweł Hanus[1,3], Agnieszka Krzyżosiak[1] , Kamila Środa-Pomianek[2], Michał Ślęzak[1]

[1]Research Group of Biology of Astrocytes, Łukasiewicz Research Network – PORT Polish Center for Technology Development, Wrocław, Poland, [2]Department of Biophysics and Neuroscience, Wroclaw Medical University, Wrocław, Poland, [3]Department of Psychiatry, Wroclaw Medical University, Wrocław, Poland

Stress is an important risk factor for mental disorders. Stress response is controlled by the hypothalamic-pituitary-adrenal (HPA) axis, which activation results in glucocorticoid (GC) secretion. Physiologically, these hormones are molecular effectors of the circadian rhythm and play crucial role in synchronizing transcriptional and metabolic activity in peripheral tissues. However, little is known about analogical regulation in the brain. We previously showed that astrocytes are a cellular target of glucocorticoid receptor (GR)-dependent transcriptional activity in the brain and this signaling contributes to central stress response. Here we investigate whether GR signaling controls circadian oscillations of metabolic genes in astrocytes and whether this regulation engages clock genes.

Primary astrocyte cells were treated with a single pulse of specific GR agonist, dexamethasone (DEX), and the expression levels of several clock genes and bona fide GR targets were monitored at 6-hour intervals by quantitative polymerase chain reaction (qPCR).

GR stimulation reliably induced the uniphasic raise of GR-responsive genes and elicited oscillations of clock gene expression with approximately 24h phase in primary mouse astrocytes. Future directions: GR- and clock gene-dependence of astrocyte- specific enzymes controlling their metabolic activity will be examined in future.

This work was funded from Norwegian Financial Mechanism 2014-2021 operated by the Polish National Science Center under the project contract 020/37/K/NZ3/02783.

Key words: astrocytes, circadian rhythm, glucocorticoid receptor, clock genes

P8.5. SorCS2 PROTECTS ASTROCYTES FROM AMYLOID BETA (Ab) – INDUCED STRESS BY MODULATING p75 NTR SIGNALING

Ewelina Ziemlińska[1], Tomasz Obrębski[1], Vannesa Schmidt[2], Thomas E. Wilnow[2], Anna R. Malik[1]

[1]University of Warsaw, Faculty of Biology, Warsaw, Poland, [2]Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

SorCS2 is a mammalian sorting receptor, which expression is highly induced in astrocytes in stroke. We hypothesised that astrocyte-expressed SorCS2 not only supports post-stroke regeneration but its protective functions also matters in Alzheimer's disease (AD), the most common cause of dementia. To date, no association between SorCS2 and AD has been found. Our research, focused on investigation of SorCS2 deletion in the AD mouse model, showed a decline in astrocyte number accompanied by profound increase in Ab peptide level, one of the attributes of AD (Network Glia Conference 2023, #341). To verify this and in search of SorCS2 interacting partners we tested the impact of stimulation with Ab-containing medium on wild type (WT) and SorCS2 knock-out astrocytes (SorCS2-KO). We stimulated astrocytes in culture for 24 and 48 hours and analysed their viability with mitochondrial reduction-based assay, followed by an examination of apoptosis and stress-related markers with a use of Western Blot (WB) and quantitative PCR (qPCR) methods. Already after 24 h of Ab exposition SorCS2-KO astrocytes showed significantly reduced cell viability which deepened in time. This was accompanied by an increase in stress and pro-apoptotic markers: phospho-p38 kinase and cleaved CASP-3 levels. In search for receptors that may be involved in the deepened apoptotic effects observed in SorCS2-KO astrocytes we checked whether the inhibition of p75 NTR receptor and its pro-apoptotic signalling will rescue the observed phenotype. Our experiments showed positive quantitative correlation between the concentration of

the antibody targeting p75 extracellular domain and the increased SorCS2-KO astrocytes cell viability. Together our results confirm the vulnerability of astrocytes to Ab burden and highlight the importance of protective SorCS2 functions in the condition of Ab load seen in AD, which in part could be dependent on p75 NTR transduced signals.

Key words: Alzheimer's disease, astrocytes

P8.6. INVESTIGATING THE MEDIATING ROLE OF ASTROCYTES IN NORADRENERGIC TRANSMISSION FOR NEUROPROTECTION

Justyna Barut[1], Katarzyna Rafa-Zabłocka[1], Michał Wilczkowski[1], Monika Bagińska[1], Rosanna Parlato[2], Grzegorz Kreiner[1]

[1]Department of Brain Biochemistry, Maj Institute of Pharmacology, Polish Academy of Sciences, Poland, [2]Institute of Anatomy and Cell Biology, University of Heidelberg, Heidelberg, Germany, Institute of Applied Physiology, University of Ulm, Ulm, Germany

Neurodegenerative diseases such as Parkinson's disease (PD) are characterized by neuroinflammation and glial reactivity. Noradrenaline provides long-term protection to dopaminergic neurons by reducing oxidative stress as well as enhancing glial activation. These observations prompted us to investigate whether astrocytes mediate noradrenergic transmission.

We induced a reactive phenotype in primary mouse astrocytes by co-treatment with IL-1 alpha-TNF alpha, or IL-1 beta-TNF alpha. Astrocytes exhibited signs of reactivity, including morphological changes, decreased GFAP expression, increased proliferation, and translocation of NF-kB to the nucleus. Cytokine stimulation also influenced astrocyte metabolism, as indicated by increased monocarboxylate transporter expression and confirmed in selected key metabolic parameters. In midbrain neuronal cultures, the number of TH+ dopaminergic neurons remained unchanged after cytokine treatment. However, when cultured with astrocytes, TH+ neuron levels decreased in a dose-dependent manner upon cytokine stimulation. Pretreatment with beta-AR agonists showed neuroprotective effects against cytokine-induced neurotoxicity.

To explore the role of noradrenergic transmission in PD, we utilized mice models with progressive degeneration of noradrenergic cells. Although no loss of TH+ cells in the SN of mutant mice was observed, we noted increased markers of neurodegeneration, including elevated *GFAP* expression, IL-10 protein and CCL2 levels – an astrocytic chemokine. Additionally, we identified 35 elevated genes in the SN that correlated with PD, including *Sgk1*, an astrocytic GR-dependent gene.

Our findings highlight the potential detrimental impact of noradrenergic degeneration on the SN/VTA and reinforce the neuroprotective role of noradrenaline, potentially mediated by astrocytes. Primary astrocytes induced by cytokines provide a valuable *in vitro* model for further research.

Key words: Parkinson's disease, neurodegeneration, astrocytes, reactive astrocytes

P9.1. TCF7L2 THALAMIC DELETION LEADS TO ALTERATIONS IN MICE'S BEHAVIORAL PROFILE AND BRAIN ENERGY METABOLISM

Suelen Baggio[1], Andrzej Nagalski[1], Kamil Koziński[1], Łukasz Szewczyk[1], Marcin Lipiec[2], Ben Hur Mussulini[3], Ksenia Meiza[2], Ewelina Knapska[2], Agnieszka Chacińska[3], Marta Wiśniewska[1]

[1]Centre of New Technologies, University of Warsaw, Warsaw, Poland, [2]Necki Institute of Experimental Biology, Warsaw, Poland, [3]IMol Polish Academy of Sciences, Warsaw, Poland

TCF7L2 is a transcriptional effector of the Wnt/β-catenin signaling pathway, connected to gene expression, cell fate, and development. This gene is vital for the liver, pancreas, and adipose tissue and has been associated with pathological processes, such as cancer, autism spectrum disorder (ASD), and type 2 diabetes. TCF7L2 is largely expressed in the thalamus, where impairments in thalamocortical connections contribute to behavioral and sensory disorders. Therefore, this study aims to understand the role of TCF7L2 in the development of brain disorders such as ASD and the connection with energy metabolism. We used a strain developed in our laboratory in which the regulator of thalamic maturation TCF7L2 is knocked out postnatally. To validate ASD-associated phenotypes, we analyzed the mice's behavioral profile through Open field, Marble-burying test, Eco-HAB, and Three-chamber test. For metabolic analysis, we used the high-resolution respirometry system Oroboros. *Tcf7l2* KO mice present a decrease in social performance, not interacting with other mice during the cage exploration and spending less time in the compartment containing social scent. They show a decrease in grooming behavior and no difference in repetitive behavior, locomotor activity, or olfactory function. These results corroborate a hypothesis that thalamic dysfunctions originating from perinatal development can be a primary cause

of social deficits and behavioral inflexibility in ASD. Regarding the metabolic parameters, upon thalamic deletion of TCF7L2, thalamic and cortical mitochondria favor oxidation of fatty acid to the detriment of pyruvate, showing an increase in β-oxidation and ketone bodies utilization. Such results demonstrate that TCF7L2 is vital in regulating energy metabolism in the thalamus, similar to its functions in metabolic organs in the periphery. In summary, our study suggests that impaired energy metabolism in thalamocortical circuits plays a role in the pathogenesis of ASD.

Key words: thalamus, Tcf7l2, behavior, energy metabolism

P10.1. MUSCLE SPINDLES IN RAT MEDIAL GASTROCNEMIUS MUSCLE AND IA PROPRIOCEPTIVE INPUT TO SPINAL MOTONEURONS IN MALE AND FEMALE ANIMALS

Jan Celichowski[1], Magdalena Piotr[1], Hanna Drzymała-Celichowska[1], Hanna Jackowiak[2], Marcin Bączyk[1], Piotr Krutki[1]

[1]Poznań University of Physical Education, Department of Neurobiology, Poland, [2]Poznań University of Life Sciences, Department of Histology and Embryology, Poland

The sexual dimorphism of muscle spindles in rat medial gastrocnemius as well as Ia monosynaptic inputs to motoneurons were studied. First, the muscles were cut transversely into serial sections and the number, density, and morphometric properties of the muscle spindles were determined. There was no significant difference ($p>0.05$) in the number of muscle spindles of male (14.45±2.77) and female (15±3.13) rats. Muscle mass was 38.89% higher in males (1.08 g *vs.* 0.66 g in females), making the density of these receptors significantly higher ($p<0.01$) in females (approximately one spindle per 51.14 mg of muscle mass *vs.* 79.91 mg in males). The morphometric properties of intrafusal muscle fibers or muscle spindles appeared to be similar in male and female rats ($p>0.05$). Second, it was investigated whether apparent sex differences in body mass and muscle force influence the proprioceptive input from muscle spindles to motoneurons. Motoneurons were investigated intracellularly in deeply anesthetized male and female rats. Monosynaptic Ia excitatory postsynaptic potentials (EPSPs) were evoked using electrical stimulation of primary afferent homonymous muscle fibers. The central latencies of EPSPs were 0.38–0.80 ms, with no differences in means between males and females. The maximum EPSP amplitude varied 2.03-8.09 mV in males and 1.24-6.79 mV in females. The mean maximum EPSP amplitude was 26% higher in males than in females (4.83±1.57 *vs.* 3.84±1.23 mV). The mean EPSP rise time, half-decay time, and total duration did not differ between the sexes. EPSP amplitudes correlated with the resting membrane potential, input resistance, and EPSP rise time in both sexes. The observed sex differences in the Ia proprioceptive input may be related either to mechanical loading differences in males and females associated with their different body mass or hormonal differences influencing the levels of neuromodulation in spinal circuits.

Supported by NCN Grant No. 2018/31/B/NZ7/01028.

Key words: muscle spindles, afferent fibers, motoneurons, electrophysiology, sex differences

P10.2. CORTICAL SOURCES OF ELECTRICAL ACTIVITY, RELATED TO THE SWITCHING TO AN ALTERNATIVE MOTOR PROGRAM IN HUMANS

Olha Korzhyk, Alevtyna Morenko

Lesya Ukrainka Volyn National University, Department of Human and Animal Physiology, Lutsk, Ukraine

This work aims to detect the cortical sources of event-related potentials while switching to an alternative motor program (paradigm Stop-Change task). A total of 35 men and 40 women, healthy, and right-handed, participated in the study. According to the Stop-Change task paradigm, each participant when receiving the presented Stop-Change signal stopped the running motor program (to press the left button with the index finger) with subsequently switched to an alternative one (pressing the right button with the middle finger). EEG recordings were analyzed in the frontal, central, and parietal lobes of the cortex. Data was processed with the method of low-resolution electromagnetic tomography – LORETA (the sLORETA software).

In the time intervals corresponding to the N2 and P3 components of the ERP, in men, generators of event-related activity were localized in the right hemisphere and gradually moved from the superior temporal gyrus (Brodmann area 38) to the supramarginal gyrus of the parietal lobe (Brodmann area 40), which can, in general, mediate increased motor attention to conflict monitoring and response selection. In women, under these conditions, a primary bilateral activity of the posterior cingulate cortex (Brodmann area 23) was observed with

a gradual narrowing over time the localization of the ERP source to the left insular cortex (Brodmann area 13), the participation of which was considered a marker of the selective reaction.

Key words: EEG, cortical sources, ERP, Stop-Change task, men, woman

P10.3. EFFECT OF LOCOMOTOR EXERCISE ON DISTRIBUTION OF VGluT1 AND VGluT2 IN THE LUMBAR SPINAL CORD OF RATS WITH COMPLETE SPINAL CORD TRANSECTION

Magdalena Paradowska[1,2]*, Karolina Godlewska[1]*, Małgorzata Skup[2], Olga Gajewska-Woźniak[2]

[1]Warsaw University of Life Sciences, Faculty of Biology and Biotechnology, Warsaw, Poland, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Group of Restorative Neurobiology, Warsaw, Poland, [2]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Group of Restorative Neurobiology, Warsaw, Poland

**Authors equally contributed to the work*

Vesicular Glutamate Transporters (VGluT1, VGluT2, VGluT3) upload glutamate (Glu) into synaptic vesicles. After spinal cord transection (SCT) at Th10, VGluT transcript levels decrease below the lesion site by 95% (VGluT1 mRNA) and by 64% (VGluT2 mRNA) in the lumbar L1-2 segments, and less (by 34%, VGluT2 mRNA) in the lumbar L3-6 segments, reflecting possible dysfunction of excitatory interneurons.

The role of these interneurons and their impact on hind limb motoneuron activity in L4-L5, in association with decreased VGluT mRNA after SCT, led us to investigate the effect of SCT and long-term locomotor training on distribution of VGluT1; VGluT2 proteins in gray matter of the L5 segment.

Experiments included intact (C, n=6), spinal (Sp, n=8), and spinal, subjected to 5 weeks of training (SpLoc, n=8) groups. Assisted hindlimb stepping on the running treadmill was video recorded and analyzed off-line. Measurements of VGluT signal intensity and distribution were done with IHC on transverse L5 sections using ImagePro Plus 7.0 software.

Six weeks after SCT, the SpLoc group showed over 4-fold increase in step-like movements, compared to the Sp group. Surprisingly, in the Sp group, IHC analysis showed no changes in VGluT1; VGluT2 signal intensity. It suggests that the level of VGluT1 which at L5 mainly comes from primary afferents, is not reduced. In interneurons compensatory post-transcriptional changes may contribute to VGluT2 maintenance. Trained animals exhibited a 35% decrease in VGluT1 and 10% decrease in the VGluT2 signal in the ventral horn, which raises the question on training-mediated adaptive mechanisms in glutamate loading.

Financial support: Polish National Science Center grant 2018/31/B/NZ4/02789; Nencki Institute Statutory Grant; POWR.03.05.00-00-Z033/17.

Key words: spinal cord, injury, VGluT1, VGluT2, motoneurons

P10.4. TARGETED ACTIVATION OF EXTENSOR SOLEUS MOTONEURONS USING AAV-MEDIATED TrkB RECEPTOR ENRICHMENT ENHANCES MOTOR FUNCTION RECOVERY AFTER SPINAL CORD TRANSECTION

Anna Głowacka[1], Olga Gajewska-Woźniak[1], Karolina Godlewska[2], Magdalena Paradowska[2], Sylwia Wieczorek[2], Małgorzata Skup[1]

[1]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Group of Restorative Neurobiology, Warsaw, Poland, [2]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Group of Restorative Neurobiology, Warsaw University of Life Sciences, Faculty of Biology and Biotechnology, Warsaw, Poland

Our previous studies showed that the expression of brain-derived neurotrophic factor (BDNF) and its high-affinity receptor TrkB is upregulated by locomotor training, and improvement of motor functions in spinal, trained animals is related to BDNF activation. Motoneurons (MNs) innervating extensor muscles in the ankle joint are particularly affected by spinal cord transection (SCT). This study investigates whether enhancing the expression of the gene encoding TrkB receptor in this MNs population can lead to locomotor function recovery following complete SCT in the adult rat.

To increase responsiveness of the ankle extensor MNs to BDNF, we used intramuscular gene transfer. TrkB receptor with C-myc tag was produced in soleus MNs from ssAAV6/2-hsyn-TrkB_Cmyc (8.2x10E12 v.c.) construct. Vectors were injected into the soleus muscles of adult Wistar rats during the surgical procedure of complete SCT at Th10. Immunofluorescence was employed to identify the localisation of c-Myc protein, tagging the exogenous TrkB receptor. Activation of the receptors was achieved through long-term locomotor training (5 weeks). Functional assessment was performed based on modified BBB locomotor scale. Three experimental

groups were used: Control (n=5), SCT-AAV-TrkB (n=7), and SCT-AAV-TrkB-Loc (n=7). We observed improvement in the functional capacity based on the increased number of "step-like movements" and alternations at 6th week, compared to animals receiving saline. We conclude that enriching the TrkB receptor pool, and stimulating neurotrophin signaling with endogenous ligand may be a therapeutic approach with promising potential.

Key words: spinal cord, motoneurons, BDNF, neurotrophins, spinal injury

P10.5. COMBINED STIMULATION OF EXTENSOR SOLEUS MOTONEURONS *VIA* DREADDS WITH INTERMITTENT TREADMILL TRAINING PREVAILS OVER LONG-TERM LOCOMOTOR TRAINING IN MAINTENANCE OF PLANTAR FOOT STEPPING AFTER SPINAL CORD TRANSECTION

Olga Gajewska-Woźniak[1], Benjun Ji[1], Karolina Godlewska[2], Magdalena Paradowska[1], Małgorzata Skup[1]

[1]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Group of Restorative Neurobiology, Warsaw, Poland, [2]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Group of Restorative Neurobiology, Warsaw University of Life Sciences, Faculty of Biology and Biotechnology, Warsaw, Poland

Targeting a specific group of hindlimb motoneurons (MNs) by gene transfer may address a common issue in experimental therapies after spinal cord transection (SCT): a failure to restore equilibrium between different groups of MNs and muscles. That is a risk when unspecific stimulation of the preserved neuronal network below the injury site is applied. We hypothesized that a selective approach may yield superior physiological effects and restore motor function more effectively.

MNs innervating extensor muscles are differently impacted by SCT than MNs of the flexor muscle acting at the ankle joint. Extensor MNs are particularly impacted long-term by losing cholinergic and glutamatergic VGluT1 inputs and content of M2 receptors.

After SCT, to restore a balance in signaling between MNs controlling antagonistic muscles acting at the ankle joint, we employed selective activation of extensor Soleus MNs through a chemogenetic tool: Designer Receptor Exclusively Activated by Designed Drug (DREADD).

DREADDs were produced from ssAAV-retro/2-hsyn-DREADD_mCherry (8.2x10E12 v.c.) construct. Vectors were injected into the Soleus muscles of adult Wistar rats one week prior to SCT at Th10. Expressed DREADDs were activated through the i.p. administration of selective ligand, Compound 21, once a week for six weeks.

We observed improvement in the functional capacity based on the increased number of "step-like movements" at 4 and 6 weeks, after 24 hours from ligand injection, compared to animals receiving saline. The number of R-L alternations cumulated from week to week in both groups with no consistent chemogenetic impact. Low expression of the mCherry gene in the spinal cord and dorsal root ganglia and mCherry fluorescence in single soleus MNs suggest that even mild chemogenetic stimulation can lead to improved motor function in rats.

Financial Support: NCN 2018/31/B/NZ4/02789 and Statutory for the Nencki Institute.

Key words: spinal cord, motoneurons, DREADD, extensor, spinal injury

P11.1. ZEBRAFISH SYNAPTOSOME-POST SYNAPTIC DENSITY LIGAND-RECEPTOR INTERACTOME ATLAS

Miłosz Chodkowski[1], Andrzej Zieleziński[2], Savani Anbalagan[2]

[1]Adam Mickiewicz University in Poznań, Poznań, Poland, [2]Institute of Molecular Biology and Biotechnology, Faculty of Biology, Adam Mickiewicz University in Poznań, Poznań, Poland

Ligand-receptor-mediated cellular signaling is essential for neurodevelopment and dysfunctional ligand-receptor interactions are implicated in autism spectrum disorders. Most of the brain disease-targeted drugs are against receptors that were tested using *in vivo* model organisms. Due to ongoing discussions in the European Parliament, the future of mammalian research is at risk and there is a need for robust alternative model organisms. Larval zebrafish with autism-like phenotypes have been used for *in vivo* phenotypic drug discovery screens. Despite the importance of ligands and receptors for drug discovery and drug companies, a database on zebrafish ligands, receptome and interactome are either unavailable or incomplete. Herein, we present the first ligand-receptor interactome zebrafish atlas. Using knowledge-based data mining and machine learning algorithms on zebrafish reference proteome, we created a database of zebrafish ligands, receptors, and interactome. To aid other researchers, we developed DanioTalk, an open-source tool which allows us-

ers to provide their -omics (proteomics or single-cell or bulk RNA-seq) data and identify genes encoding ligands, receptors and interactome. DanioTalk also lists all the potential drugs that can target the ligands and receptors based on orthology with human proteins. Applying DanioTalk to publicly available zebrafish brain synaptosomal and postsynaptic density proteome, we identify all potential synaptic ligand-receptor interactions and drugs that can target them. Our resource will aid researchers interested in the functions of protein-based ligand-receptor interactions in zebrafish neuronal remodeling and drug discovery.

Key words: ligand, receptor, autism, synapse, drug, zebrafish

P11.2. DISINHIBITION OF RYANODINE RECEPTORS AND THEIR OVEREXPRESSION MIGHT SUPPORT CALCIUM WAVE PROPAGATION IN NEURONS AND CONTRIBUTE TO ABERRANT CALCIUM HOMEOSTASIS IN THE DENDRITIC BRANCH

Joanna Jędrzejewska-Szmek

Nencki Institute, Poland

Calcium (Ca) is a second messenger playing an important role in many neuronal processes and linked to learning and memory. Aberration in Ca regulation can lead to neurodegeneration and cell death. Ca dynamics inside the cell is tightly regulated: Ca is excruded to the extracellular space by transmembrane pumps, buffered in the cytosol by Ca-binding proteins, stored in intracellular organella such as endoplasmic reticulum (ER) and if necessary released by activated by Ca ryanodine receptors (RyR) and IP3 receptors. CA1 pyramidal neurons express RYR2 in the dendrites and soma and RyR3 in spines containing ER. RyR3 in the spine neck serve as spine Ca transducer amplifying dendritic Ca close to the spine. Using a spatial stochastic reaction-diffusion model of a dendritic branch we investigated whether RyR2 in the dendrite can solely support Ca wave propagation following synaptic stimulation in health and disease. We used 50 um long dendrites with 3 different dendritic diameters (1.2, 2.4, 6.0 um). Ca dynamics was modeled with pump- and buffer-reactions and with ER mechanisms (pumps, RyR2, and optionally store-operated calcium entry (SOCE)). We show that even when RyR2 receptors are not inhibited by calmodulin, Ca wave can not exceed 15 um with smaller Ca wave extent in thinner dendrites (up to 10 um). ER morphology of interconnected tubes supports farther Ca wave propagation than ER of the shape of a single large tube. The extent of Ca wave propagation depends on the amplitude and duration of initial Ca elevation in the dendrite and does not depend on SOCE due to a much faster temporal activation of RyRs than SOCE. With RyR2 overexpression in the ER membrane and large inital Ca elevations a low peak calcium wave (peak ~200 nM) can propagate for more than 25 um, suggesting that in Alzheimer's disease computations in the whole dendritic branches might be abnormal. This phenomenon might also play an important role in inhibitory plasticity on a dendritic branch.

Key words: calcium, computational model, neurodegeneration, ryanodine receptors

P11.3. ACTIVITY-DEPENDENT POLYADENYLATION OF mRNAs IN THE RAT BRAIN

Bozena Kuzniewska[1], Pawel Krawczyk[2], Francois Pauzin[3], Jacek Milek[1], Clive Bramham[3], Andrzej Dziembowski[2], Magdalena Dziembowska[1]

[1]Laboratory of Molecular Basis of Synaptic Plasticity, Centre of New Technologies, University of Warsaw, Poland, [2]Laboratory of RNA Biology, International Institute of Molecular and Cell Biology, Poland, [3]Mohn Center for Research on the Brain, University of Bergen, Norway

Local translation of numerous synaptic proteins is essential to the maintenance and plasticity of neuronal synapses. One of the major determinants of mRNA stability and translation is the poly(A) tail. Poly(A) tail is deposited during mRNA maturation in the nucleus, still for some RNAs, its extension may occur in the cytoplasm, allowing for a context-specific regulation of translation. It has been proposed that some dendritically localized mRNAs may undergo activity-induced polyadenylation. However, the mechanism and functional impact of neuronal cytoplasmic mRNA polyadenylation are largely unknown.

We applied Oxford Nanopore direct RNA sequencing to measure the genome-wide mRNA poly(A) tail dynamics upon neuronal activity. We analyzed mRNA poly(A) tail length in rat synaptoneurosomes stimulated *in vitro* for 10 minutes. Our preliminary data show that indeed a number of mRNAs display lengthening of poly(A) tails in response to *in vitro* NMDA-R stimulation. Furthermore, we used a model of LTP (long-term synaptic plasticity) induced *in vivo* in rats. LTP was induced by

high-frequency stimulation of the medial perforant path input to the dentate gyrus on one side of the rat brain (contralateral non-stimulated side served as control). As a result of these experiments we obtained a dataset of genome-wide poly(A) tail dynamics induced by LTP in the dentate gyrus. We will show and discuss the population of mRNAs that dynamically change their poly(A) tail lengths upon the stimulation in both models.

Key words: polyadenylation, local translation, synaptic plasticity, LTP

P12.1. DELETION OF DIAPHANOUS RELATED FORMIN 1 PRESERVES DIABETIC PERIPHERAL NEUROPATHY IN MICE – A PRELIMINARY STUDY

Kamila Zglejc-Waszak[1], Agnieszka Korytko[1], Andrzej Pomianowski[2], Judyta Juranek[1]

[1]Department of Human Physiology and Pathophysiology, School of Medicine, Collegium Medicum, University of Warmia and Mazury in Olsztyn, Poland,
[2]Department of Internal Diseases with Clinic, Faculty of Veterinary Medicine, University of Warmia and Mazury in Olsztyn, Poland

Diabetic peripheral neuropathy (DPN) is a nerve damage caused by long-term diabetes. Several biological processes underlying DPN have been identified such as impaired slow axonal transport, alternations in axonal diameter, myelin thickness, myelin irregular shape and myelin infoldings in diabetic sciatic nerve. All these processes are related to the modulations of actin cytoskeleton. Diaphanous related formin 1 (Diaph1) with its actin-binding ligands such as profilin as well as cofilin, are involved in actin polymerization. The aim of our study was to decipher Diaph1's role in DPN. Thus, eight weeks old mice, C57BL/6 wild-type (WT) and Diaph1 knockout (DKO), were injected intraperitoneally with streptozotocin or vehicle for five consecutive days and sacrificed 24 weeks after the last injection. The results showed that in both type 1 diabetes (T1D) groups motor nerve conduction velocity (MNCV) was lower than in respective control groups. Nevertheless, the MNCV of DKO mice was higher than that of WT mice. We suppose that the deletion of Diaph1 may improve MNCV in mice and thus delay DPN progression. Our studies showed that T1D decreases actin and profilin amount in sciatic nerve harvested from WT mice. On the contrary, we did not observe a decline in ACTB and profilin in DKO groups. Hence, we may speculate that the deletion of Diaph1 may affect actin dynamic regulation by cofilin. Indeed, we observed higher ratio of cofilin/actin in sciatic nerve harvested from DKO than in WT mice. Finally, Diaph1 may be a crucial switch in actin polymerization as well as in cytoskeleton reorganization of peripheral nervous system and thus be involved in the progression of DPN. Deletion of Diaph1 seems to be nerve protective, preventing from DPN progression in diabetic mice.

Funded by: National Science Centre, Poland (Grant UMO-2018/30/E/NZ5/00458).

Key words: diabetes, sciatic nerve, neuropathy, Diaph1, actin cytoskeleton, mouse

POSTER SESSION 2

P13.1. LACK OF MITOCHONDRIAL CHAPERONE TRAP1 IN MICE AFFECTS NEURONAL RESPONSE TO STRESS AND MITOCHONDRIA METABOLISM

Aleksandra Stawikowska, Bożena Kuźniewska, Magdalena Dziembowska

Centre of New Technologies, University of Warsaw, Poland

HSP90 proteins are essential molecular chaperones highly conserved in evolution. Although the mitochondrial HSP90 paralogue, TRAP1 was discovered more than 20 years ago a detailed understanding of its function remains elusive. TRAP1 was shown to be involved in protection from oxidative stress and cell death, implicated in metabolic regulation and mitochondrial dynamics.

Recently, using gene editing technology, we generated a new transgenic knock-in mouse line with the truncation of TRAP1 (p.Gln639Ter) resulting in significant downregulation of TRAP1 expression. We found that Trap1$^{p.Gln639Ter}$ mutant mice (Trap1 MUT) exhibit changes in behavior and neuronal synaptic plasticity as compared to wild-type mice. In the current study we aimed at investigating the effects of TRAP1 mutation on mitochondria metabolism and cellular stress response in the brain. We analyzed hippocampi isolated from young and adult TRAP1 mice and analyzed signaling pathways activated after cellular stress. We found a significant increase in the level of P-S6K and P-eIF2a in adult Trap1 MUT mice as compared to WT mice. To analyze consequences of TRAP1 mutation for mitochondria metabolism in the synapse we used synaptoneurosomes (SN), fraction enriched in synapses, freshly isolated from the mouse brain. Using this model, we measured activity of respiratory chain complex I and II and we found a significant increase in the activity of respiratory complex I and a decrease in the activity of respiratory complex II in Trap1 MUT mice as compared to WT. Next, we measured consumption of energy substrates using MitoPlate™ and we observed the decreased consumption of succinate and increased consumption of pyruvic and malic acid. We also analyzed the level of reactive oxygen species (ROS) and ATP in SN and we didn't found differences between genotypes.

Key words: TRAP1, mitochondria metabolism, stress response

P13.2. THE POWER OF MODEL: DEVELOPMENT OF DEPRESSIVE-LIKE BEHAVIOR IN MICE EXPOSED TO CHRONIC OR SUBCHRONIC SOCIAL DEFEAT STRESS

Patrycja Ziuzia[1], Laura Bergauer[2], Michał Ślęzak[1]

[1]Łukasiewicz Research Network – PORT Polish Center for Technology Development, Life Sciences and Biotechnology Center, Wrocław, Poland,
[2]BioMed X Institute, Heidelberg, Germany

Major depressive disorder (MDD) is one of the main causes of public health concern, affecting approx. 300 million people of all ages. Considering that major risk factor for developing MDD is stress exposure, it is crucial to provide research on molecular basis of stress response with validated rodent models, exhibiting both physiological and behavioral phenotypes corresponding to those observed in human disease.

One of the MDDs hallmarks is disrupted functioning of hypothalamus-pituitary-adrenal (HPA) axis, which controls release of steroid hormones e.g., glucocorticoids (GCs). Increased concentration of GCs in the blood, results in hyperactivation of glucocorticoid receptors (GRs), leading to crucial alterations of the stress response regulation. Although GRs are ubiquitously expressed in the central nervous system (CNS), our former studies revealed that among other glial cells, astrocytes play major role in mediating GR-dependent outcomes of Chronic Social Defeat Stress (CSDS, 14 days) paradigm.

The aim of this project was to study the contribution of astrocytic GRs signalling to a shorter stress exposure, as well as the role of stress duration on developing depressive-like behavior. To achieve that GRs were selectively eliminated from astrocytes of male mice (Aldh1l1-CreER^{T2} x GR$^{flox/flox}$, C57Bl/6J background). Afterwards, a Subtreshold Social Defeat Stress (SSDS, 3 days) paradigm was performed and both individual and social interactions were monitored with classical tests (e.g., light-dark box, social avoidance).

In contrast to CSDS, we did not observe alterations of social interaction and anxiety-like behavior in mice exposed to SSDS, irrespective of the genotype. Our results show that CSDS is better suited to examine the contribution of GR signaling in astrocytes to depressive- and anxiety-like behavior than SSDS.

Literature: Tertil et al., Glucocorticoid receptor signaling in astrocytes is required for aversive memory formation, 2018. Translational Psychiatry 8(1): 255. Yang et al., The Effects of Psychological Stress on Depression. Current Neuropharmacology. 2015;13: 494–504.

Key words: astrocytes, glucocorticoid receptor, depressive-like behavior, Chronic Social Defeat Stress, Subtreshold Social Defeat Stress

P13.3. EFFECT OF VARIABLE DOSES OF NICKEL OXIDE NANOPARTICLES ON BEHAVIOR, BLOOD BIOCHEMISTRY AND MARKERS OF OXIDATIVE STRESS FROM THE VITAL ORGANS OF ALBINO MICE IN A SEX SPECIFIC MANNER

Furhan Iqbal

Bahauddin Zakariya University, Multan, Pakistan

POSTER WITHDRAWN

P13.4. DISTINCT microRNA SIGNATURES OF CHILDHOOD TRAUMA IN HUMAN SERUM AND SPERM: IMPLICATIONS FOR POTENTIAL INTERGENERATIONAL TRANSMISSION

Magdalena Gomółka, Weronika Tomaszewska, Adria-Jaume Roura Canalda, Bożena Kamińska-Kaczmarek, Ali Jawaid

Nencki Institute of Experimental Biology, Warsaw, Poland

Childhood trauma is an important risk factor for psychiatric and physical ailments during adulthood. Emerging evidence from rodent studies suggests that some behavioral and metabolic symptoms of childhood trauma are transmissible across generations. However, the exact mechanisms underlying the transmission of the effects of trauma to the germline for intergenerational transmission remain elusive. This project aims to systematically examine small RNAs in the serum and sperm samples from human trauma cohorts to identify molecular cascades that could potentially carry the effects of trauma to the germline.

Small RNA sequencing (sRNA-seq) followed by RT-qPCR assays were performed to identify and validate miRNA changes in the serum of children with recent trauma in the form of paternal loss and maternal separation (PLMS), and the sperm of adult men with a history of complex trauma prior to the age of 17.sRNA-seq revealed differential expression of 48 miRNAs in the serum of PLMS children *vs.* controls; whereas 29 miRNAs are altered in the sperm of trauma-exposed men compared to controls. Pathway analysis and functional relevance of the differentially expressed miRNAs suggest a close association with cholesterol and lipoprotein signaling. Notably, miR-223-3p, which was similarly upregulated

in the blood and sperm samples from these trauma cohorts targets SR-B1: the receptor for high-density lipoproteins and is implicated in cholesterol biosynthesis. This study found distinct overlapping miRNA changes in serum and sperm after childhood trauma. Guided by these results, our current efforts are focused on modeling the role of lipids and lipid-associated factors in the intergenerational effects of early postnatal trauma *via* ethologically relevant mouse models and *ex vivo* approaches.

Key words: childhood trauma, microRNAs, epigenetic inheritance

P13.5. ELECTROMAGNETIC FIELD EXPOSURE: ADAPTIVE STIMULANT OR CO-FACTOR FOR STRESS-RELATED DISEASES?

Maciej Klimiuk, Hanna Kletkiewicz, Angelika Klimek, Agnieszka Siejka, Justyna Maliszewska, Joanna Wyszkowska, Milena Jankowska, Paulina Idczak, Anna Nowakowska, Maria Stankiewicz, Justyna Rogalska

Nicolaus Copernicus University, Department of Animal Physiology and Neurobiology, Toruń, Poland

Recently, the interest in medical applications of extremely low-frequency electromagnetic fields (EMF) is growing. However, the overall direction of the influence of EMF is still unresolved. Furthermore, it has been shown that EMF activates stress response, potentially contributing as a co-factor to stress-related diseases.

The aim of this research was to evaluate the influence of 50Hz EMF, with low (1mT) and high (7mT) intensity on the expression of pro-/anti-apoptotic factors (Bcl-2, Bak) and concentration of stress-related markers (CRH, CORT).

Three-months old male rats (Wistar strain) were exposed 3 times to 50Hz EMF at intensities of 1 or 7mT (each exposure lasting a week, 1h/day). After each exposure, a part of the animals was sacrificed to collect hippocampi and adrenal glands. RT-qPCR was performed to measure relative expression of Bcl-2 and Bak mRNA, while ELISA was used to determine levels of CRH and CORT.

The results showed that low-intensity EMF upregulated factors associated with cell survival, with no significant impact on proteins related to stress reactions. In contrast, high-intensity EMF induced a severe stress response and disrupted expression of pro-/anti-apoptotic factors.

Thus, we conclude that low-intensity EMF exposure yields no significant stress reaction and promotes cell survival in the hippocampus, while high-intensity may act as a severe stressor and could possibly contribute as a co-factor in nervous system-related diseases.

Understanding the properties of EMF is crucial both for developing novel therapeutic interventions as well as ensuring a safe environment for human habitat. Investigating the impact of EMF on brain plasticity opens up new possibilities for therapies aimed at improving cognitive function and addressing various neurological conditions, but we have to be wary of a possible drawbacks of such treatment.

Key words: electromagnetic field, HPA axis, BCL2, stress response, hormesis

P13.6. THE IMMUNE CHECKPOINT EXPRESSION IN THE BRAIN AND BLOOD CELLS IS ASSOCIATED WITH THE OCCURRENCE OF DEPRESSIVE SYMPTOMS: A STUDY IN AN ANIMAL MODEL OF DEPRESSION BASED ON WISTAR KYOTO RATS

Katarzyna Curzytek[1], Anna Gąsiorek[2], Stanisław Malicki[3], Marta Kubera[1]

[1]Department of Experimental Neuroendocrinology, Maj Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland, [2]Department of Microbiology, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Kraków, Poland, [3]Department of Microbiology, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Kraków, Malopolska Centre of Biotechnology, Jagiellonian University, Kraków, Poland

Major depression disorder (MDD) is a complex mental disease with a growing prevalence in the human population worldwide. Despite many years of intensive research, the mechanism of the development of depressive disorders remains elusive, and the disease manifests itself in various ways, from changes in energy, mood, and behavior to physical symptoms. Growing evidence suggests that depression is accompanied by the activation of the immuno-inflammatory pathways. Antidepressants used so far in the treatment of MDD have certain immunomodulatory properties, nevertheless, the search for new therapeutic targets is extremely urgent. Therefore, the aim of the present study was to investigate the role of immune checkpoints (ICP), namely programmed cell death protein 1 (PD-1) and its ligand, programmed death-ligand 1 (PD-L1), in the mechanism of development and course of depressive disorders. We conducted the experiments in Wistar Kyoto (WKY)

male rats – an animal model of treatment-resistant depression, and Wistar strain rats as control animals. Our studies revealed decreased hippocampal and cortical PD-L1 gene expression in Wistar Kyoto rats compared to Wistar rats. Moreover, the decrease in PD-L1 expression in brain structures was associated with an increase in PD-1 expression in primary blood mononuclear cells (PBMC) isolated from WKY rats. Reduction in PD-L1 expression in the brain and elevation of PD-1 in PBMC isolated from WKY rats may suggest that depressive disorder correlates with ICP dysregulation in the nervous system. Therefore, more research is needed to assess ICP function, both in the nervous and immune systems, which will help us find a connection between depression and the accompanying inflammation.

This work was supported by grant 2021/43/B/NZ6/02203 National Science Centre, Poland.

Key words: depression, immune checkpoint, PD-1, Wistar Kyoto

P13.7. INACTIVATION OF α1A-ADRENERGIC RECEPTOR AFFECTS ANXIETY- AND DEPRESSIVE-LIKE BEHAVIOR OF MICE IN CHRONIC RESTRAINT STRESS-INDUCED MODEL OF DEPRESSION AND MODULATES CITALOPRAM EFFECT ON EXPRESSION OF SOME GENES: INSIGHTS FROM FEMALE α1A KNOCKOUT MICE

Michał Wilczkowski, Katarzyna Chorązka, Piotr Chmielarz, Katarzyna Maziarz, Adam Bielawski, Katarzyna Rafa-Zabłocka, Monika Bagińska, Agnieszka Zelek-Molik, Irena Nalepa

Maj Institute of Pharmacology, Polish Academy of Sciences, Department of Brain Biochemistry, Kraków, Poland

Noradrenergic transmission disruption is a key feature of stress-related psychiatric disorders like depression. Within the components of noradrenaline signaling, α1–adrenergic receptor (α1-AR) that consists of three subtypes (α1A, α1B, α1D), appears to be critically involved in modulating depression by facilitating the cellular response to antidepressants. We aimed to study the behavioral response and gene expression of female α1A-AR knockout (AKO) mice exposed to chronic stress and an antidepressant, citalopram.

Mice were subjected to 21 days of chronic restraint and since the day 7, concurrently treated with citalopram. Depressive-like behaviors and anxiety level, as well as the impact of citalopram on these behaviors, were assessed using tail suspension (TST) and elevated plus maze tests (EPM). The prefrontal cortex was isolated and mRNA expression of depressive disorder-related genes were evaluated using Low Density TaqMan arrays (TLDA).

Bodyweight gain assessment confirmed the stress model's effectiveness. Further findings showed a reduced immobility time following citalopram administration in stressed wild-type mice (WT), but not in AKO mice. Moreover, chronic restraint stress increased anxiety in WT mice, evidenced by reduced time in the open arm of the EPM, while no such effect was observed in AKO mice. Molecular experiments showed changes in mRNA expression of depression-related genes, including COMT, TNF, and TP53 (p53 protein). In stressed AKO mice, COMT mRNA expression was lower compared to the AKO control group and stressed WT mice. Further, the regulation of TNF and TP53 genes varied depending on the genotype. In stressed AKO mice treated with citalopram, TNF and TP53 genes exhibited distinct expression patterns compared to stressed WT mice.

Our results revealed the significance of α1A-AR subtype in modulating stress and depression-like responses in female mice, at the same time indicating the importance of this receptor for the effect of citalopram.

This research was funded by National Science Centre, Poland,grant number 2015/17/B/NZ7/03018 (Opus 9) and statutory funds of the Maj Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland.

Key words: α1A–adrenergic receptor, chronic stress, prefrontal cortex, depression-related genes

P13.8. POTENTIAL EFFECT OF SLEEP DEPRIVATION ON THE GUT – *DROSOPHILA MELANOGASTER* MODEL

Joanna Jędrusik, Karolina Warzecha, Milena Damulewicz

Jagiellonian University, Department of Cell Biology and Imaging, Krakow, Poland

Jet lag is a condition of organism caused by disruption of circadian rhythms. In most cases it affects people who travel and change multiple time zones. However, a similar phenomenon is also increasingly affecting people whose lifestyles cannot be coordinated with the internal clock, such as shift workers. Among the wide range of adverse side-effects associated with the phase shift of the sleep-wake cycle, a highly common are gastrointestinal problems. It has already been proven that jet lag causes changes in the expression of genes in the

gut – including those related to inflammation. Here we investigated the relationship between short term sleep deprivation and gene expression changes using *Drosophila melanogaster* model. Therefore, one-day-old males underwent 16 hours of mechanical sleep deprivation. Next, we performed analysis of gene expression from middle part of the gut. We focused on clock genes, and two genes encoding proteins strongly connected with nervous system – *npf* and *ninad*. Our study unravels potential disruption in gut physiology following sleep disturbance on molecular level. Since many people suffer from sleeping disorders it is important to conduct fundamental studies in this area.

Key words: jet lag, sleep deprivation, gut disruption, *Drosophila melanogaster*

P13.9. BEHAVIORAL CHARACTERISTICS OF CHRONIC PSYCHOSOCIAL CROWDING STRESS MODEL IN RATS

Agnieszka Zelek-Molik[1], Weronika Surdej[1], Agnieszka Potasiewicz[2], Agnieszka Nikiforuk[2], Michał Wilczkowski[1], Irena Nalepa[1], Grzegorz Kreiner[1]

[1]Maj Institute of Pharmacology, Polish Academy of Sciences, Department of Brain Biochemistry, Poland, [2]Maj Institute of Pharmacology, Polish Academy of Sciences, Department of Behavioral Neuroscience and Drug Development, Kraków, Poland

The psychosocial nature of the crowding stress model (CS) relies on the animals' exposure to proximity to companions and competition for access to drinking water or food. It makes CS similar to social stressors in humans that may result in stress-related pathology. Our previous studies showed disruptions in synaptic transmission and glutamate receptor levels in the frontal cortex of CS rats, and the rats' inability to habituate to stress conditions. This study aimed to assess whether chronic CS induces behavioral deficits in rats.

Male Wistar rats were overcrowded for 14 days while the control (CON) were kept under standard conditions. Open Field (OF), Elevated Plus Maze (EPM), Novel Object Recognition (NOR), and Social Interactions (SI) behavioral tests were performed to assess whether CS procedure evokes anxiety-like behaviors.

We found that CS rats gained less weight than CON during the stress procedure. Compared to CON, CS rats spend less time in the central zone of the OF apparatus and their exploration measured by rearing was decreased. In the EPM test, stressed rats exhibited augmented stereotypic behavior measured by grooming and also spend less time in open arms. In the NOR test, stressed rats presented a decrease in the discrimination index connected to impairment in recognizing the novel object. In the SI test, CS rats spent the same time playing together. There were no differences in interaction behaviors like sniffing, anogenital sniffing or grooming. However, vocalization analysis recorded during the SI test revealed that stressed rats vocalized less, and the reduction was concerned mainly with high-frequency (reward-connected) calls. Moreover, calls of stressed rats were shorter, and with higher peak frequency.

Our results revealed that chronic CS triggers anxiety-like behavior and visual memory deficits which point out CS as a promising model to study the mechanisms underlying psychosocial stress-related pathologies.

Key words: chronic stress, open field, elevated plus maze, novel object

P14.1. EFFECTS OF A MOTHER'S CAFETERIA DIET ON HISTOLOGICAL PARAMETERS AND THE EXPRESSION OF RECEPTORS BELONGING TO THE KISSPEPTIN SYSTEM IN THE TESTES OF THE OFFSPRING

Emilia Grzeda[1], Julia Matuszewska[1], Dominika Kawka[2], Monika Kaczmarek[2], Joanna Śliwowska[1]

[1]Faculty of Veterinary Medicine and Animal Sciences, Poznan University of Life Sciences, Poznan, Poland, [2]Institute of Animal Reproduction and Food Research PAS, Olsztyn, Poland

Unhealthy diet contributes to the development of the global obesity epidemic and is a risk factor for fertility disorders[1]. It seems likely that maternal obesity leads to alterations in the reproductive capacity of the offspring *via* prenatal and postnatal programming. To mimic the effects of a high-sugar and a high-fat diet, which induce obesity in animals, the cafeteria (CAF) diet is used[2].

We hypothesized that the maternal cafeteria diet has adverse effects on: the male offspring's reproductive functions due to morphological and molecular – *Kiss1, Kiss1r, Esr1, Esr2, Ar*, and *Lhcgr* expression, alterations in the testes.

Rat mothers were fed the CAF diet before and during pregnancy and lactation. Male offspring were sacrificed on postnatal days (PNDs) 40 and 60, total RNA was extracted from the testes, and gene expression was

measured by real-time PCR. Morphological parameters of the testes were evaluated after hematoxylin-eosin staining.

We found that male offspring of CAF mothers had: decreased diameter of seminiferous tubules, luminar epithelium diameter and height; a lower number of Sertoli cells; a lower percentage of semen distribution at PNDs 40 and 60; and alterations in the mRNA levels of tested genes. At PND 40 and 60, CAF male offspring had higher *Ar* mRNA level compared to the control (C). At PND 40, CAF males had higher *Kiss1* and lower *Kiss1r* mRNA levels compared to C.

We conclude that the mother's CAF diet leads to alterations in reproductive outcomes in male offspring *via* dysregulation of the kisspeptin system in the testes.

The study was funded by PRELUDIUM grant 2019/35/N/NZ9/00663 to JM, and statutory funding from the Poznan University of Life Sciences (506-511-09-00) to JHS.

References: 1. Barker DJ. The Fetal and Infant Origins of Adult Disease. BMJ 1990; 2. Grzęda E, et al. Animal Foetal Models of Obesity and Diabetes – From Laboratory to Clinical Settings. Front Endocrinol 2022.

Key words: obesity, cafeteria diet, prenatal programming, kisspeptin, testes, estrogen receptor, androgen receptor

P14.2. EFFECT OF CORTICOSTERONE ON THE GENE EXPRESSION IN THE CONTEXT OF GLOBAL HIPPOCAMPAL TRANSCRIPTION

Grzegorz Juszczak[1], Adrian Stankiewicz[2], Aneta Jaszczyk[1]

[1]Institute of Genetics and Animal Biotechnology, Department of Animal Behavior and Welfare, Jastrzebiec, Poland, [2]Institute of Genetics and Animal Biotechnology, Department of Molecular Biology, Jastrzebiec, Poland

Glucocorticoids are involved in physiological response to stress but processes taking place in brain in response to glucocorticoids are still poorly understood. To fill existing gaps in knowledge we performed a transcriptomic experiment testing effects of prolonged treatment with corticosterone ranging from 5 to 28 days. This approach enabled us an assesment of replicability of findings and identification of time-dependent processes. We also performed a global assesment of hippocampal transcriptome to enable better understanding of the effects induced by glucocorticoids. Experiment was performed in adult male mice (Swiss-Webster) that received corticosterone in drinking water. Analysis of hippocampal transcriptome was performed with RNA sequencing. The analysis showed increasing number of genes with altered expression (from 228 do 597) depending on the duration of treatment with corticosterone. We also found that the most affected transcripts are coded by genes with relatively low or moderate basal level of expression. This observation can be explained by the fact that transcription is a relatively slow process compared with translation and, therefore, effective regulation of transcriptome may be restricted only to genes with lower basal expression.

Key words: corticosterone, transcriptome, hippocampus

P15.1. DEEP LEARNING APPROACHES TO IDENTIFICATION AND DELINEATION OF CORTICAL AREAS IN THE MARMOSET CORTEX

Agata Kulesza[1], Sylwia Bednarek[1], Marcello G.P. Rosa[2], Piotr Majka[1]

[1]Laboratory of Neuroinformatics, Nencki Institute of Experimental Biology of the Polish Academy of Sciences, Warsaw, Poland, [2]Monash University Node, ARC Centre of Excellence for Integrative Brain Function, Monash University, Clayton, Australia

The cerebral cortex is subdivided into functionally distinct areas, traditionally distinguished based on the distribution and size of the neuronal bodies (cytoarchitecture) and the direction and density of myelinated axons (myeloarchitecture). The delineation of the cortex into areas and layers is, in most cases, performed manually in a laborious process requiring substantial expertise in neuroanatomy. This manual approach is typically a bottleneck in large-scale, high-throughput applications where several areas are to be delineated using objective criteria in large numbers of animals.

We report on a deep learning pipeline for the automated identification of cortical areas in the entire cortex of the marmoset monkey (*Callithrix jacchus*). The process relies on microscopic (0.5 µm/px) images of serial sections stained with the Nissl method and consists of three components: segmentation of the cerebral cortex, estimation of the density and size of the neuronal somata, and identification of the cortical areas based on series of cortical profiles (i.e., unambiguously defined lines that connect the pial with the white matter).

To train the network, we took advantage of the repository of several hundred outlines of selected cortical areas in twenty hemispheres of the marmoset cerebral cortex, in which areas were delineated manually based on both cyto- and myeloarchitecture, as part of the Marmoset Brain Connectivity Atlas project. This allowed us to compare the performance of two networks: one relying on cortical profiles derived from 3D reconstructions of the brain hemisphere and another utilising individual 2D sections independently. The preliminary results demonstrate that the cytoarchitectonic profiles are a reliable source of training data for deep-learning solutions to identify cortical areas based on their cytoarchitectonic characteristics.

Acknowledgments: National Science Centre (2019/35/D/NZ4/03031) National Health and Medical Research Council (APP1194206).

Key words: deep learning, segmentation, histology, cortex

P15.2. IDENTIFICATION OF GENES AND SIGNALING PATHWAYS REGULATING PROLIFERATION AND DIFFERENTIATION OF RAT SPINAL CORD CENTRAL CANAL NEURAL PROGENITOR CELLS

Krzysztof Miazga, Urszula Sławińska, Marek Bekisz, Małgorzata Zawadzka

Nencki Institute of Experimental Biology, Polish Academy of Science, Warsaw, Poland

The spinal cord central canal ependyma is a niche for neural progenitor cells (ependymal NPCs), which after spinal cord injury in lower vertebrates (e.g., zebrafish) proliferate and differentiate into neurons and, therefore, may be involved in the tissue reconstruction and restitution of lost functions. However, in mammals, these cells differentiate mainly in astrocytes forming a glial scar that often limits neural regeneration. Understanding the molecular mechanisms involved in proliferation and differentiation of ependymal NPCs may contribute to the development of new therapies for spinal cord injury treatment based on the manipulation of their fate. The present study aimed to identify genes and signaling pathways which might be involved in the regulation of proliferation and differentiation of rat spinal ependymal NPCs after spinal cord injury. To this end, we microdissected ependymal cells from the tissue sections of the spinal cord central canal collected from rats 5 days after spinal cord transection and control rats and compared their transcriptomes. RNAseq data were subjected to bioinformatic analysis in order to identify genes specifically regulated in ependymal cells. Gene Ontology and Protein-protein Interaction String analyses indicated TGF-β and WNT signaling pathways to be selectively upregulated in central canal cells. Moreover, we identified two transcription factors KLF5 and Elf3 uniquely upregulated in central canal cells and subsequently confirmed the localization of their protein products in ependymal cell nuclei. We propose the above signaling pathways and transcription factors as potentially involved in the control of the proliferation and/or differentiation of ependymal cells in response to spinal cord injury.

Key words: rat spinal cord, ependymal cells, neural progenitor cells, RNAseq

P15.3. DEEP LEARNING APPROACHES IN OBSERVER-INDEPENDENT EXPLORATION OF CYTOARCHITECTURAL PROPERTIES OF THE NON-HUMAN PRIMATE CEREBRAL CORTEX

Adam Datta[1], Agata Kulesza[1], Sylwia Bednarek[1], Marcello Rosa[2], Piotr Majka[1]

[1]Nencki Institute of Experimental Biology of the Polish Academy of Sciences, Laboratory of Neuroinformatics, Warsaw, Poland, [2]Monash Biomedicine Discovery Institute, Department of Physiology and Neuroscience Program, Clayton, Australia

The cerebral cortex is a laminar structure that can be divided into cytoarchitectonically defined areas and layers. While it has been extensively investigated for over a century, there is still no consensus regarding its structural and functional parcellation. At the same time, delineating areas that are agreed upon is still laborious and depends on extensive neuroanatomical knowledge. To this end, the development and implementation of deep learning techniques provides additional support for the rapid processing of a large amount of information-rich high-resolution microscopic images and brings a chance to alleviate both obstacles: the time-consuming nature of the process and observer bias.

We propose a U-Net deep learning neural network model for semantic segmentation of the cerebral cortex into cortical layers. This solution was tested using two different datasets: profiles generated from a small sample of brain sections stained with NeuN and profiles obtained from Nissl-stained sections of the whole brain of the non-human primate, the common marmoset monkey (*Callithrix jacchus*). Specifically, we analyze examples of koniocortex, dysgranular, and agranular cor-

tical areas with diverse, clear, and agreed-upon laminar composition.

The model applied to a small sample of NeuN-stained sections confirms the feasibility of segmenting the layers with accuracy ranging from 0.67 for layer IV to 0.96 for layers II–III, V–VI, and white matter. Using a larger dataset reduced the observed discrepancy in accuracy between layer IV and other layers.

The study demonstrated that the U-Net deep learning network model is an adequate tool for detecting the cytoarchitectonic properties of the primate cerebral cortex and automated identification of the individual cortical layers. As a result, it allows for a more robust segmentation, similar to that achieved by expert neuroanatomists, thereby significantly reducing the time required for manual annotation.

Key words: cerebral cortex delineation, neural networks

P15.4. ANALYSIS OF TRANSCRIPTOMES AND DIFFERENTIATION FATE OF EMBRYONIC BRAINSTEM PROGENITOR CELLS GROWN *IN VITRO* UNDER DIFFERENT EXPERIMENTAL CONDITIONS

Urszula Sławińska, Anna Kwaśniewska, Marek Bekisz, Krzysztof Miazga, Małgorzata Zawadzka

Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

To understand the influence of specific environmental conditions on transcriptome and differentiation fate of rat embryonic progenitor cells (EPCs), the fetal brainstem EPCs were grown in the presence of either Shh/FGF4 (S) or EGF/bFGF (E). Isolated cells effectively proliferated *in vitro*, creating neurospheres (S1 and E1), capable to form secondary neurospheres (S2) or monolayers (E2). RNAseq followed by bioinformatic analysis of transcriptomes of cells exposed to different conditions showed significant differences in gene expression. Comparing passages, we found that in S1 the most upregulated genes were related to neurogenesis and nervous system development as well as axon growth processes, while in S2 the upregulated genes were related to the organization of genetic material in the cell as chromatin and nucleosome formation. Higher expression of genes involved in neurogenesis was also found in the E1 *vs.* E2 cells. When compared S1 *vs.* E1, higher expression of genes associated with neuronal differentiation and nervous system development was indicated in S1. In the latest, we also found higher expression of genes involved in the differentiation of serotonergic neurons. Next, we examined the differentiation fate of pretreated cells (S1, E1, S2, E2). In all variants, a higher percentage of Sox2+ DCX+ cells were detected in cultures exposed to a neuron rather than in a glia-promoting medium, with the highest percentage in E2. As DCX is considered to be expressed in neuroblasts and young neurons, this variant may have the biggest potential to create neurons in a conducive environment. However, the highest percentage of cells double positive for NeuN+ and 5-HT+ was observed in the S1 group suggesting their ability to differentiate into serotonergic neurons. Concluding, EPCs can adopt different phenotypes *in vitro*. They may also develop different phenotypes when exposed to the specific environmental signals of the recipient's nervous tissue (e.g., spinal cord *vs.* brain).

Key words: progenitor cells, fetal brainstem, transcriptomes, differentiation fate

P15.5. MODELING NEUROSCIENTIFIC RESEARCH USING VIRTUAL REALITY ENVIRONMENTS, AND EXAMPLES OF VR APPLICATION AREAS

Beata Sokołowska[1], Ewa Sokołowska[2]

[1]Mossakowski Medical Research Institute, Polish Academy of Sciences, Bioinformatics Laboratory, Warsaw, Poland, [2]The John Paul II Catholic University of Lublin, Faculty of Social Sciences, Institute of Psychology, Department of Developmental Psychology, Lublin, Poland

Virtual reality (VR) offers interesting and worthwhile opportunities for neuroscience research and therapy, and public health. Neuroscientists and clinicians point out that diagnostic tests using VR environments (VREs) have high ecological value, accuracy, sensitivity and specificity in identifying various dysfunctions/deficits in examining subjects with serious diseases. Extensive research is being conducted in clinical and non-clinical populations, and studies with healthy individuals additionally serve to explore the capabilities and limitations of IT/ICT (including natural aging processes and supporting neurogeriatric care). Our model research was conducted using a non-immersive VRE. Healthy adult volunteers participated in virtual training sessions, performing cognitive-motor exercises using the dominant and non-dominant hand, and the same tasks on a posturographic platform. The results, together with the proposed analytical approach (based

on an error-counting algorithm and supervised classification methods), showed perfect recognition of the body side, i.e., functional lateralization of the brain. This concerned both the recognition of handedness and postural asymmetry of the exercisers. In addition, virtual scores were compared with the results of classical real tests, presenting their comparability. Our research, as well as other modeling/experimental studies and clinical observations, show the great potential of new IT/ICT tools. Moreover, VR has the potential to become the gold standard in (neuropsychological) diagnostics. In summary, it should also be noted that VR systems require the fulfillment of certain criteria, indicated, e.g., by the National Academy of Neuropsychology and the American Academy of Clinical Neuropsychology, for the implementation of innovative digital technologies for research and clinical purposes. However, currently, an important limitation of novel VREs is the sometimes observed symptoms of cybersickness in their users.

Key words: neuropsychology, cognitive-motor exercise and training, brain functions, functional lateralization, virtual reality

P15.6. NOVEL DATA ON THE TOLERANCE OF CEREBELLAR VESSELS FOR TEMPORARY OCCLUSION USING AWAKE TESTING

Natalia Lehman[1], Chiara Spezzani[2], Matan Bone[3], Yana Al-Inaya[4], Fariba Amiri[5], Jack Wellington[6], Monika Martinek[7], Raghuram Sampath[8], Kathleen Spears[9], Meghan Rodriquez[9], Saleem Abdulrauf[10]

[1]Department of Neurosurgery and Paediatric Neurosurgery, Medical University of Lublin, Lublin, Poland, [2]University of Florence, Florence, Italy, [3]University of Manchester, Manchester, United Kingdom, [4]Neuroscience, Curie Institute, Orsay, France, [5]Vrije Universiteit Amsterdam, Amsterdam, The Netherlands, [6]Cardiff University School of Medicine, Cardiff Wales, United Kingdom, [7]Saint Louis University, St Louis Missouri, United States, [8]Kaiser Permanente of Northwest, Sunnyside, Oregon, United States, [9]University of Missouri-Kansas City, St. Joe, Missouri, United States, [10]George Washington University, Washington DC, United States

POSTER WITHDRAWN

P16.1. CHARACTERIZATION OF NOVEL MOUSE MODELS OF TUBEROUS SCLEROSIS FOR THE STUDY OF DEVELOPMENTAL BASIS OF AUTISM SPECTRUM DISORDER

Marcin Lipiec[1], Mohammad Abdelfattah[1], Karolina Bogaj[2], Joanna Urban-Ciećko[2], Mateusz Grabowski[3], Jarosław Barski[3], Ewelina Knapska[1]

[1]Nencki Institute of Experimental Biology, Laboratory of Emotion Neurobiology, Warsaw, Poland, [2]Nencki Institute of Experimental Biology, Laboratory of Electrophysiology, Warsaw, Poland, [3]Center for Experimental Medicine, Medical University of Silesia, Katowice, Poland

Tuberous sclerosis complex (TSC) is a genetic disorder caused by the mutation in either TSC1 or TSC2 genes. These mutations lead to overactivation of the mTOR pathway – a signaling pathway associated with various cellular processes, including cell growth, proliferation, protein synthesis and synaptogenesis. TSC affects multiple organs, including the brain, leading to the development of benign tumors, as well as various neurological disorders, such as seizures, developmental delay or intellectual disability. TSC patients are also at a disproportionately increased risk of an autism spectrum disorder (ASD) diagnosis. The genetic link between TSC and ASD makes the *Tsc1/2* knockout animals a good model for elucidating autism's etiology. To study the connection between TSC and ASD and the developmental basis of the latter, we established two novel mouse models with a conditional knockout of the *Tsc2* gene. One of the leading hypotheses suggests that an important factor in autism's etiology is an imbalance in excitatory to inhibitory neurotransmission in the brain. To further explore this idea, the *Tsc2* knockout in our new mouse lines is induced specifically in either excitatory or inhibitory neurons early in gestation. This study provides an initial set of histological (e.g., myelin; cytochrome C oxidase stainings), electrophysiological (whole-cell patch-clamp) and behavioral (open field, Eco-HAB) data, that revealed significant differences between the knockout and wild-type animals. Our research prove that these new models can be a valuable tool for further, in-depth studies of the molecular mechanisms and developmental abnormalities that lead to autism.

Key words: Tuberous sclerosis complex, autism spectrum disorder, mTOR, whole-cell patch-clamp, social interaction, Eco-HAB

P16.2. SOCIAL POSITION EFFECT ON PLASMA PRO-INFLAMMATORY CYTOKINE LEVEL AFTER SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION APPLIED IN A RAT MODEL OF PARKINSON'S DISEASE

Oliwia Harackiewicz, Beata Grembecka, Irena Majkutewicz, Wojciech Glac, Danuta Wrona

Department of Animal and Human Physiology, Faculty of Biology, University of Gdańsk, Poland

Parkinson's disease (PD) is a neurodegenerative disorder that has been widely studied in animal models. It has been shown that PD is also assosiated with neuroinflammation and an alteration in the immune system functionality. Subthalamic nucleus deep brain stimulation (DBS-STN) is an effective method of alleviating motor symptoms of PD and has immunomodulative properties. Animal studies suggest an influence of social position on the functioning of the rat's immune system.

The aim of the experiment was to assess the influence of social position of rats with PD model on the plasma levels of pro-inflammatory cytokines: interleukin 6 (IL-6) and interferon γ (INF-γ) after DBS-STN.40 adult male Wistar rats underwent social interaction test to determine their social position, received unilateral DBS-STN implantation and 6-hydroxydopamine (6-OHDA) infusion into the SNpc (substantia nigra pars compacta). Following recovery rats received DBS-STN (n=21) or SHAM (control, n=19) 1 hour stimulation. PD model was verified by tyrosine hydroxylase (TH) positive cells detection in SNpc. After stimulation blood samples have been taken and analysed using ELISA method to determine IL-6 and IFN-γ levels.

We found that plasma level of IL-6 was significantly lower in dominant (D) rats after DBS-STN (DBS-6OHDA) compared to submissive (S) rats ($p \leq 0{,}05$) and to control groups (D/S SHAM VEH; $p \leq 0{,}001$). There was no significant differences between other groups. The plasma level of IFN-γ was significantly elevated in D rats of DBS-6OHDA group compared to S ($p \leq 0{,}0001$) and D rats of SHAM group ($p \leq 0{,}01$). The level of IFN-γ was lower in S rats of DBS-6OHDA group compared to S of SHAM group, and in S rats of SHAM group compared to D rats, however those differences were not statistically significant.

The obtained results suggest a potential role of PD model rat's social position in modulating the plasma levels of pro-inflammatory cytokines after DBS-STN application.

Key words: deep brain stimulation, subthalamic nucleus, rat model of Parkinson's disease, social position, cytokine

P16.3. N-ACETYLCYSTEINE AND ARIPIPRAZOLE IMPROVE SOCIAL BEHAVIOR AND COGNITION, AND MODULATE BRAIN BDNF LEVELS IN A RAT MODEL OF SCHIZOPHRENIA

Elżbieta Lorenc-Koci, Kinga Kamińska, Zofia Rogóż

Maj Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland

Treatment of negative symptoms and cognitive disorders in patients with schizophrenia is still a serious clinical problem. The aim of our study was to compare the efficacy of chronic administration of the atypical antipsychotic drug aripiprazole (7-{4-[4-(2,3-dichlorophenyl)-1-piperazinyl] butoxy}-3,4-dihydro-2(1H)-quinolinone; ARI) and the well-known antioxidant N-acetylcysteine (NAC) both in alleviating schizophrenia-like social and cognitive deficits and in reducing the decreases in the levels of the brain-derived neurotrophic factor (BDNF) in the prefrontal cortex (PFC) and hippocampus (HIP) of adult Sprague-Dawley rats, that have been induced by chronic administration of the model compound L-buthionine-(S, R)-sulfoximine (BSO) during the early postnatal development (p5-p16). ARI was administered at doses of 0.1 and 0.3 mg/kg while NAC at doses of 10 and 30 mg/kg, alone or in combination. Administration of higher doses of ARI or NAC alone, or co-treatment with lower, ineffective doses of these drugs significantly improved social and cognitive performance as assessed in behavioral tests. Both doses of NAC and 0.3 mg/kg of ARI increased the expression of BDNF mRNA in the PFC, while all doses of these drugs and their combinations enhanced the levels of BDNF protein in this brain structure. In the HIP, only 0.3 mg/kg ARI increased the levels of both BDNF mRNA and its protein. These data show that in the rat BSO-induced neurodevelopmental model of schizophrenia, ARI and NAC differently modulated BDNF levels in the PFC and HIP.

This work was also supported by the Statutory Found of the Institute of Pharmacology, Polish Academy of Sciences.

Key words: neurodevelopmental model of schizophrenia, schizophrenia-like symptoms, levels of BDNF mRNA and its protein, aripiprazole, N-acetylcysteine

P16.4. INCREASED NEURONAL ACTIVITY AND mTOR HYPERACTIVATION LEADS TO DEGRADATION OF BAF COMPLEX SUBUNIT – Brg1

Shiwani Kumari[1], Karolina Bogusz[1], Matylda Macias[1], Ewa Liszewska[1], Magdalena Bakun[2], Justyna Jackiewicz[1], Weronika Zajko[1], Jacek Jaworski[1]

[1]International Institute of Molecular and Cell Biology in Warsaw, Poland, [2]Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland

Mammalian target of rapamycin (mTOR) is a kinase essential for cell metabolism and growth in most cell types. In neurons, mTOR is crucial for neuronal development and plasticity. Dysregulation of mTOR activity has been implicated in a group of disorders known as mTORopathies, with notable examples including tuberous sclerosis complex (TSC) and associated brain disorders such as epilepsy. Although mTOR is predominantly cytoplasmic, several groups have reported its nuclear presence. With the mass spectrometry analysis, we identified Brg1, the catalytic subunit of the BAF chromatin remodelling complex, as one of the nuclear mTOR interactors. Therefore, in this study , we aimed to explore the mTOR-Brg1 interaction in the nucleus and its implications for neuronal development and disease. We used *in vitro* cultured rat neurons, and our data confirmed that mTOR-Brg1 interaction increases upon kainic acid (KA) and revealed that Brg1 is phosphorylated by mTOR. We also observed that the modulation of mTOR as well as proteasome affects Brg1 nuclear presence, suggesting Brg1 degradation in the nucleus upon KA treatment. In agreement with KA treatment results, we observed the downregulation of Brg1 expression upon TSC2 loss, which leads to mTOR hyperactivation in neurons. Ca^{2+} imaging and morphometric analysis revealed several similarities between neurons with silenced TSC2 and Brg1. Altogether, our data suggest that neuronal activity leads to changes in Brg1-containing BAF complex function *via* mTOR.

The research was financed under the NCN MAESTRO grant 2020/38/A/NZ3/00447.

Key words: mTOR, BAF complex, Brg1, TSC

P16.5. THE INFLUENCE OF KML-29, INHIBITOR OF ENDOCANNABINOIDS ENZYMATIC DEGRADATION, ON THE DIFFERENT STAGES OF MEMORY AND MEMORY DISORDERS PROVOKED BY AN ACUTE INJECTION OF MK-801 IN MICE

Marta Kruk-Slomka, Ewa Kedzierska, Jolanta Orzelska-Gorka, Grazyna Biala

Department of Pharmacology and Pharmacodynamics, Medical University of Lublin, Poland

Schizophrenia is a serious mental disorder, with e.g., memory-loss. The treatment of schizophrenia is complicated. One of the possible strategies for the modulation of cognitive symptoms of schizophrenia is connected with the endocannabinoid system (ECS). ECS is composed of cannabinoid (CB: CB1 and CB2) receptors, and endocannabinoids, which are degraded by fatty acid hydrolase (FAAH) and monoacylglycerol lipase (MAGL). Thus, the function of ECS might be modulated in a directly, through CB receptor ligands or indirectly by FAAH and MAGL inhibitors. However, the influence of ECS through indirect manner in the context of cognitive processes remains poorly understood.

The aim of the experiments was to evaluate the indirect impact of ECS, using MAGL inhibitor: KML-29 on the different stages of memory (acquisition, consolidation and retrieval), as well as on the memory disturbances typical for schizophrenia in an acute N-methyl-D-aspartate (NMDA) receptor hypofunction animal model of schizophrenia (i.e., injection of NMDA receptor antagonist – MK-801).

We assessed different memory stages in mice using the passive avoidance (PA) test. The deficit in PA performance was expressed as the difference between retention and training latencies and is taken as an index of latency (IL).

An acute administration of KML-29 (20 and or 40 mg/kg) had a positive effect on the memory processes in the PA test in mice. Additionally, the combined administration of PA-ineffective dose of KML 29 (5 mg/kg) attenuated the MK 801-induced cognitive impairment (0.6 mg/kg) in mice in the all stages of memory.

Our results suggest that the indirect regulation of endocannabinoids concentration in the brain through the use of selected inhibitors (e.g., KML-29) may positively affect memory disorders and thus increase the effectiveness of modern pharmacotherapy of schizophrenia.

Funding: NCN: MINIATURA 4 (no.2020/04/X/NZ7/00123); Statutory Funds of the Medical University of Lublin, Poland DS 23/23).

Key words: endocannabinoids, schizophrenia-like cognitive disorders, FAAH and MAGL inhibitor, NMDA-receptor hypofunction, passive avoidance test, mice

P16.6. NMDA ANTAGONIST ENHANCED-HIGH FREQUENCY OSCILLATIONS (130-180Hz) IN THE PIRIFORM CORTEX ARE DRIVEN BY THE OLFACTORY BULB IN FREELY MOVING RATS

Jacek Wróbel[1], Władysław Średniawa[2], Daniel K. Wójcik[1], Mark J. Hunt[1]

[1]Laboratory of Neuroinformatics, Nencki Institute of Experimental Biology, Warsaw, Poland, [2]Laboratory of Neurophysiology of Mind, Nencki Institute of Experimental Biology, Warsaw, Poland

In rodents, NMDAR antagonists, such as ketamine and MK801, enhance high frequency oscillations (HFO) 130-180 Hz measured in local field potentials (LFP) in many brain regions. Our recent studies have shown that the olfactory bulb (OB) is an important generator of this rhythm. The aim of the study was to examine whether systemic injection of MK801 could enhance HFO in the piriform cortex (PC), one of the main targets of the OB, and to what extent the OB drives activity in this area. Simultaneous LFP from the OB and PC were recorded after systemic injection of 0.15 mg/kg MK801 in freely moving male Wistar rats. Thirty minutes after MK801 injection rats received microinfusion (0.5 µg muscimol or saline) to the OB or PC. Tetrodotoxin was also infused to rats with guides in the PC. Systemic injection of MK801 increased the power of HFO in both the OB and the PC which was significantly higher in the OB compared to the PC. Microinfusion of muscimol to the OB produced an immediate reduction in HFO power in both the OB and PC. Changes in HFO power in the OB and PC positively correlated. Further, slow rhythms in the OB drove HFO locally and in the PC. By contrast infusion to the PC produced a gradual reduction in HFO power in the PC without affecting the OB. TTX produced an immediate reduction in HFO power selectively affecting the PC. These findings suggest, that activity of OB efferent pathways play a critical role in the generation of HFO post NMDA receptor antagonists in downstream targets.

This work was supported by the National Science Centre grant: 2021/41/B/NZ4/03882.

Key words: HFO, olfactory bulb, piriform cortex, NMDA antagonist, MK801, muscimol, TTX, rat

P16.7. ROLE OF CXCR4/CXCL12 AND CXCR2/CXCL1 SIGNALLING IN THE CROSSTALK OF GLIAL CELLS IN THE *IN VITRO* RAT MODEL OF NEONATAL ASPHYXIA

Justyna Gargas, Justyna Janowska, Malgorzata Ziemka-Nalecz, Joanna Sypecka
MMRI PAS, Poland

Neonatal hypoxia-ischemia (HI) is still one of the causes of neurological problems among newborns. Unfortunately, the only available therapy is therapeutic hypothermia, used only in cases of moderate or severe HI. There is a need to find new strategies for effective therapy. It seems that studying glial cell interactions, including their secretory profile, is a new, promising target for potential therapies.

Primary mixed glial cultures were established from the brains of Wistar rat pups. Then, after 12 days of mixed culture, individual glial fractions (microglia, oligodendrocyte progenitors/OPCs) were isolated and subjected to the oxygen-glucose deprivation (OGD) procedure, mimicking HI. The cells were cultured as monofractions or their co-cultures. After 24 hours, cells and culture media were collected and analyzed using ultra-sensitive ELISA and Luminex kits.

At 24 hours after OGD the CXCL12 secretion by microglia is nearly 2-fold higher than in control. Another very interesting finding concerned the down-regulated expression of CXCR-4, which is a specific receptor for CXCL12. The immunocytochemical analysis of CXCR4 expression of OPCs showed decreased receptor density on the cell surface after OGD. The analysed OPCs were also less advanced in their differentiation process, as deduced from the cell morphology. We also analyzed the secretion of the CXCL-1, as a chemokine that plays an important role in regulating the immune response by being a chemoattractant for immune cells. ELISA assay indicated that at 24 hours after OGD the CXCL1 secretion by OPCs is over 5-fold higher than in control. In the studies we conducted, we showed no change in the expression of CXCR2, which is the receptor for CXCL1.

Studies conducted are aimed at finding HI biomarkers as targets for potential therapies. The expression and secretion of chemokines is essential for modulating inflammation and, physiological cell function, as well as and influences their migratory potential.

Key words: glial cells, rat model of neonatal asphyxia, chemokines

P16.8. ACTIVATION OF INTRACELLULAR SIGNALING PATHWAYS IN MOTONEURONS BY SYNAPTIC EXCITATION IN PRESYMPTOMATIC SOD1-G93A ALS MOUSE MODEL

Kamil Grycz[1], Francesco Roselli[2], Daniel Zytnicki[3], Marcin Bączyk[1]
[1]Poznań University of Physical Education, Poland, [2]Ulm University, Germany, [3]Université Paris Cité, France

In the presymptomatic stage of amyotrophic lateral sclerosis (ALS) spinal motoneurons (MN) display reduced intrinsic excitability and synaptic excitation levels. The Ca/CaMKIV/CREB signaling pathway was shown to regulate both synaptic scaling of excitatory inputs and intrinsic excitability. Based on this we hypothesize that MN homeostatic breakdown could be related to dysfunction in activity-dependent intracellular pathways.

To stimulate the MN intracellular pathway we used 20-minute of 400Hz unilateral vibration of the Achilles tendon of SOD1 and WT mice. This activates the primary afferents of triceps surae (TS) muscles and provides powerful excitatory drive to TS MNs. The response of CaMKIV/CREB and in parallel ERK/pS6 pathway was probed by quantitative immunofluorescence of selected activity markers in CTB-labeled TS MNs.

We showed that the vibration protocol induced 20% increase of pCaMKIV, pCREB and pS6 proteins in WT but not in SOD1 MNs. This implies that CaMKIV/CREB pathway in SOD1 mice is impaired. We then aimed to rescue this pathway by activating cAMP-mediated signaling with cAMP hydrolysis inhibitor – Rolipram, and by reducing AMPA receptor deactivation with AMPAkine. We found that injection of Rolipram resulted in a 20% increase of pCREB and pS6. On the other hand, AMPAkine showed only a moderate tendency to increase pCREB IF level.

A dysregulation of CaMKIV pathway may have an impact on the disease progression since nuclear calcium and CaMKIV mediate prosurvival transcriptional programs through the activation of CREB. Pharmacological activation of cAMP/CREB signaling may therefore provide a novel therapeutic option for ALS management by restoring the actions of activity-dependent neuroprotective pathways to regain firing homeostasis and reduce disease progression.

Supported by: NCN OPUS 2019/35/B/NZ4/02058.

Key words: ALS, motoneurons, signaling pathway, CREB, CaMKIV, pS6

P16.9. THE IMPACT OF SELECTIVE PHOSPHODIESTERASE-4 INHIBITOR – ROLIPRAM, AND AMPA RECEPTOR AGONIST – AMPAKINE ON SPINAL MOTONEURON ELECTROPHYSIOLOGICAL PROFILE IN SOD1 G93A MOUSE MODEL OF ALS

Piotr Zawistowski[1], Kamil Grycz[1], Francesco Roselli[2], Daniel Zytnicki[3], Marcin Baczyk[1]

[1]Poznań University of Physical Education, Department of Neurobiology, Poznań, Poland, [2]Department of Neurology, Ulm University, Ulm, Germany, [3]Université Paris Cité, Paris, France

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by the progressive loss of upper and lower motoneurons (MN). Previous research show decreased excitability and synaptic excitation of spinal MNs during the presymptomatic phase of the disease. Interestingly, increasing MNs excitation with chemogenetic rescues the deranged synaptic structures and decreases the disease markers.

We tested two approaches to enhance the MN synaptic excitation levels. First, we used Ampakine to increase the AMPA receptor activation. Next, we used Rolipram to inhibit cAMP degradation and activate the cAMP/PKA signalling pathway. *In vivo* intracellular recordings of MNs were made to evaluate the impact of our interventions. Unilateral 400 Hz Achilles tendon vibration was used to evoke compound EPSPs in TS MNs, and the maximal response amplitude was compared pre- and post-drug administration. We also examined the effects on MN passive membrane properties.

Results show no significant difference in max amplitude of induced EPSPs pre- and -post Ampakine administration (11.38±1.03 mV *vs.* 12.82±1.66 mV). However, further analysis showed that when the EPSP response was normalized by cells' input conductance, a strong increase in maximal EPSP amplitude was seen for the highest input conductance cells. Similarly, Rolipram evoked only a modest 9.21±4.54 mV *vs.* 10.20±5.02 mV increase in the EPSP amplitude. However, this increase was not correlated with cells' input conductance. Both interventions did not affect MN passive membrane properties.

Ampakine shows potential for upregulating spinal MN synaptic excitation in ALS, while Rolipram primarily targets intracellular pathways and has a secondary impact on synaptic excitation efficiency.

Supported by NCN OPUS 2019/35/B/NZ4/02058.

Key words: ALS, EPSP, motoneurons, CaMKIV/CREB

P16.10. THE ROLE OF PARKIN PROTEIN IN MAINTAINING CIRCADIAN RHYTHMICITY IN *DROSOPHILA MELANOGASTER*

Kamila Zientara, Milena Damulewicz

Department of Cell Biology and Imaging, Faculty of Biology, Jagiellonian University, Kraków, Poland

Parkinson's disease (PD) is one of the most common age-related neurodegenerative disorders, connected with the loss of dopaminergic neurons in the substantia nigra of the midbrain. Among genes identified as contributing in PD development are *parkin* and *pink,* involved in the regulation of mitochondrial integrity. PINK1 protein activates Parkin, which starts process of ubiquitination and degradation of damaged mitochondria on the pathway called mitophagy. Growing number of evidences show that there is strong connection between the development of neurodegenerative diseases and circadian clock disruption.

Drosophila melanogaster is an important model organism in the study of circadian rhythmicity. Its clock network consists of 150 neurons divided into 7 groups, which makes research simplier. The most important are the sLNv neurons, which express clock neurotransmitter Pigment Dispersing Factor (PDF). They send projections to the dorsal brain where their terminals show daily changes in the complexity. This rhythmicity provides synaptic plasticity and differences in the postsynaptic partners across the day. The aim of this work was to check whether *Drosophila* PD model shows disruption in pacemaker neuronal plasticity.

We used flies with *park* mutation and with *park* silencing specifically in sLNv, respectively. We analyzed locomotor activity and sleep profile to check whether PD model has circadian disruption. Then, we collected heads at selected time points, at the beginning of the day and at the beginning of the night, and using anti-PDF immunostaining we visualized cell bodies and terminals.

Our results showed that indeed, PD model flies showed reduced amount of sleep, which was more fragmented. Moreover, we observed abnormal projections in the dorsal brain and disrupted rhythmicity in branching complexity.

Taking together, our results showed that sleep problems observed in *park* mutants are connected with disruption in clock neurons functioning.

Key words: Parkinson's disease, park mutation, *Drosophila melanogaster*, circadian rhythmicity

P16.11. TRAP-1 MUTANT MICE – A NOVEL MOUSE MODEL OF AUTISM-ASSOCIATED NEURODEVELOPMENTAL DISORDER MANIFEST ALTERATIONS IN SYNAPTIC MITOCHONDRIA NUMBER

Marta Magnowska

University of Warsaw, Poland

Neurons critically depend on mitochondrial function to establish membrane excitability and to execute the complex processes of neurotransmission and plasticity. Recently it was shown, that synapses are the regions of the neuron with the highest energy consumption, thus they have the highest demand for mitochondrial ATP production. Additionally, dysregulated synthesis of mitochondrial proteins may contribute to the pathomechanism of neurodevelopmental disorders.

We created a new mouse model of autism-associated neurodevelopmental disorder, based on the human mutation in *TRAP-1* gene. TRAP-1 mutant mice display behaviors characteristic for ASD such as social behavior deficits. TRAP1 is a mitochondrial chaperone from HSP-90 family engaged in the regulation of mitochondrial stress response. Mitochondrial functions are intrinsically linked to their morphology and membrane ultrastructure. For a detailed analysis of mitochondria morphology and organization in the hippocampi of TRAP1 mutant mice, heterozygous and wild-types, we used Serial Block Face-Scanning Electron Microscopy (SBF-SEM). Mitochondria shape and volume reconstruction was performed in RECONSTRUCT software. We compared the morphology and number of synaptic mitochondria in TRAP-1 mutant, heterozygous and wild-type mice and found significant reduction of the number of mitochondria in mutants as compared to wild-types.

Key words: neuronal mitochondria, ASD, synaptic plasticity

P17.1. WORKING MEMORY CONTENT OUTSIDE THE FOCUS OF ATTENTION: EVIDENCE FROM SINGLE-NEURON RECORDINGS IN HUMANS

Katarzyna Paluch[1], Mikołaj Magnuski[1], Władysław Średniawa[1], Davor Ivanovski[2], Wojciech Fortuna[3], Katarzyna Smarzewska[3], Paweł Tabakow[3], Harish Babu[2], Jan Kamiński[1]

[1]BRAINCITY, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland, [2]SUNY Upstate Medical University, Syracuse, United States, [3]Wroclaw Medical University, Wroclaw, Poland

Working memory (WM) is an ability to hold and manipulate a small amount of information in mind. The prevailing model of WM, supported by multiple animal and human studies, postulates that retention of information is accomplished *via* persistent neuronal spiking. However, in virtually all of these studies WM content was not only remembered but also continuously attended. To unconfound memory and attention recent electrophysiological and fMRI studies used cues to shift attention across different WM items. Interestingly, they observed correct recall of WM items without detectable, accompanying activity during the delay period. A new, activity-salient theory of WM storage was proposed postulating that unattended memoranda are coded without neuronal spiking.

To test this hypothesis we directly measured spiking of single neurons in humans when preferred stimulus was held in memory and within/outside the focus of attention. Such recordings are possible in patients suffering from refractory epilepsy in whom depth electrodes are implanted for seizures monitoring. We used adapted retro-cue task and replicated behavioral results of neuorimiging studies, showing costs (lower recall accuracy) of attention shifts. We replicated results of previous single neuron studies, showing persistent activity for attended items held in WM. Finally, for the first time we recorded neuronal activity when items were held in WM but outside attention focus. Using machine learning (SVM) during delay period we were able to successfully decode attended, but not unattended WM items. Representation of attended WM item was stable in time, decoder trained on first delay generalized to the second one.

Key words: working memory, attention, retro-cue, single neurons

P17.2. THE INFLUENCE OF THE CHOLINERGIC AND RELAXIN-3 SIGNALLING ON THE ACTIVITY OF INTERPEDUNCULAR NUCLEUS NEURONS – A POSSIBLE NEURONAL SUBSTRATE FOR THE FAMILIARITY/NOVELTY PROCESSING

Gabriela Stopka[1], Patryk Sambak[1], Aleksandra Trenk[1], Anna Gugula[1], Andrew Gundlach[2], Mohammad Akhter Hossain[2], Anna Blasiak[1]

[1]Department of Neurophysiology and Chronobiology, Institute of Zoology and Biomedical Research, Jagiellonian University, Poland,
[2]Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

The correct response to novel stimuli is crucial in adapting to changing environment. Recently studies related the crucial role of the interpeduncular nucleus (IPN) along with the medial habenula and the ventral tegmental area in familiarity/novelty signalling. Also, it is known that stress is a main factor that can lead to the development of disorders manifested in incorrect responses to novel stimuli. The highly stress-sensitive brain structure is the nucleus incertus (NI), the main source of neuropeptide relaxin-3 (RLN3) in the brain. In addition, the IPN is densely innervated by NI. However, the pattern of a specific receptor for RLN3 (RXFP3) expression in IPN, and the effect of activation of this receptor and nicotine on IPN neurons activity remain unknown. Therefore, we aimed to verify the impact of nicotine and RXFP3 receptor agonist (A2) on the activity of IPN neurons. Using whole-cell patch-clamp and multi-electrode array *ex vivo* techniques, we noted the sensitivity of IPN neurons on both drugs. We examined the impact of nicotine on the activity of IPN neurons directly innervated by NI neurons by using optogenetics. We observed the single IPN neurons sensitive to nicotine and opto-stimulation of NI fibres in IPN containing brain slices, which can imply a role of the NI-IPN axis in familiarity signalling. Then, using the RNA-scope *in situ* hybridization we showed the co-expression of α5-subunit nicotinic receptor and RXFP3 in specific IPN subnuclei. Moreover, viral-based immunofluorescent staining revealed co-localization of the NI-originating and RLN3 positive fibres in IPN, which indicates the crucial role of RLN3/RXFP3 signalling in NI-IPN axis.

In fine, we suggest that RLN3/RXFP3 signalling and NI-IPN axis can constitute an important part of the neuronal mechanism underlying response to novel stimuli, consequently involving this pathway in stress-related novelty preference disturbances.

Funding: National Science Centre, Poland (UMO-2018/30/E/NZ4/00687).

Key words: nuclues incertus, interpeduncular nucleus, relaxin-3, RXFP3, nicotine, novelty preference

P17.3. INFLUENCE OF PROCAINE INJECTION INTO THE UNILATERAL OLFACTORY BULB ON THE BEHAVIORAL RESPONSE ELICITED BY CONTRALATERAL ELECTRICAL STIMULATION OF THE VENTRAL TEGMENTAL AREA

Grażyna Jerzemowska, Aleksandra Piwka, Jolanta Orzeł-Gryglewska

Department of Animal and Human Physiology, Faculty of Biology, University of Gdansk, Gdansk, Poland

In the present study, we investigated the involvement of temporary inactivation by the injection of procaine as a non-specific blocker of sodium channels (20% (w/v); volume: 0.5 µl; experimental group) into the olfactory bulb (OB) (Artificial Cerebrospinal Fluid injection as a control, ACSF group; volume: 0.5 µl) on the behavioral activity in rats exposed to electrical stimulation of the midbrain ventral tegmental area (VTA). In all of the rats used in this experiment (Wistar, n=5), a latency/stimulation frequency curve-shift paradigm, which assesses the motor and motivational aspects of appetitive behavior, was measured. Contralateral OB-VTA relationships were analyzed in rats, with feeding response, as an appropriate behavioral reaction.

The contralateral procaine injection into the OB on behavioral response during the VTA- stimulation had prolonged latency of response to this stimulation, which was manifested by a significant reaction threshold (+21.64%) ($p<0.01$). However, in each rat, these results varied. In three rats, a significant deterioration of the reaction was observed, which was manifested by an increased reaction threshold (+19.82%, +36.96, and +48.61%) and an extension of the reaction latency, during frequency changes (from 17.71 Hz to 81.38 Hz). Nonetheless, in the two of the five rats, after contralateral procaine injection into the OB, during unilateral VTA-stimulation, no changes occurred in the reaction threshold (+7.81%, -5.58%) (changes at the level ±10%), as well as no changes occurred in the latency reaction at particular frequencies (17.71-81.38 Hz) of stimulation, as compared to the control (ACSF injection into the OB).

The observed effect depends on the places of the injected chemical agent within the OB area.

The research was funded by the Ministry of Education and Science of Poland funding for statutory research and development activities of the Department of Animal and Human Physiology of the University of Gdansk.

Key words: olfactory bulb, ventral tegmental area, procaine

P17.4. SHINING THE LIGHT ON THE DOPAMINERGIC SYSTEM: ELECTROPHYSIOLOGICAL INSIGHTS FROM VTA/SNc

Karolina Nowalińska, Magdalena Walczak, Martyna Marzec, Tomasz Błasiak

Department of Neurophysiology and Chronobiology, Institute of Zoology and Biomedical Research, Faculty of Biology, Jagiellonian University in Kraków, Poland

There exists a neural pathway that suggests light may influence the activity of neurons within ventral tegmental area (VTA) and substantia nigra compact part (SNc) – the primary source of dopamine in the mammalian brain. The involved polysynaptic pathway originates from M4-type retinal ganglion cells that project to the ventral lateral geniculate nucleus/intergeniculate leaflet (vLGN/IGL). From there, the innervation extends to the lateral habenula (LHb), and subsequently from LHb to the VTA/SNc, either directly or through the rostromedial tegmental nucleus.

Given the previously reported effects of light stimuli on LHb neurons activity, we aimed to investigate whether dopaminergic neurons within the VTA/SNc region exhibit responses to light stimuli. To address this question, we conducted *in vivo* electrophysiological recordings of putative dopaminergic neurons in albino rats under urethane anesthesia. During the recordings, pulses of light stimuli were delivered to the animal's eyes. Our study also accounted for spontaneous changes in brain state occurring during urethane anesthesia.

We observed the existence of a subpopulation of neurons within the VTA/SNc that exhibit suppression of electrical activity in response to light stimulation. Furthermore, for a subset of these neurons, the responses to light pulses were dependent on the brain state and/or whether the stimulated eye was ipsilateral or contralateral to the recording site.

These findings warrant further research to explore the following inquiries: Do the light-induced responses of dopaminergic neurons correlate with alterations in dopamine release along the ascending dopaminergic pathways? Could these changes influence motivation levels and motor control in animals? Additionally, within this context, could these findings have implications for an animal's decision-making regarding body orientation and movement direction?

Key words: ventral tegmental area, substantia nigra compact part, light, dopaminergic neurons, *in vivo* electrophysiology

P17.5. LEARNING INFLUENCES THE SYNAPTIC INPUTS AND OUTPUTS OF GABAERGIC INTERNEURONS IN THE BARREL CORTEX OF MICE

Dominik Kanigowski, Joanna Urban-Ciećko

Nencki Institute of Experimental Biology, Polish Academy of Sciences, Laboratory of Electrophysiology, Warsaw, Poland

The neocortex contains three main classes of GABAergic interneurons: somatostatin- (SOM), parvalbumin- (PV), and ionotropic serotonin 5HT3a receptor-expressing cells. The last group is divided into vasoactive intestinal polypeptide-expressing (VIP) and non-VIP-expressing cells. Multiple lines of evidence indicate that GABAergic interneurons are crucial for information processing as well as for memory consolidation and learning. Here, we raised a question of whether a simple model of learning in mice influences the excitatory synaptic input and output of SOM-, PV-, and VIP-interneurons. To address this question we exposed mice to a conditioning paradigm where tactile stimulation of whiskers was paired with electrical tail shocks or to pseudoconditioning where these stimulations were applied randomly. Following the learning procedures, we performed *in vitro* whole-cell patch-clamp recordings in the mice barrel cortex. Electrophysiological experiments revealed that conditioning increases the amplitude as well as the rise time and decay time of spontaneous excitatory postsynaptic currents (sEPSCs) recorded from low-threshold spiking SOM interneurons in layer IV of the cortical representations of stimulated whiskers. Next experiments also showed that pseudoconditioning prolongs the EPSC decay time of PV interneurons. However, no changes were observed in VIP interneurons regarding the parameters of sEPSCs. Moreover, recordings of optogenetically evoked inhibitory postsynaptic currents in excitatory neurons showed elevated inhibition of these cells by SOM and PV interneurons after conditioning. Summarising, our results imply that changes in excitatory drive of GABAergic interneurons are specific to the interneuron classes and the type of learning, whereas the modifications of the GABAergic outputs are more uniform, only differing in terms of the type of learning.

National Science Centre UMO-2015/18/E/NZ4/00721 to J.U.C.

Key words: somatostatin interneurons, parvalbumin interneurons, VIP interneurons, barrel cortex, classical conditioning, *in vitro* electrophysiology

P17.6. THE VISUAL TEMPORAL ORDER THRESHOLD IS POSITIVELY ASSOCIATED WITH THE MULTIVARIATE MULTISCALE ENTROPY OF RESTING-STATE EEG ACTIVITY

Monika Lewandowska[1], Marcin Hajnowski[2], Krzysztof Tołpa[2], Tomasz Piotrowski[3], Joanna Dreszer[1]

[1]Institute of Psychology, Faculty of Philosophy and Social Sciences, Nicolaus Copernicus University in Toruń, Poland, [2]Centre for Modern Interdisciplinary Technologies, Nicolaus Copernicus University in Toruń, Poland, [3]Institute of Engineering and Technology, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Toruń, Poland

Temporal information processing in the milliseconds range is considered essential for cognition whereas the resting-state brain's signal complexity can mirror task-induced activity. The aim of this study was to determine the relationship between the visual temporal order threshold (vTOT), the minimum gap between two successive stimuli required for accurate identification of their before-after relation, and the complexity of resting-state EEG (rsEEG) signal, calculated using the multivariate MultiScale Entropy (mMSE) algorithm. The rsEEG data with eyes closed were acquired in 71 healthy adolescents and young adults (37 women, mean age=17.48±1 year) who underwent the psychophysical measurement of vTOT. The Area Under Curve (AUC) that represents the total complexity, the MaxSlope and the AvgEnt – the metrics of entropy at fine and coarse scales, respectively – were determined for the electrode sets corresponding to the 7 networks extracted by Yeo et al. (2011). We found positive correlations between the vTOT and the AUC for the channels linked to the default mode, ventral attention, limbic, frontoparietal and somatomotor networks. In addition, the greater the MaxSlope values for the ventral attention and limbic networks, the higher the vTOT. The AvgEnt parameters for the default mode, ventral attention and somatomotor networks were positively associated with the vTOT, as well. Our outcomes indicate that the temporal order perception is reflected in the total, fine and coarse entropies of rsEEG signal. The vTOT, associated with fine and coarse rsEEG complexity, suggests that both short- and long-distant functional connections in the brain are related to the temporal information processing in the millisecond range.

Reference: Yeo BTT, Krienen FM, et al. (2011) The organization of the human cerebral cortex estimated by intrinsic functional connectivity. Journal of Neurophysiology 106(3): 1125–1165.

Supported by the National Science Centre grant no. 2015/18/E/HS6/00399.

Key words: visual temporal order threshold, resting state, EEG, multivariate MultiScale Entropy

P17.7. THE PHYSIOLOGICAL AND MORPHOLOGICAL EFFECTS OF PERINATAL EXPOSURE TO FLUOXETINE IN MOUSE DORSAL RAPHE NUCLEUS SEROTONERGIC NEURONS

Agnieszka Kania[1], Bartosz Bobula[1], Nikola Multan[2], Michał Kiełbiński[1], Marcin Siwiec[1], Grzegorz Hess[1]

[1]Maj Institute of Pharmacology, Polish Academy of Sciences, Cracow, Poland, [2]Jagiellonian University in Cracow, Poland

Selective serotonin reuptake inhibitors, commonly known as SSRI drugs, remain widely used to treat major depressive disorder (MDD), which is also prevalent among pregnant women. Like depression itself, treatment with SSRIs might have an unknown effect when it comes to child's development. Our main interest was to assess safety of one of the most commonly used SSRI, fluoxetine, in the brain serotonergic system. We aimed to compare inhibitory synaptic transmission in the DR as well as to evaluate the effects of the 5-HT7 receptor activation in the DR serotonergic neurons after treatment. We tested whether fluoxetine exposure throughout gestation and lactation has any profound effects on the function and morphology of the DR neurons in the mouse offspring as they reach adulthood.

C57BL/6 dams were provided fluoxetine water solution, or pure water, throughout the entire pregnancy and until weaning. As the male and female offspring reached 8 to 12 weeks, their brains were dissected, cut, and slices were used to perform whole cell patch clamp electrophysiological recordings. 5-HT7 receptor agonist LP-211 was administered *via* the incubation medium. Each examined DR cell was filled with biocytin and immunostained for tryptophan hydroxylase (marker of serotonergic neurons). Scholl analysis was performed to assess cell morphology. The results indicate no significant change in basal sIPSC frequency, and the frequency after 5-HT7 agonist administration in both male and female offspring. However, it was found that the mean amplitude of sIPSCs was decreased after 5-HT7 activation in male mice treated with fluoxetine.

Key words: depression, fluoxetine, patch clamp, 5-HT7R, nervous system development

P17.8. CLONIDINE INHIBITS INTERICTAL EPILEPTIFORM EVENTS IN PREFRONTAL CORTEX PYRAMIDAL NEURONS

Weronika Kołba, Bartłomiej Szulczyk

Department of Pharmacodynamics, The Medical University of Warsaw, Warsaw, Poland

Clonidine is an alpha-2 adrenergic receptor agonist used to treat high blood pressure and attention deficit hyperactivity disorder (ADHD). The aim of this study was to assess the influence of this drug on short-lasting (interictal) epileptiform discharges.

Interictal epileptiform events were recorded from prefrontal cortex pyramidal neurons with the use of patch-clamp technique. Slices were obtained from young rats. Zero magnesium, elevated potassium extracellular solution was used to evoke interictal discharges. These events were spontaneous depolarizations which evoked action potentials.

We found that clonidine (100 μM) potently inhibited the frequency of interictal epileptiform discharges. Moreover, we found that this drug hyperpolarized the membrane potential recorded in zero magnesium, elevated potassium extracellular solution. Further experiments will be conducted to assess which ionic channels are involved in the effect of clonidine on interictal discharges.

Interictal events may occur in EEG in patients with ADHD and may contribute to symptoms of this disease. Therefore, inhibition of interictal discharges by clonidine may partially explain beneficial effects of this drug in patients with ADHD.

This study was sponsored by the Medical University of Warsaw student mini-grant no: FW3/4/F/MG/N/22.

Key words: prefrontal cortex, patch-clamp, clonidine, interictal discharges

P17.9. PROTEIN S-PALMITOYLATION IN HIPPOCAMPAL SYNAPTIC PLASTICITY

Tomasz Wójtowicz[1], Agata Pytyś[1], Anna Buszka[1], Matylda Roszkowska[2], Eli Kerstein[3], Rhonda Dzakpasu[3], Katarzyna Kalita-Bykowska[2], Jakub Włodarczyk[1]

[1]Nencki Institute of Experimental Biology, Laboratory of Cell Biophysics, Warsaw, Poland, [2]Nencki Institute of Experimental Biology, Laboratory of Neurobiology, Warsaw, Poland, [3]Georgetown University, Department of Physics, Washing DC, United States

Understanding of the mechanisms of synaptic plasticity and neuronal network code lies at the center of contemporary neurobiology. Recently, post-translational protein modification S-palmitoylation which involves covalent addition of palmitic acid has been proposed to play a crucial role in synaptic plasticity and learning. However, it is largely unknown how this modification affects synaptic function. To determine to what extent S-PALM is required for neuronal plasticity, we have recorded neuronal spiking in 14-day-old primary neurons cultured on multi-electrode arrays. We have found that a long-term increase in neuronal spiking after associative stimulation of network nodes was abolished in cultures treated with depalmitoylating agent NtBuHA. Next, we recorded extracellular field potentials in rat hippocampal slices incubated with NtBuHA. We have found that in the CA1 region, pharmacological treatment impaired both short and long-term synaptic plasticity in both stratum oriens and stratum radiatum. Next, we have studied S-PALM profiles following the induction of chemical long-term potentiation (cLTP) with acyl-biotinyl exchange assay (ABE) method. We have identified synaptic proteins (i.e., PSD-95, Gα13, synaptophysin) which were specifically up- or down-regulated following cLTP and those for which S-PALM state remained (i.e., SNAP25, VAMP2). Altogether, our findings suggest that protein S-PALM is crucial for synaptic plasticity in hippocampal excitatory synapses and neuronal spiking following enhanced neuronal network activity. Changes to protein S-PALM levels can occur rapidly (in a matter of minutes) and are protein-specific rather than proteome-wide. We hope that these findings will shed more light on S-PALM's role in healthy brain function and contribute to the understanding of diseases of the nervous system that negatively affect cognitive functioning in people.

Research funded by the Polish National Science Center (grant 2019/34/E/NZ4/00387).

Key words: neuronal plasticity, protein S-palmitoylation, postranslational modifications, learning and memory

P17.10. THE BOOST IN INITIAL FORCE DEVELOPED BY FAST MOTOR UNITS STIMULATED WITH PULSES AT VARIABLE INTERVALS IN THE RAT MEDIAL GASTROCNEMIUS MUSCLE

Katarzyna Kryściak, Hanna Drzymała-Celichowska, Jan Celichowski

Poznan University of Physical Education, Department of Neurobiology, Poznan, Poland

The initial development of force during unfused tetanic contraction of fast motor units is characterized by two phenomena: extra force production (boost) followed by force decrease (sag). So far, the boost and sag have been studied in unfused tetanic contractions evoked at constant stimulation frequency. However, during voluntary movements, the muscle fibers of the motor units work in unfused tetanic contractions evoked by motoneuronal discharges at variable intervals. Therefore, the aim of the study was to verify whether the two phenomena occur in unfused tetanic contractions with variable stimulation frequency and whether, and to what extent, they depend on the level of this variability, stimulation history and type of motor unit. Additionally, we have tested the influence of the initial doublet of stimuli (frequent in voluntary activity of motoneurons) on the boost and sag. To record activity of single motor unit axon isolated from the ventral root was stimulated. The stimulation protocol allowed to determine the basic contractile properties for motor units: single twitch, 500 ms unfused tetanic contraction at constant stimulation frequency (35 Hz) and then at randomly varying interpulse intervals (three variation ranges of ± 2, ± 5 and ± 7 ms), repeated three times once per second. We have used and analyzed 3 different patterns with randomly varying intervals. The experiments revealed that: regardless of the applied pattern, unfused tetanic contractions at variable interpulse intervals presented boost and sag; both phenomena occurred in FF and FR units, although they had different characteristics; regardless of the stimulation pattern and type of motor unit, the first out of three contractions was characterized by the most visible boost and sag; the same results were obtained for unfused contractions beginning with the doublet of stimuli.

Key words: boost, sag, motor unit, rat, medial gastrocnemius

P17.11. THE EFFECT OF TENT2 CYTOPLASMIC POLY(A) POLYMERASE KNOCKOUT ON ELECTROPHYSIOLOGICAL PROPERTIES OF NEURONS

Patrycja Wardaszka[1], Tomasz Wojtowicz[2], Magdalena Dziembowska[1]

[1]Centre of New Technologies, University of Warsaw, Poland, [2]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Poland

TENT2 is a cytoplasmic poly(A) polymerase. It catalyzes the process of polyadenylation, an elongation of poly(A) tails at the 3' ends of mRNA. This process is considered to increase mRNA stability. Polyadenylation occurs mainly in the nucleus, before the transport to the cytoplasm. However, it can also occur in the cytoplasm of neurons. TENT2 is expressed in several brain structures including hippocampus of a mouse brain. Nevertheless, whether this enzyme's activity may affect any neuronal function remains unknown. Here we have analyzed passive membrane properties and membrane excitability of CA1 pyramidal neurons in acute hippocampal slices of wild-type and an in-house generated Tent2 KO mice. We found that Tent2 KO neurons exhibited increased rheobase, the minimal electrical current that is necessary to elicit an action potential and the frequency of evoked action potentials compared to wild-type neurons. In addition, the voltage-gated sodium channels (NaV) currents were measured. In Tent2 KO neurons the maximal value of NaV currents were reached at lower voltage. Next, we have performed recordings of evoked field potentials in Sch-CA1 projection in acute hippocampal slices. In agreement with patch-clamp results, Tent2 KO mice exhibited enlarged amplitude of population spike signal while excitatory postsynaptic potentials were unafected. In conclusion, lack of TENT2 resulted in increased responsiveness of neuronal membrane to excitation, thus making CA1 pyramidal neurons become more excitable. Cytoplasmic polyadenylation mediated by TENT2 may play a regulatory mechanism for local translation in neurons and affect the function of CA1 hippocampal neurons.

Supported by GRIEG 2019/34/H/NZ3/00733 (Norway Grants).

Key words: TENT2, cytoplasmic polyadenylation

P17.12. ELECTROPHYSIOLOGICAL TYPE-SPECIFIC MODULATION OF VIP-EXPRESSING INTERNEURONS THROUGH GABABRS IN THE PRIMARY SOMATOSENSORY CORTEX

Karolina Bogaj, Joanna Urban-Ciećko

Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Vasoactive intestinal polypeptide-expressing interneurons (VIP-INs) belong to the 5-hydroxytryptamine 3a (5HT3a) receptor-expressing neuron class, which contribute to one of three major populations of GABAergic (Gamma-aminobutyric acid) cortical neurons, next to parvalbumin (PV)- and somatostatin (SST)-expressing interneurons. Primary function of VIP-INs within the neuronal circuitry is to release excitatory cells from the inhibition, provided predominantly by SST-INs. Despite our vast knowledge of VIP-IN function their electrophysiological properties still remain under intense investigations.

Here we characterized the influence of GABAbR modulation on VIP-IN activity in layer 2/3 of the somatosensory cortex in mice. GABAbRs are well-established modulators of slow and prolonged inhibitory action, present on both synaptic sites. We performed *in vitro* whole-cell patch-clamp recordings in acute brain slices. Using principal component analysis with k-means unsupervised clustering and GABAbR pharmacological agents, we found that layer 2/3 VIP-INs can be clustered into 3 main types according to their electrophysiological properties. Analysis of intrinsic excitability and sEPSCs (spontaneous excitatory postsynaptic currents) showed that types 1 and 2 are modulated through GABAbRs whereas type 3 is insensitive to the modulation *via* these receptors.

P17.13. CHANGES IN ELECTROPHYSIOLOGICAL PROPERTIES OF SPINAL MOTONEURONS IN RESPONSE TO ALTERED LEVELS OF BDNF IN BLOOD SERUM AND HINDLIMB MUSCLES. STUDIES ON WILD-TYPE AND BDNF KNOCKOUT RATS

Norbert Grzelak[1], Piotr Krutki[1], Marcin Bączyk[1], Dominik Kaczmarek[2], Włodzimierz Mrówczyński[1]

[1]AWF Poznań, Department of Neurobiology, Poznań, Poland, [2]AWF Poznań, Department of Physiology and Biochemistry, Poznań, Poland

In the present study, we would like to determine whether altering the concentration of brain-derived neurotrophic factor (BDNF) in serum and/or skeletal muscle modifies the electrophysiological properties of spinal motoneurones (MNs). Wild-type and heterozygous *BDNF* knockout (HET, SD-BDNF) rats were used in this study. Animals were divided into four groups: control, knockout, control trained and knockout trained. The latter two groups were subjected to moderate-intensity endurance training to increase BDNF levels in serum and/or hind limb muscles. Passive, threshold and rhythmic properties of MNs as well as inputs from peripheral afferents were studied in each studied group of rats. In addition, BDNF and other neurotrophins including glial cell-derived neurotrophic factor (GDNF), neurotrophin-3 (NT-3), nerve growth factor (NGF), and neurotrophin-4 (NT-4) were measured in serum and in selected hind limb muscles such as tibialis anterior (TA), medial gastrocnemius (MG), and soleus (Sol). Moreover, levels of BDNF-specific receptors – TrkB, as well as indicators of muscle contractile activity: interleukin-15 (IL-15) and myoglobin (MYO/MB) were also measured in these muscles.

In BDNF knockout rats, reduced serum levels of all NFs tested were found, while its remained unchanged in hind limb muscles. Reduced blood levels of NFs did not affect the electrophysiological properties of MNs. Endurance training did not change the serum levels of any of the NFs tested, but significantly increased the levels of BDNF and GDNF in fast muscles – TA and MG in both groups of trained rats with different genotypes. In addition, the trained rats showed reduced excitability in fast-type MNs. However, there were no changes in the parameters of postsynaptic potentials recorded from the motoneurones of all groups tested.

These results suggest that BDNF and GDNF derived from muscles may be key factors in altering the excitability of spinal MNs in response to enhanced physical activity.

1. Norbert Grzelak, Piotr Krutki, Marcin Bączyk, Dominik Kaczmarek, Włodzimierz Mrówczyński.

Influence of altered serum and muscle concentrations of BDNF on electrophysiological properties of spinal motoneurons in wild-type and BDNF-knockout rats. Sci Rep. 2023 Mar 20;13(1): 4571. doi: 10.1038/s41598-023-31703-8.

Key words: spinal motoneurons, BDNF, neurotrophins, endurance training

P17.14. SHORT-LASTING ANOSMIA IN RATS AFTER GADOLINIUM INFUSION TO THE NARES: PRELIMINARY FINDINGS

Wiktoria Podolecka, Mark Hunt
Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Anosmia is an olfactory dysfunction which worsens the sense of smell. It is present in many diseases, such as COVID-19, Parkinson's disease or Alzheimer's disease. Most rat models of anosmia are either unreliable or associated with high levels of mortality. Here, we describe a protocol for producing short-lasting, reversible anosmia in adult rats. In this study, either gadolinium (50 µl, 60 mg/ml) or saline (50 µl) was infused bilaterally to the nares. Olfactory function was assessed using a hidden cookie test. Nasal respiration in the olfactory bulb (OB), was measured as a marker of sensory neuron input from the nasal epithelium. Respiratory rhythm (1-10 Hz) was recorded after every conducted hidden cookie test. Finally, histological sections of the nasal epithelium were collected to directly assess damage to the nasal epithelium. We found gadolinium infusion was associated with a marked increase in time to find the hidden cookie compared to control rats, an effect that lasted at least 10 days. Further, gadolinium infused rats had a significant reduction in the respiration rhythm which followed a similar time course to disturbances in the hidden cookie test. Histological analyses revealed damage to the epithelium which was not present in control rats. Together these findings demonstrate that gadolinium infusion to the nares of rats can be used as a safe alternative model to produce anosmia. Our findings suggest that gadolinium produces its effects by reducing excitatory drive of olfactory sensory neurons to the OB.

The authors wish to thank NCN (grant 2021/41/B/NZ4/03882) for funding this project.

Key words: anosmia, respiratory rhythm, gadolinium, hematoxylin and eosine, olfactory bulb, hidden cookie test

P17.15. THE POSSIBLE ROLE OF NGF AND RELAXIN-3 MODULATION OF INTERPEDUNCULAR NUCLEUS IN THE CONTROL OF ANXIETY AND STRESS RELATED BEHAVIOURS

Sylwia Drabik, Aleksandra Trenk, Anna Guguła, Patryk Sambak, Angelika Kaleta, Gabriela Stopka, Anna Błasiak
Department of Neurophysiology and Chronobiology, Institute of Zoology and Biomedical Research, Jagiellonian University, Krakow, Poland

Interpeduncular nucleus (IPN) is a highly complex and evolutionary-conserved, midbrain structure, anatomically divided into seven subnuclei, which neuronal populations express different chemical markers. IPN is densely innervated by medial habenula (MHb) originating, cholinergic fibers which are known to mediate the aversive effects of nicotine and its withdrawal, fear and anxiety and novelty preference. Another important source of IPN innervation comes from nucleus incertus (NI) – a highly stress-sensitive structure involved in the control of anxiety, arousal and stress responses, and the source of relaxin-3 (RLN3) neuropeptide, the highly specific ligand for relaxin family peptide receptor 3 (RXFP3). Interestingly, IPN is characterized by a high level of expression of the nerve-growth factor (NGF) receptor TrkA, and NGF was shown to control stress- and anxiety-related behaviors. Taken together these data we hypothesise that IPN-NI axis is involved in stress response control and remains under the modulatory influence of NGF.

Multiplex *in situ* hybridization allowed us to characterise the distribution of mRNA for TrkA, and its co-expression with RXFP3 as well as with vGAT1 and GABA- neurons marker). Multielectrode array recordings revealed both excitatory and inhibitory effects of NGF administration on IPN neurons. Moreover, during whole-cell patch clamp recordings we observed NGF evoked inward whole-cell current in IPN cells. Finally, viral based neural tract-tracing of NI neurons innervating IPN shown a distinct innervation pattern in septal area and ventral hippocampus.

Obtained results proved GABAergic nature of TrkA/RXFP3 co-expressing IPN neurons. NGF administrations confirmed its ability to modulate activity of IPN neurons. Moreover, tract-tracing results suggest that NI-IPN axis is involved in stress response.

Key words: interpeduncular nucleus, nucleus incertus, nerve growth factor, relaxin-3, anxiety

P18.1. UNDERSTANDING FUNCTIONAL BRAIN REORGANISATION FOR NATURALISTIC PIANO PLAYING IN NOVICE PIANISTS

Alicja Olszewska[1], Maciej Gaca[1], Dawid Droździel[1], Agnieszka Widlarz[2], Aleksandra Herman[1], Artur Marchewka[1]

[1]Nencki Institute of Experimental Biology, Laboratory of Brain Imaging, Warsaw, Poland, [2]The Chopin University of Music, Department of Choir Conducting and Singing, Music Education and Rhythmics, Warsaw, Poland

Learning to play the piano is a unique complex task, integrating multiple sensory modalities and higher-order cognitive functions. Longitudinal neuroimaging studies on adult novice musicians show training-related functional changes in music perception tasks. The reorganisation of brain activity while actually playing an instrument was studied only on a very short time-frame of a single fMRI session, and longer interventions have not yet been performed. Thus, our aim was to investigate the dynamic complexity of functional brain reorganisation while playing the piano within the first half year of musical training.

We scanned twenty-four novice keyboard learners (female, 18-23yo) using fMRI while they played increasingly complex musical pieces after 1, 6, 13 and 26 weeks of training.

Playing music evoked responses bilaterally in the auditory, inferior frontal and supplementary motor areas, and the left sensorimotor cortex. The effect of training over time, however, invoked widespread changes encompassing the right sensorimotor cortex, cerebellum, superior parietal cortex, anterior insula and hippocampus, among others. As the training progressed, the activation of these regions decreased while playing music. *Post-hoc* analysis revealed region-specific time-courses for independent auditory and motor regions of interest.

These results suggest that while the primary sensory, motor and frontal regions are associated with playing music, the training decreases the involvement of higher-order cognitive control and integrative regions, and basal ganglia. Moreover, training might affect distinct brain regions in different ways, providing evidence in favour of the dynamic nature of brain plasticity.

Key words: motor learning, music training, neuromusicology, experience-dependent neuroplasticity, functional neuroplasticity

P18.2. PRESERVED SELECTIVITY IN OCCIPITOTEMPORAL BUT NOT TEMPOROPARIETAL CORTICES IN CHILDREN WITH READING AND SPELLING DEFICITS

Agnieszka Dębska, Marta Wójcik, Katarzyna Jednoróg

Nencki Institute of Experimental Biology, Poland

Fluent reading and spelling requires effective orthographic and phonological representations (i.e., knowledge how to spell and pronounce words). In developmental dyslexia deficits in both areas are often reported. We designed an fMRI study in the Rapid Adaptation Paradigm to examining neural selectivity patterns for orthographic and phonological processing in children with differential reading and spelling deficits. Polish children (9.32-13.18 y.o.) were selected based on various literacy skills deficits: children with dyslexia (n=34), typical readers and spellers (n=43), isolated poor readers (n=14), isolated poor spellers (n=19), poor readers and spellers (n=26). In the scanner we repeatedly presented words that shared phonology but differ in orthography (homophones, e.g., kret-kred), shared both (kret-kret) or differed in both (kret-noga).

The results of the fMRI-RA analyis showed a disruptive selectivity pattern in the phonological brain region (left temporoparietal) in all children with literacy deficits compared to typical readers and spellers but preserved selectivity in an orthographic region (left ventral occipitotemporal).

Key words: fMRI-RA, reading, spelling, VOT, dyslexia

P18.3. INVOLVEMENT ON ANTARIOR CINGULATE CORTEX IN SOCIAL BUFFERING DURING FEAR MEMORY EXTINCTION

Tomasz Górkiewicz, Konrad Danielewski, Ksenia Meyza, Ewelina Knapska

Nencki Institute of Experimental Biology, Poland

It has been shown in many social species that when conspecific animals are together, they are less sensitive to stress and recover faster from aversive experiences. This phenomenon is termed social buffering. Social support during the exposure-based psychotherapy has been suggested to have an important influence on the course of exposure treatment, however some clinical trials show that individual therapy may be more effec-

tive than group therapy. The mechanisms of social influence on fear extinction remain unknown. To study neuronal correlates of social buffering in fear extinction, we have developed a rat model. In our model rats showed significant lowering of fear response during fear extinction when exposed to fear-associated stimuli with a companion. However, the effect was transient and disappeared when rats were tested individually on the next day. Next, we moved to investigating the neuronal mechanisms of social buffering. First, using c-Fos protein as a marker of neuronal activation, we measured activation of several brain structures after testing animals together or alone. We have found differences in two regions of the prefrontal cortex: anterior cingulate cortex (ACC) and prelimbic cortex. Then, we chemogenetically blocked the ACC or input from the ACC to the central nucleus of the amygdala (CeA). We found that the ACC-CeA projection is causally involved in social buffering effect. This manipulation diminished social buffering.

Key words: social buffering, anterior cingulate cortex, fear extinction

P18.4. INPUT SPECIFICITY OF NMDA-DEPENDENT GABAERGIC PLASTICITY IN THE HIPPOCAMPUS

Grzegorz Wiera, Jadwiga Jabłońska, Jerzy Mozrzymas
Wroclaw Medical University, Poland

Sensory experience and learning modify brain circuits primarily by the long-lasting plasticity of excitatory (E) and inhibitory (I) synapses. Numerous stimulation patterns that induce excitatory plasticity, also concurrently elicit long-term potentiation (iLTP) or depression (iLTD) at inhibitory GABAergic synapses. However, the rules for the interdependency of excitatory and GABAergic plasticity remain unclear. To describe them, we simultaneously recorded IPSCs and EPSCs in pyramidal cells (PCs) of hippocampal CA1, stimulating parvalbumin (PV) or somatostatin (SST) positive interneurons (INs) using optogenetics and Schaffer collaterals using a bipolar electrode. Plasticity was induced by NMDA application.

Our experiments have shown that optogenetic stimulation of PV and SST INs in the hippocampal CA1 activated two different inhibitory inputs to PCs with distinct IPSC kinetics and short-term plasticity. Interestingly, after NMDA infusion for 2'30'' excitatory CA3→CA1 synapses expressed LTD (average EPSC before: 155.0 ± 20.4 pA, after: 110 ± 16 pA n=11, p=0.031, paired t test), while inhibitory SST→PC developed stable iLTP (average IPSC before: 64.3 ± 8.8 pA, after: 75.4 ± 7.2 pA, n=6, p=0.012) and PV→PC synapses were not plastic (before: 107 ± 23 pA, after: 113 ± 27 pA, n=12, p=0.47). Next, we checked the interdependence of E and I plasticity using different inhibitors of matrix metalloproteinases. Our data indicated that heterosynaptic NMDA-dependent iLTP at inhibitory synapses is also expressed when excitatory plasticity is abolished by MMP-9 inhibitor. Together, these findings demonstrate that: the sign of inhibitory plasticity depends on the type of presynaptic interneuron, thus the GABAergic plasticity is input specific; the interdependence of E and I plasticity can be uncoupled pharmacologically. Presented results significantly expand our knowledge of the local interplay between excitatory and inhibitory synapses.

NCN grant 2021/43/B/NZ4/01675.

Key words: synaptic plasticity, inhibitory synapses, GABA

P19.1. THE CENTRAL ROLE OF DOPAMINE IN LEARNING AND MOTIVATION – A THEORETICAL REVIEW

Olgierd Borowiecki
Nicolaus Copernicus University in Toruń, Poland

In this theoretical work, the association between memory systems and dopamine is reviewed. Multidisciplinary research on memory shows a division between hippocampal-dependent and hippocampal-independent memory systems known as the dichotomy between declarative and procedural, goal-oriented and habitual, or Model-Based and Model-Free memory systems. Recently, the division has been linked to the computations done by place cells in the hippocampus and landmark cells in the dorsolateral striatum (Geerts et al., 2020). Complementary, dopamine is linked to encoding the information in both systems (Haber, 2016; Lisman, Grace, 2005), as well as mediating motivation in the hippocampal-independent system. This work highlights the neurocircuitry of hippocampal-dependent and hippocampal-independent systems together with research specifying the role that dopamine plays in these systems.

Geerts, J. P., Chersi, F., Stachenfeld, K. L., Burgess, N. (2020). A general model of hippocampal and dorsal striatal learning and decision making. *Proceedings of the National Academy of Sciences*, *117*(49), 31427–31437. Haber, S. N. (2016). Corticostriatal circuitry. *Dialogues in*

Clinical Neuroscience, *18*(1), 7–21. Lisman, J. E., Grace, A. A. (2005). The Hippocampal-VTA Loop: Controlling the Entry of Information into Long-Term Memory. *Neuron*, *46*(5), 703–713.

Key words: memory, learning, dopamine, hippocampus, striatum

P20.1. SUMO-SPECIFIC PROTEASE SENP3 INTERACTS WITH TAU UNDER LONG-TERM MITOCHONDRIAL STRESS

Lukasz Samluk, Piotr Ostapczuk, Magdalena Dziembowska
Centre of New Technologies, University of Warsaw, Warsaw, Poland

Apart from their main task, cellular energy production, mitochondria influence many aspects of cell biology as they are important signaling organelles. Mitochondrial dysfunction can cause some pathological conditions, such as neurodegenerative diseases. Long-term mitochondrial stress has been shown to trigger early steps in the formation of Tau protein aggregates characteristic of Alzheimer's disease, but also to trigger responses that counteract aggregation on a larger scale. In the present study, we analyzed the interactome of Tau under mitochondrial stress conditions using a co-immunoprecipitation approach followed by mass spectrometry analysis. Long-term mitochondrial stress was modeled by the knockout of the accessory subunit of mitochondrial complex I, NDUFA11, in HEK293T cells transfected with Tau-encoding plasmids. We demonstrated an increase in the interaction of Tau with SENP3, a SUMO-specific protease, in NDUFA11-deficient cells. The interaction between Tau and SENP3 was confirmed by Western blotting and confocal microscopy using proximity ligation assay. The cellular fractionation showed that SENP3 was mainly localized in the nucleus, but we also found a small fraction of SENP3 in the cytoplasm, where it interacted with Tau under mitochondrial stress. Reducing oxidative stress with N-acetyl-L-cysteine, a well-known ROS scavenger, did not alter the interaction between Tau and SENP3, suggesting that reactive oxygen species are not involved in this process. Downregulation of *SENP3* mediated by siRNA resulted in a significant decrease in the interaction between Tau and SENP3. The decrease in Tau-SENP3 interaction led to the increased formation of Tau aggregates observed under the confocal microscope in NDUFA11 KO cells but not in HEK293 wild-type cells. Therefore, we consider the enhanced Tau-SENP3 interaction to be a protective response that counteracts Tau protein aggregation on a bigger scale under long-term mitochondrial stress.

Key words: mitochondrial stress, neurodegeneration, Tau protein

P20.2. LONG-TERM MITOCHONDRIAL STRESS INDUCES EARLY STEPS OF Tau AGGREGATION AND TRIGGERS RESPONSES COUNTERACTING Tau AGGREGATION ON A BIGGER SCALE

Piotr Ostapczuk, Magdalena Dziembowska, Łukasz Samluk
Centre of New Technologies, University of Warsaw, Warsaw, Poland

Mitochondria are nowadays recognized as very important signaling organelles. Moreover, defective mitochondria are increasingly associated with the development of neurodegenerative diseases, such as Alzheimer's disease, in which Tau protein aggregates are observed in patients' brains. In the present study, we report that under long-term mitochondrial stress (LMS) Tau undergoes enhanced dimerization, which is the first step of protein aggregation. LMS was induced by prolonged rotenone treatment of HEK293T or SH-SY5Y cells and by NDUFA11 knockout in HEK293T cells. We observed a significant increase in reactive oxygen species (ROS) levels in both cell lines under applied mitochondrial stress conditions. Oxidative stress and Tau dimerization in HEK293T were significantly reduced by cells treatment with NacetylLcysteine, a well-known ROS scavenger which indicated that early steps of Tau protein aggregation may be triggered by oxidative imbalance. We found that in cells upon LMS, phosphorylation of S6K1 protein, which is the mTOR pathway component, was increased, like in brains of Alzheimer's disease patients. In order to check if increased S6K1 phosphorylation was involved in Tau protein aggregation we treated HEK239T NDUFA11 knockout cells with the mTOR and S6K1 inhibitor, which caused the elevation of Tau aggregation. In contrast, stable overactivation of the mTOR pathway caused a further increase of S6K1 phosphorylation and reduced Tau oligomerization. We also analyzed the interactome of endogenous Tau in SH-SY5Y cells in control conditions and under mitochondrial stress conditions using a co-immunoprecipitation approach followed by mass spectrometry

analysis. We revealed increased interaction of Tau and a heat shock protein – HSP90B1. The inhibition of the activity of chaperons from the HSP90 family or specific HSP90B1 downregulation caused the increase in Tau aggregation, suggesting that they are counteracting Tau protein aggregation on a bigger scale.

Key words: Tau protein, Alzheimer's disease, neurodegeneration, mitochondrial stress, mTOR pathway

P20.3. DEPLETION OF NEURODEGENERATION-ASSOCIATED PROTEIN TDP-43 PERTURBS CELLULAR ENERGY METABOLISM IN MOTOR NEURONS

Ismail Gbadamosi, Ali Jawaid

Laboratory for Translational Research in Neuropsychiatric Disorders, BRAINCITY: Center of Excellence for Neural Plasticity and Brain Disorders, Nencki Institute of Experimental Biology, Warsaw, Poland

Amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) are two incurable neurodegenerative disorders (NDDs) with considerable clinical and molecular overlaps. Cytoplasmic mislocalization and aggregation of protein TDP-43 in neurons and glia is the molecular hallmark of a majority of ALS and FTLD cases. Clinically, metabolic conditions that are conventionally considered unfavourable, such as type 2 diabetes mellitus and dyslipidaemia, are associated with better prognosis in ALS and FTLD. To ascertain whether changes in metabolism are critically linked to neurodegeneration in these TDP-43 proteinopathies, we depleted TDP-43 *via* RNA interference in NSC34 mouse motor neurons followed by a comprehensive cellular metabolic profiling. Transcriptomic analyses revealed increased expression of genes related to glucose transport, glycolysis, pyruvate metabolism and AMPK signalling following TDP-43 depletion. Functional metabolic assays confirmed that TDP-43 knockdown increased glucose uptake and glycolysis, as well as oxidative phosphorylation in NSC34 cells resulting in the exacerbated generation of reactive species. An overall increase in glycolytic flux and oxygen consumption upon TDP-43 knockdown was further confirmed by metabolic flux analysis. Finally, we showed that defects in cellular energy sensing are likely responsible for these metabolic changes as indicated by the dysregulated activity of the cellular energy sensor, AMPK. Taken together, these results reveal that TDP-43 loss-of-function, a prodromal event in TDP-43-associated NDDs, is associated with a constellation of cellular metabolic perturbations suggestive of hypermetabolism and impaired energy sensing. Characterization of metabolic changes in NSC34 cells after TDP-43 aggregation followed by *in vivo*/*ex vivo* validations are the subjects of our ongoing investigations.

Key words: ALS, motor neuron, TDP-43, energy metabolism, AMPK

P20.4. LIPIDS MODULATE MICROGLIAL PHAGOCYTOSIS OF AMYLOID BET

Izabela Lepiarz-Raba, Taufik Hidayat, Sandra Binias, Bartłmiej Gielniewski, Ali Jawaid

Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Alzheimer's disease (AD), the most common cause of dementia, is characterized by pathological deposition of amyloid-β (Aβ) in the brain. Extracellular accumulation of Aβ involves an imbalance between the level of Aβ production and clearance. Aβ clearance is primarily the function of microglia, the brain-resident immune cells that are increasingly implicated in the pathogenesis and pathophysiology of neurodegenerative disorders. Microglia are highly sensitive to environmental stimuli and respond to homeostatic changes in the brain and the periphery by altering their phagocytic properties and inflammatory outputs. These functional adaptations in microglia are closely linked to changes in their metabolism. This provides a unique opportunity to harness beneficial properties of the microglia *via* targeting their metabolism.

Human microglia-like (HMC3) cells were incubated with lipids and lipoproteins or exposed to lipid starvation and serum starvation. Aβ (1-42) uptake and degradation was assessed using ELISA. Unbiased bulk RNA sequencing was employed to determine molecular cascades responsible for observed effect.

Supplementation of HMC3 microglia with lipids, as well as lipoproteins, impaired Aβ uptake. On the contrary, lipid starvation enhanced microglial uptake of Aβ and this effect was blocked by lipid concentrate. Moreover, Aβ internalized by microglia upon lipid starvation is efficiently degraded, while only a minor fraction of the Aβ internalized by microglia upon serum starvation is degraded over 24 hours. Both lipid and serum starvation induced transcriptomic changes in molecular cascades relevant to cholesterol biosynthesis, activation of gene expression by SREBF and metabolism of steroids.

Lipids play bidirectional role in microglial Aβ phagocytosis. Further molecular underpinnings of the mod-

ulation of phagocytosis by lipids and the selectivity of their effect are the subjects of our ongoing investigations.

Key words: microglia, phagocytosis, amyloid beta, lipids, Alzheimer's disease

P20.5. THE IMPORTANCE OF COMPARTMENTATION OF POLYAMINE METABOLISM IN THE HIPPOCAMPUS FOR THE DIFFERENTIAL SENSITIVITY OF CA1-3 REGIONS TO EXCITOTOXICITY

Aleksandra Kaczyńska[1], Małgorzata Beręsewicz-Haller[2], Aleksandra Owczarek[1], Katarzyna Skowrońska[3], Magdalena Zielińska[3], Barbara Zabłocka[2], Michał Węgrzynowicz[1]

[1]Mossakowski Medical Research Institute, Polish Academy of Sciences, Laboratory of Molecular Basis of Neurodegeneration, Warsaw, Poland, [2]Mossakowski Medical Research Institute, Polish Academy of Sciences, Molecular Biology Unit, Warsaw, Poland, [3]Mossakowski Medical Research Institute, Polish Academy of Sciences, Department of Neurotoxicology, Warsaw, Poland

Polyamines (PAs) are small biomolecules, that can control a variety of processes, including neuroprotection, although the exact mechanisms of their action are often complex and not fully recognized. The aim of this study was to verify the hypothesis that the hippocampus is characterized by regional compartmentation of PAs metabolism, what may determine specific phenotypes of individual regions of this structure.

Spatial distribution of mRNAs of PAs metabolism-related genes was studied with Allen Brain Atlas. The experimental work was performed using WT mice and mouse model of loss of arginase 2 (Arg2), a first enzyme in PAs synthesis pathway, responsible for conversion of arginine (Arg) to ornithine (Orn). Distribution of Arg2 protein was analyzed using immunostaining. Levels of Arg and Orn was measured with HPLC and activity of arginase was assayed by fluorimetric test. The role of PAs synthesis pathway for protection from neuronal injury was studied using organotypic cultures of rat hippocampal slices.

Region CA2, known for its exceptional resistance to neurotoxic stimuli, was identified to feature a unique profile of PAs-related gene expression. Arg2 protein was specifically expressed in pyramidal neurons of CA2, and absent in other regions. Arginase activity followed the regional distribution of Arg2. Loss of Arg2 resulted in accumulation of Arg and reduction of Orn as well as in loss of arginase activity. Inhibition of PAs synthesis in organotypic slice model of excitotoxicity was found to induce injury of, otherwise protected, CA2 pyramidal neurons.

My data suggest a distinct PAs metabolism in hippocampal subregions. Arg2, the only hippocampal isoform of arginase, seems to be a main supplier of Orn for intensive production of PAs in CA2, a pathway that appears to support the protection of pyramidal neurons of this region from excitotoxicity.

Key words: polyamines, hippomcampus, arginase, neuroprotection, excitotoxicity

P20.6. PROTECTIVE EFFECT OF SELECTED NATURAL COMPOUNDS AGAINST ERASTIN-INDUCED MITOCHONDRIAL DYSFUNCTION IN BV2 MICROGLIAL CELLS

Agata Adamczyk[1], Anna Wilkaniec[1], Renata Wolińska[2], Magdalena Bujalska-Zadrożny[2]

[1]Mossakowski Medical Research Institute, PAS, Department of Cellular Signalling, Warsaw, Poland, [2]Medical University of Warsaw, Department of Pharmacodynamics, Warsaw, Poland

Microglia-mediated neuroinflammation is the main factor involved in the pathogenesis of several neuropsychiatric disorders such as autism and neurodegenerative diseases including Alzheimer's and Parkinson's disease. Mitochondria are pivotal to triggering inflammation and stimulating innate immune signaling cascades to intensify the inflammatory response in front of different stimuli. Mitochondrial reactive oxygen species (ROS) influence and regulate a number of key aspects of mito-inflammation, therefore strategies directed to reduce or neutralize mitochondrial ROS levels might have a beneficial effect on inflammatory-related disorders. This work aimed to evaluate the antioxidative and anti-inflammatory properties of natural compounds isolated from plants such as Cannabidiol (CBD), Thymoquinone (TQ), and Berberine (BBR) against erastin-induced damage in BV2 microglial cells and mouse hippocampal HT22 neuronal cells. Cell viability, mitochondrial function, and ROS assays were performed to assess the protective effect of these natural compounds. Our results, based on the superoxide anion radical ($O_2^{\bullet-}$) detection using a hydroethidine (HE) probe, demonstrated that TQ at a concentration of 1 μM exhibited considerable antioxidant activity in both BV2 and HT22 cells treated with 1 μM erastin. JC-10 mitochondrial membrane potential (ΔyM) assay revealed significant mitochon-

drial dysfunction evoked by erastin that was attenuated by both TQ and BBR. However, neither TQ nor BBR prevented mitochondrial ROS generation analyzed by MitoSOX-based assay. Among the tested compounds, exclusively CBD attenuated the lipopolysaccharide (LPS)-induced inflammatory response in BV2 microglial cells in a concentration-dependent manner. In conclusion, these results may provide new prospects for the therapeutic manipulation of mito-inflammation in the context of inflammatory brain diseases.

Key words: cytoprotection, mitochondrial dysfunction, oxidative stress, mitoflammation, BV2 cells

P20.7. GPR183 ANTAGONIST PREVENTS IMMUNE CELL MIGRATION TO THE BLOOD-BRAIN BARRIER *IN VITRO* DURING INFLAMMATION

Fionä Caratis[1], Bartosz Karaszewski[2], Tomomi Furihata[3], Aleksandra Rutkowska[4]

[1]Department of Anatomy and Neurobiology, Medical University of Gdansk, Poland, [2]Brain Diseases Center and Department of Adult Neurology, Medical University of Gdansk & University Clinical Center, Gdansk, Poland, [3]Laboratory of Clinical Pharmacy and Experimental Therapeutics, School of Pharmacy, Tokyo University of Pharmacy and Life Sciences, Hachioji, Tokyo, Japan, [4]Brain Diseases Center and Department of Anatomy and Neurobiology, Medical University of Gdansk, Poland

Multiple sclerosis (MS) is a chronic, progressive, neuroinflammatory and neurodegenerative disease characterised by the entry of peripheral immune cells into the central nervous system *via* a damaged blood-brain barrier (BBB). During MS, the Epstein-Barr virus-induced gene 2 (EBI2 or GPR183), alongside its natural ligand the oxysterol 7α,25OHC, are known to be increased. Indeed the GPR183/oxysterol pathway is involved in several neuroinflammatory and neurodegenerative disorders and plays a key role in modulating innate immunity. GPR183, activated by 7α,25OHC, coordinates immune cell positioning enabling proper humoral and cellular immune responses. This coordinated lymphocyte positioning is possible with a tightly regulated concentration gradient of 7α,25OHC formed by cells expressing the enzymes necessary for 7α,25OHC synthesis (CH25H and CYP7B1) and degradation (HSD3B7). The infiltrating immune cells then propagate the inflammatory signalling and attack the myelin sheaths surrounding the neuronal axons, leading to their neurodegeneration and death. We specifically showed that brain microvessels express the GPR183 receptor as well as the enzymes necessary for 7α,25OHC synthesis and that the oxysterol pathway is upregulated in brain's plaques in multiple sclerosis but also in the cerebrospinal fluid of MS patients. Using human *in vitro* BBB models, comprised of endothelial cells, pericytes and astrocytes, we characterised the expression of GPR183 and GPR183-related enzymes after inflammatory stimuli and how they impact the BBB permeability. Finally, we investigated immune cells migration patterns towards our *in vitro* BBB model. The BBB was stimulated with inhibitor of the GPR183/oxysterol pathway and showed that immune cell migration is dependent on the GPR183/oxysterol pathway thus representing a therapeutic target in MS by modulating this pathway directly at the BBB to prevent immune cell migration towards the brain parenchyma.

Key words: EBI2, GPR183, MS, immune cell migration

P20.8. LONG-TERM HYPERGLYCEMIA AFFECTS EXPRESSION OF DIAPH1 AND ITS CYTOSKELETON LIGANDS IN EPIDERMIS OF DIABETIC PATIENTS

Bernard Kordas, Robert Modzelewski, Wojciech Matuszewski, Jarosław Szuszkiewicz, Michał Załęcki, Joanna Wojtkiewicz, Elżbieta Bandurska-Stankiewicz, Judyta Juranek

University of Warmia and Mazury, Poland

Over the past few decades, diabetes has gradually become one the top non-communicable disorders in the modern world. A range of high glucose-mediated effects may contribute to the pathogenesis of diabetic neuropathy, including cytoskeleton protein glycation and axonal transport alteration. In this study we aimed at capturing molecular changes in expression of Diaph1 and related proteins involved in cytoskeleton integrity, cellular movement and axonal transportation in epidermal cells and nerve endings in skin biopsies collected from long term diabetic patients.

Type 2 diabetic patients (n=16, 21-82 yrs old) and non-diabetic controls (n=12, 25-50 yrs old) were enrolled in the study. Prior to enrollment, all subjects provided informed consent. The study was approved by the University Institutional Ethics Committee. Skin specimens were obtained under local anesthesia using sterile disposable biopsy punchers. Expression of PGP 9.5 (used as a neuronal marker), Diaph, actin, liprin, and profilin

was analyzed by immunohistochemistry. For each protein, stained area fraction and stained nerve fiber count were calculated using ImageJ.

The immunostained area fraction was significantly larger for actin and profilin, and slightly larger for Diaph1 and liprin in epidermal basal cells of diabetic patients. On the contrary, the number of PGP 9.5-positive nerve fibers was significantly lower in the same group of patients, marking the clear division between neuronal and non-neuronal components of the skin.

Long-term hyperglycemia leads to a reduced number of sensory nerve endings in the epidermis and to an increased, likely compensatory, presence of Diaph1 and its cytoskeletal ligands in degenerating epidermis of diabetic patients. This observation highlights the importance of Diaph1 signaling in diabetes and provides background for further translational studies.

Funding: NCN Miniatura-1 2017/01/X/NZ5/01350.

Key words: diabetes, neuropathy, Diaph1, cytoskeleton, nerve endings

P21.1. IDIOSYNCRASY OF ANTISENSE OLIGONUCLEOTIDE TARGETING PROTEIN-CODING GENE EMBEDDED WITH NON-CODING RNA *IN VIVO*

Md Hasan Ali, Savani Anbalagan

Institute of Molecular Biology and Biotechnology, Faculty of Biology, Adam Mickiewicz University in Poznań, Poznań, Poland

Antisense oligonucleotides (ASO) are powerful tools to alter gene expression and ASO's are even under clinical use and clinical trials to treat human diseases. Whether ASO's targeting protein-coding genes embedded with non-coding RNA's affect non-coding RNA expression or function is relatively unknown. While studying how glial cells regulate axonal morphogenesis in larval zebrafish, we made a serendipitous observation that ASO targeting a splice site of one of our candidate protein-coding genes led to defects in axonal morphogenesis. We observed ASO-induced intron retention events and increased gene expression. The splice site-targeted ASO-induced phenotype was not rescued by candidate gene translation-blocking ASO's, thus potentially ruling out the role of truncated protein. However, the phenotype was rescuable by the knockdown of embedded non-coding RNA. We believe our results highlight a blind spot in ASO-based research and call for a careful evaluation of results from ASO studies when targeting protein-coding genes embedded with non-coding RNAs.

Key words: axon, morphogenesis, ASO, zebrafish

P21.2. THE INFLUENCE OF CEREBROSPINAL FLUID ON THE THERAPEUTIC POTENTIAL OF NEURAL STEM CELLS

Klaudia Radoszkiewicz, Anna Sarnowska

Translational Platform for Regenerative Medicine, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland

Over the last few years, we have seen that human neural stem cells (hNSCs) show promising outcomes when used for neurological disease cell therapy, however, several issues should be further investigated even on the preclinical level. Our current knowledge regarding neurogenesis is still not well understood, thus, more research is needed to address the limitations and effectiveness of the therapy and to investigate what laboratory conditions would be able to mimic the physiological brain environment. It has been suggested previously that the cerebrospinal fluid (CSF) which is a natural component of the brain niche, plays a vital role not only in brain development, but also in NSCs' survival, proliferation, and differentiation processes, although its exact role in adult neurogenesis is much less clear. There is a very limited number of data regarding its influence on NSCs. Thus, in our study, we preincubated human NSC line with the human CSF leftovers from healthy donors (in whom the reason for collecting CSF was the suspicion of neurological disease that has not been confirmed) to obtain closer to the physiological brain environment and to assess NSCs' fate and their therapeutic abilities *in vitro* and *ex vivo*. We observed the significant changes in the secretory potential of CSF-treated NSCs, and, moreover, their elevated neuroprotective potential after co-culture with ischemically damaged by oxygen-glucose deprivation (OGD) organotypic rat hippocampal slices culture (OHC) in comparison to the cells cultured in the standard conditions. This study exposed the critical importance of nutritional supplementation regarding NSC culture maintenance and therapeutic properties and brings hope for understanding the mechanisms underlying brain function and disease, what may ultimately lead to the development of new therapeutic interventions for neurological disorders.

The work was supported by the National Science Centre grant no. NCN 2018/31/B/NZ4/03172.

Key words: neural stem cells, ischemic stroke, cerebrospinal fluid, neuroprotection, cell therapy

P22.1. TUNNEL VISION IN RETINITIS PIGMENTOSA PATIENTS LEADS TO NEGATIVE CONTRAST MOTION-ACUITY IMPAIRMENT: BEHAVIORAL AND fMRI EVIDENCE

Marco Ninghetto[1], Tomasz Gałecki[2], Kamil Szulborski[2], Artur Marchewka[1], Kalina Burnat[1]

[1]Nencki Institute of Experimental Biology, Poland, [2]Department of Ophthalmology, Medical University of Warsaw, Warsaw, Poland

POSTER WITHDRAWN

P22.2. USAGE OF NOVEL TRP ION CHANNELS COMBINED WITH MELANOPSIN TO SIGNAL TRANSDUCTION

Anna Galińska, Bartłomiej Bałamut, Jagoda Płaczkiewicz, Andrzej Foik

International Centre for Translational Eye Research, Institute of Physical Chemistry Polish Academy of Sciences, Warsaw, Poland

Vision is a fundamental sense essential for life quality and function independently. The main reasons for visual impairment and blindness are retinal diseases, for example retinitis pigmentosa and macular degeneration with age. The main common feature of these diseases is the degeneration of cones and rod photoreceptors in the retina. Although there is some promising research, there are still no effective treatments to restore visual function in suffering people.

The loss of rods and cones does not affect other retinal cell layers, including Bipolar and Retinal Ganglion cells. Intrinsically photosensitive retinal ganglion cells (ipRGCs) are considered a third type of photoreceptor. They are distinguished by a unique function – an expression of Melanopsin. As a result of the ipRGCs transduction cascade, Melanopsin target Transient Receptor Potential channels (TRPs). TRPs are ion channels that play a crucial role in responding to various environmental stimuli, including light. Disruptions in their proper function are associated with multiple diseases, including glaucoma and diabetic retinopathy. Therefore, the viral administration of TRPs combined with Melanopsin into the retina may significantly enhance the response to the light stimulus. Our aim was to check if TRPs combined with Melanopsin will modulate signal in activated cells.

We created AAV viral plasmids carrying TRP channels and Melanopsin, and investigated their potential by single-channel current flowing electrophysiology using the patch-clamp technique. Our preliminary results suggest that the complementation of TRPs with opsins may significantly change the response to the light stimulus in the case of non-photoreceptor cells expressing opsins.

Key words: TRPs, Melanopsin, vision, visual impairments, AAV vectors

P22.3. SHEDDING LIGHT ON CALCIUM DYNAMICS AND MEMBRANE POTENTIAL CONTROL WITH OPTOGENETICS

Bartłomiej Bałamut, Jagoda Płaczkiewicz, Karolina Saran, Andrzej Foik

International Center for Translational Eye Research, Institute of Physical Chemistry, Polish Academy of Science, Warsaw, Poland

The project's primary objective is to develop a tool that utilizes coloured light to stimulate retinal circuitry. Calcium is one of the retina's regulatory mechanisms, as intercellular calcium levels control the ion channels in all cells involved in phototransduction. [1] In the case of bipolar cells, calcium plays a significant role in modulating their response during hyperpolarization or depolarization. The optogenetic tools employed for retinal stimulation rely on the passive influx of ions from the extracellular space. However, intracellular Calcium is indispensable for phototransduction, ON bipolar cell signal processing, and neurotransmitter release. Calcium interacts with signal transfer *via* gap junctions and chemical synapses in various ways, influencing the magnitude and kinetics of the postsynaptic response. The proposed approach aims to simultaneously enhance the response to light by utilizing multiple pathways. The first pathway involves melanopsin, which activates G protein-coupled pathways, causing the release of calcium ions into the intracellular space. Coupling this pathway with TRP-like calcium-gated channels would accelerate and amplify the depolarization/hyperpolarization process of bipolar cells. [2] Channelrhodopsin and ChrimsonR are the primary tools for altering membrane voltage and source of extracellular calcium influx into the cell. These findings suggest that our multimodal optogenetic approach holds promise for inducing higher membrane currents through synergistic effects, advancing retinal circuit stimulation techniques.

[1] Akopian, Abran, Witkovsky, Paul, "Calcium and retinal function" Molecular Neurobiology, 113-132# (2002). [2] Križaj, D., Cordeiro, S., Strauß, O" "Retinal TRP channels: Cell-type-specific regulators of retinal homeostasis and multimodal integration" Progress in Retinal and Eye Research, vol. 92.

Key words: Retinal circutry; Calcium regulation; Optogenetic tools; Melanopsin; coloured light; retina stimulation

P22.4. NEW APPROACH FOR DELIVERY OF GENE THERAPY TO CONES, USING MODIFIED RABIES VIRUS

Jagoda Płaczkiewicz[1], Lucyna Piórkowska[1], Samuel Du[2], Krzysztof Palczewski[2], Andrzej Foik[1]

[1]Institute of Physical Chemistry Polish Academy of Sciences, Poland, [2]Center for Translational Vision Research, University of California, Irvine, United States

Vision is providing the reception of information from the external environment, which is crucial for maintaining a high quality of life. However, there are estimated 285 million vision-impaired and 39 million blind people worldwide. That is why it is crucial to look for effective therapies that will slow down the disease progression and restore vision. Recently, viral gene therapies providing defective genes or optogenetic tools appeared to be the most effective ways to restore vision.

Rabies Virus is an attractive candidate for gene delivery due to the fast and high expression of multiple proteins encoding genes, which can be potentially used in gene therapy of degenerative diseases. However, delivery of therapeutic genes to the target cells is a key step in gene therapy, and RV infections are not cell-type unique, therefore gene delivery cannot be specifically controlled. Key RV protein, involved in mediating of interaction with host cells surface receptors and subsequent infection is envelope glycoprotein (G). Pseudotyping of G-deleted RV (RVΔG) with a properly designed chimeric G protein, can restrict RV infection to specific cell types.

Most of inherited retinal degeneration diseases are the result of mutations in rods, leading to their loss, which progressively leads to degeneration of cones. Despite the failure to transmit vision to the brain, cones are present for longer period in humans and animals, therefore they are excellent target for gene therapy approaches in early stages of degeneration. Therefore, we aim to pseudotype RV to reach remaining cones, using Rod-derived cone viability factor (RdCVF).

We created viral vectors pseudotyped with RdCVF, that were intravitreally administrated to the mice retina. Immunohistochemical analysis of eyes cross sections, revealed that our pseudotyping approach enables modified viral particles to infect cones specifically.

Key words: Retina, retinal degeneration, gene therapy, pseudotyping

P22.5. NEURAL UNDERPINNINGS OF VISUAL AWARENESS INVESTIGATED WITH TRANSCRANIAL MAGNETIC STIMULATION

Justyna Hobot[1], Kristian Sandberg[2], Michał Wierzchoń[3]

[1]Jagiellonian University, Institute of Psychology, Poland, [2]Aarhus University, Center of Functionally Integrative Neuroscience, Poland, [3]Jagiellonian University, Centre for Brain Research, Poland

The presentation discusses the application of transcranial magnetic stimulation (TMS) to investigate neural correlates of consciousness (NCCs) as measured with visual identification task accuracy, visual awareness ratings, and measures of metacognitive efficiency: the ability to judge one's perception accurately. The first study investigated the involvement of PFC. We applied Theta Burst Stimulation (TBS) protocols to the left anterior medial prefrontal cortex (aMPFC) to induce plasticity-like effects. The TBS protocol was applied before the behavioral testing. The results indicated that cTBS led to higher metacognitive efficiency than a sham. The second study examined whether single-pulse TMS (spTMS) applied to the primary motor cortex (M1) 450 ms after a stimulus presentation can influence visual awareness. The results revealed that in the congruent trials (where the response hand used in the identification task matched the one stimulated in the M1 condition), there were higher visual awareness ratings in the M1 condition compared to the control. Longer RTs for visual awareness ratings were observed in the M1 condition, indicating the incorporation of additional evidence into visual awareness judgments. Finally, the amplitudes of spTMS-induced motor-evoked potentials (MEPs) were associated with the visual awareness ratings and exhibited higher values in the congruent trials, suggesting they can serve as an indirect measure of accumulated evidence. Based on the reported findings, we argue that the aMPFC and M1 can contribute to visual awareness judgments. We also discuss the theoretical implications of those findings for the theories of consciousness, highlighting the importance of PFC (as postulated by, e.g., higher-order theories of consciousness) and the impact of non-visual information on visual awareness judgments.

Key words: consciousness, visual awareness, Transcranial Magnetic Stimulation

P22.6. IMPROVEMENT OF RETINAL CONDUCTIVITY BY THE INCREASE OF SYNAPTOPHYSIN EXPRESSION IN A MOUSE MODEL OF DIABETIC RETINOPATHY

Marita Pietrucha-Dutczak, Radosław Dutczak, Iwona Matuszek

Chair and Department of Physiology, Medical University of Silesia, Katowice, Poland

Diabetic retinopathy (DR) is a common ocular complication of diabetes, as it's estimated that one third of patients with diabetes will develop DR. Complications of this disease may lead to visual impairment, including blindness, and cause emotional distress, reduce patient's quality of life and generate huge costs of treatment. Nowadays, DR treatment methods are invasive and applied at the sight-threatening stages of DR. Therefore, it is important to understand the mechanisms leading to the development of this ocular dysfunction, especially considering early stages of DR. This pathology was traditionally defined as vascular disease, but there is accumulating evidence that neurodegeneration also occurs in diabetic retina, probably prior to visible microvascular damage.

The aim of these study was to examine basic mechanisms underlying the development and progression of DR and to establish whether α-lipoic acid (α-LA), a natural antioxidant, affects the survival and function of retinal neurons, especially retinal ganglion cells.

Diabetes in mice was induced by intraperitoneal administration of streptozotocin. After diabetes had developed, α-LA was injected twice a week. At the end of experiment animals were euthanized, retinas and optic nerves were collected and processed for western blot analysis and immunohistochemistry. During the experiment the retinal function was tested by electroretinography.

We observed higher amplitudes of oscillatory potentials in mice supplemented with α-LA than in diabetes mice. Moreover, α-LA decreased the expression of synaptophysin and pro-inflammatory cytokines. Functional alteration in retina precedes the structural changes. Additionally, α-LA reduces local inflammation and inhibits the development of DR. Knowledge about the supplementation of α-LA in the patients undergoing electroretinography may be crucial to obtain reliable results.

Key words: diabetic retinopathy, α-lipoic acid, electroretinography, streptozotocin

P22.7. EFFECT OF CHOLINERGIC MODULATION ON THE VISUAL PROCESSING IN RAT

Katarzyna Kordecka[1], Anna Galińska[1], David Lyon[2], Andrzej Foik[1]

[1]Ophthalmic Biology Group, International Centre for Translational Eye Research, Institute of Physical Chemistry, Polish Academy of Sciences, Warsaw, Poland, [2]Department of Anatomy & Neurobiology, University of California, Irvine, California, USA

Basal Forebrain (BF) is predominantly characterized by its' cholinergic projection patterns to the visual cortex. The functional contribution of this input is only starting to become understood. We propose that cholinergic modulation coming from BF will significantly impact single neuronal responses of the primary visual cortex (V1) in rats. The aim of this project is to understand the Basal Forebrain's role in the processing of the visual information in the V1 and its effect on the visual system activity. We used viral tracing and optogenetic stimulation of neuronal circuits paired with electrophysiological recordings in the primary visual cortex to answer this question. Precisely, we injected the modified Rabies virus (RV) into the V1 to retrogradely trace inputs coming from the BF. We hypothesize that the manipulation of the BF changes the selectivity of single cells in the V1. Indeed, our preliminary results confirm this hypothesis. The most prominent observation in our experiment is a significant change in firing rate when showing various directions of drifting gratings at optimal Spatial Frequency (SF), Temporal Frequency (TF), and Size. However, this change was different for different layers (depth) in the cortex. All layers tend to have a lower firing rate; however, the cell around layer IV tends to have an increased firing rate. Perhaps the most important result is the change in the optimal stimulus size. Most cells showed decreased optimal stimulus size, and the difference between conditions tends to be stronger in the upper layers than in the deep layers of the V1. Our preliminary results suggest that the Basal Forebrain plays a substantial role in the modulation of the center-surround interactions.

The project is supported by the National Science Center, Poland (2019/34/E/NZ5/00434) and (2020/39/D/NZ4/01881).

Key words: basal forebrain, visual cortec, electrophysiology

P22.8. ASYMMETRY IN SELECTIVE AND NON-SELECTIVE COVERT AND OVERT ATTENTION. AN EFRP STUDY

Agnieszka Fudali-Czyż[1], Marta Szewczyk[2], Łukasz Grzeczkowski[3], Paweł Augustynowicz[2]

[1]Pedagogical University of Krakow, Department of Neurocognitive Psychology, Poland, [2]The John Paul II Catholic University of Lublin, Department of Experimental Psychology, Poland, [3]Humboldt University of Berlin, Department of Psychology, Germany

Fimm et al. (2015) showed a right visual field attentional advantage (slower responses to targets presented in the left visual field) as a result of fatigue in covert attention (without eye movements). Meanwhile, in an eye-tracking study, Palladini et al. (2016) also found a right-sided attentional advantage but in relation to the overt type of attention. We tested whether attentional asymmetry differs between selective and non-selective overt and covert attention. We conducted the experiment in the eye fixation-related potentials (EFRP) paradigm, which allows us to control brain activity related to eye movements. Thus, it broadens the scope of possibilities to study EEG correlates of attention by its overt aspect (Fudali-Czyż et al., 2018). The task of right-handed subjects (N=23, aged 20-30 years) was to indicate whether the target T is rotated (90°) to the left or right side. The letter was displayed alone ("non-selection attention") or appeared surrounded by distractors ("Ls") ("selective attention"). The stimuli appeared 4° from the center of the screen and could be perceived without saccadic eye movements ("covert attention", n=256 trials) or 11° from the center of the screen, forcing the participant to make a saccadic eye movement to notice them ("overt attention", n=256 trials). Reactions were faster to the right targets only in "covert attention", regardless of the selectivity conditions. On the contrary, in "overt attention", we found shorter saccades to the left side and a larger amplitude of the so-called lambda response (positive EFRP potential recorded from posterior electrodes about 100 ms after the onset of the visual fixation). The amplitude of lambda response for right targets was larger from the right than from the left electrodes. So, despite fatigue, the natural dominance of the right cerebral hemisphere for visuospatial attention was preserved in "overt attention", regardless of the selectivity conditions.

Bibliography: 1. Fimm, B., Willmes, K., & Spijkers, W. (2015). Differential effects of lowered arousal on covert and overt shifts of attention. Journal of the International Neuropsychological Society, 21(7), 545-557.2. Fudali-Czyż, A., Francuz, P., & Augustynowicz, P. (2018). The effect of art expertise on eye fixation-related potentials during aesthetic judgment task in focal and ambient modes. Frontiers in Psychology, 9, 1972.3. Paladini, R.

E., Diana, L., Nyffeler, T., Mosimann, U. P., Nef, T., Müri, R. M., & Cazzoli, D. (2016). The asymmetrical influence of increasing time-on-task on attentional disengagement. Neuropsychologia, 92, 107-114.

Key words: covert attention, overt attention, non-selective attention, selective attention, attentional asymmetry, eye fixation-related potentials, EEG, eye-tracking

P23.1. IMPACT OF MATERNAL CHILDHOOD TRAUMA ON METABOLIC COMPOSITION AND microRNA CONTENT OF HUMAN MILK

Magdalena Gomółka[1], Patrycja Chudzicka-Ormaniec[1], Weronika Tomaszewska[1], Anna Ziomkiewicz-Wichary[2], Ali Jawaid[1]

[1]Nencki Institute of Experimental Biology, Polish Academy of Sciences, Laboratory of TREND (Translational Research in Neuropsychiatric Disorders), Centre of Excellence for Neural Plasticity and Brain Disorders (BRAINCITY), Warsaw, Poland, [2]Jagiellonian University, Department of Anthropology, Institute of Zoology and Biomedical Research, Cracow, Poland

Traumatic experiences, especially during childhood, can have pervasive effects on the physical and mental health of individuals. Recent evidence suggests that children born to mothers with a history of childhood trauma show disrupted developmental trajectories and an increased risk for behavioral and metabolic perturbations. In this study, we investigate the impact of maternal childhood trauma on the metabolic composition and small RNAs in human milk and ascertain their association with early development and behavior of the infants.

Small RNA sequencing (sRNA-seq) followed by qPCR assays were performed to identify and validate small RNAs in the milk from lactating mothers with varying levels of childhood trauma (n=112). Milk was fractionated into skimmed and fat fractions, followed by RNA extraction from the fat fraction that was further processed for sRNA-seq. Additionally, analysis of short-, middle, and long-chain fatty acids was performed on the whole milk. We then examined the small RNA and metabolomic changes in the milk in the context of childhood trauma severity, as well as, infant temperament and head circumference.

Our results reveal increased head circumference in the infants born to women with severe childhood trauma. Furthermore, a history of severe childhood trauma was associated with increased middle-chain fatty acids, as well as, differential expression of 3 specific miRNAs, miR-142-3p, miR-142-5p, and miR-223-3p in the milk. Notably, milk expression of miR-223-3p showed a moderate correlation with infant behavior and the overall changes in milk were not confounded by any symptoms indicative of post-partum depression in the mothers.

In conclusion, this study highlights changes in milk metabolome and miRNA as potential signatures of childhood trauma in humans. However, further evidence is warranted to establish a mediating role for these changes in altering the development and behavior of the children born to mothers with a history of childhood trauma.

Key words: microRNA, childhood trauma, milk, sequencing

P23.2. MEASURING INDIVIDUAL PREFERENCES FOR DIVERSE TASTES IN GROUP-HOUSED MICE

Mateusz Rycerz, Maria Kalinowska, Joanna Sadowska, Alicja Puścian, Fahmida Haque, Anna Bryksa

BRAINCITY – Centre of Excellence for Neural Plasticity and Brain Disorders, Nencki Institute, Polish Academy of Sciences, Poland

Understanding what is rewarding to an individual is indispensable for effective influence over their actions. Although much is known about the power of preferred rewards in conditioning behavior, the functional brain underpinnings of the process are still poorly understood.

In the following research, we develop methods for assessment of individual taste preferences in group-housed mice. To that end, we use naturalistic, automated testing in Eco-HAB, an assay recording murine behavior 24h/day. The longitudinal character of the experiments allows testing the changes in preferences over time. We repeatedly exposed animals to two different tastes of candied milk of equal nutritional value and measured the individual intake during time-constrained sessions each day.

We show that mice display individual preferences for diverse tastes of condensed milk. When pre-tested under single-housing conditions, mice usually start intake from their preferred taste and then swap to the other, showing favor for variability. Further, we show that after being pre-exposed to one taste of condensed milk and subsequently presented with a selection between a familiar and a new taste, mice tend to opt for the latter. Nonetheless, this inclination diminishes over time with repeated instances of choice.

In conclusion, we show that mice have individual preferences for different flavors and that they are more solidified when animals have no contact with other conspecifics. The developed methodological framework will serve for further studies on the neural background of individual preferences, as based on the assessment of voluntary behavior.

Key words: reward, preference, mice, naturalistic tasting

AUTHOR INDEX

DOSKONAŁA NAUKA – EXCELLENT SCIENCE

Co-financed by the program "Excellent Science" of the Minister of Education and Science (DNK/SP/566112/2022, "16th International Congress of the Polish Neuroscience Society").

Dofinansowano z programu „Doskonała nauka - Wsparcie konferencji naukowych" Ministra Edukacji i Nauki, na podstawie umowy nr DNK/SP/566112/2022. Tytuł projektu: "16th International Congress of the Polish Neuroscience Society".

Celem projektu jest organizacja w dniach 20-23.09.2023 r. międzynarodowej konferencji naukowej Polskiego Towarzystwa Badań Układu Nerwowego (PTBUN) w Toruniu, w Instytucie Psychologii Uniwersytetu Mikołaja Kopernika w Toruniu (UMK) oraz Akademickim Centrum Kultury i Sztuki „Od Nowa". Konferencja będzie organizowana wspólnie przez PTBUN oraz UMK. Celem konferencji organizowanej w Toruniu, w 2023 r. jest zapewnienie najwyższego poziomu merytorycznego spotkania polskich naukowców z innymi naukowcami pracującymi w wiodących międzynarodowych ośrodkach neuronaukowych. Dzięki staraniom organizatorów, wykłady plenarne zgodzili się wygłosić wybitni specjaliści w obszarach badań nad rozwojem układu nerwowego, pamięcią, empatią, przetwarzaniem sensorycznym, rytmami dobowymi i snem, neurodegeneracją, optogenetyką. Wykładowcy plenarni przyjadą z wiodących ośrodków neuronaukowych, m.in. z Holandii, Wielkiej Brytanii, Izraela, Szwajcarii. Celem sympozjów będzie przedstawienie uczestnikom najnowszych osiągnięć w dziedzinach neurobiologii, neuropsychologii, neurologii, kognitywistyki i innych dziedzin neuronauki. Poza wykładami plenarnymi oraz sympozjami naukowymi, podczas konferencji osiągnięcia przedstawą także zwycięzcy konkursu o Nagrodę J. Konorskiego, organizowanego dorocznie przez PTBUN. Specjalna sesja ustna będzie dedykowana młodym badaczom, którzy zaprezentują obiecujące wyniki własnych badań. Nieodłączną częścią programu konferencji będą sesje posterowe, cieszące się wielką popularnością szczególnie wśród młodych badaczy. Warto dodać, że podczas prezentacji posterowych, często zawiązywane są współprace naukowe. Organizatorzy szacują, że w konferencji weźmie udział ponad 300 uczestników z licznych uniwersyteckich ośrodków europejskich. Wspólna organizacja wydarzenia przez PTBUN oraz UMK pozwoli na stworzenie dogodnej platformy do wymiany myśli naukowej, przyczyni się do rozwoju polskiej nauki oraz zapewni promocję Polski i Torunia w środowisku neuronaukowym.

Kwota dofinansowania projektu: 191 600 zł

Całkowita wartość projektu: 324 600 zł

www.ane.pl