and increased repetitive behaviours with limited interests of environment. Recent studies have revealed that purinergic signalling (hyperpurinergia) is one of a key features of autism. Our aim was to establish a reliable model of ASD in our lab utilizing a broad range of behavioural experiments in order to investigate the role of P2X7 in autism. We injected Poly(I:C) (PIC) in two doses to pregnant C57Bl/6 mice: 3 mg/kg on E12.5 and 1.5 mg/kg on E17.5 respectively. Offsprings were weaned 4 weeks of age and behavioural studies started from 8 weeks of age. We performed social preference test, measured the body temperature and sensorymotor coordination (rotarod). We used self grooming and marble burying test in order to investigate manifestation of repetitive behaviour and measured the sensorymotor gating with Prepulse Inhibition (PPI). After behavioural experiments animals were sacrificed. Para-sagittal sections of the cerebellar vermis were cut and Purkinje cells were counted. Synaptosome fractions were made from half brains of animals and examined by electron microscopy. Striatum and Hippocampus monoamine content were measured by HPLC. We compared PIC treated offsprings with naive animals (n = 10–16 animals/group). PIC treated animals showed decreased sociability and sensorymotoric coordination but we did not find change in body temperature of PIC animals. MIA animals showed increased repetitive behaviour in the marble burying and self grooming test. Quantitative Purkinje cell dropout was found in PIC mice and electron microscopy of half brain revealed ultrastructural abnormalities in them. Higher level of monoamins were detected in ASD mice compared to the control group. Based on these results this model seem to be suitable to measure the effect of different compounds or genetic deletion on PIC induced ASD symptoms in rodents.

Keywords Poly(I:C), autism, P2X7R

P17

Effect of extracellular vesicles derived from distinct brain cells on Aβ toxicity and assembly: focus on microglia derived vesicles

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Alzheimer's disease (AD) is a neurodegenerative disorder. The patho-histological features in AD are intracellular accumulation of neuro-fibrillary tangles and extracellular senile plaques. Plaque deposition leads to recruitment and activation of microglial cells, which induces neuroinflammation and drives neurodegeneration.Recent evidence show that soluble pre-fibrillar Aβ species, rather than insoluble fibrils, are highly neurotoxic and correlate with disease severity.Hence, preventing formation of soluble Aβ and its interaction with neurons is a major goal in AD. Despite massive efforts, how extracellular factors regulate assembly of Aβ peptide and neurotoxic activity of Aβ species is still largely undefined. Recent studies indicate that Extracellular Vesicles(EVs),including exosomes and PM-derived microvesicles(MVs), may influence Aβ neurotoxicity. Our findings reveal that production of microglial MVs(m-MVs) is strikingly high in patients with mild cognitive impairment and AD as compared to healthy controls and positively correlates with markers of neurodegeneration and hippocampal atrophy. Furthermore we found that MVs isolated from the CSF of AD patients are toxic to cultured hippocampal neurons. Through in vitro studies we demonstrate that the m-MVs promote generation of neurotoxic soluble species from almost inert Aβ aggregates, which is mediated by lipid components of MVs. Our findings suggest that m-MVs favor formation of neurotoxic Aβspecies throughout the brain, possibly representing the mechanism behind transynaptic spread of Aβ in AD. On the other hand, studies conducted by Yuyama et al., 2012, 2014, and An et al., 2013, suggest that exosomes produced by neurons may exert opposite action by neutralizing neurotoxicity of soluble Aβ. To verify if the overall effect of exosomes and MVs on Aβneurotoxicity may vary depending on parental cell type we are currently studying the influence of EVs (exosomes &MVs) derived from distinct brain cells on Aβ toxicity and assembly.

Keywords Extracellular vesicles (EVs), Alzheimer's disease (AD), neurotoxicity

P18

GnRH level regulation in the hypothalamus of female rats of different age

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In recent years the study of age-related derangements of the gonadotropin releasing hormone (GnRH) synthesis and secretion resulting from both the GnRH gene expression changes and interaction of glia with GnRH-ergic neurons of the hypothalamus is a focus of attention. It was demonstrated earlier that this could result from the decreased activity of monoaminergic and peptidergic systems that control the GnRH preovulatory secretion surge initiation, specifically from the loss of the signal coming from the suprachiasmatic nuclei (SCN) of the hypothalamus. This signal is critical for the emerging of the GnRH regular cyclic secretion, which is mediated prominently by vasoactive intestinal peptide (VIP). We have studied age-related changes in the biogenic amines and VIP content in the hypothalamic structures responsible for the GnRH synthesis and secretion. It has been shown by us that the GnRH level in the median eminence with the arcuate nuclei (ME-Arc) of the hypothalamus of 22-month-old rats is half as high compared to that of 7–8-month-old animals. Beside that, the VIP level in the SCN tended to decrease, with the norepinephrine, dopamine, and 5-hydroxyindoleacetic acid levels decreased significantly in the median preoptic area of the hypothalamus responsible for the GnRH synthesis and in the ME-Arc exercising its secretion into the portal vein of the pituitary. It has been shown that the initial phase of the reproductive failure with 13–14-month-old animals having irregular estrous cycles is characterized by gradual disappearance of the normal biogenic amine diurnal dynamics in the studied hypothalamic structures, which could be due to the loss of regulatory signals coming from the SCN.

Keywords GnRH, biogenic amines, hypothalamus

P19

Toxicity of amyloid beta 1-40 and 1-42 on SH-SY5Y cell line

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Objectives Amyloid beta plaques are primary hallmark of Alzheimer's disease, which is characterized by specific neurodegeneration. Amyloid beta peptide – the main plaque component- was shown to be neurotoxic in animal models, primary neuronal cultures and immortalized cell lines. However, the results are often controversial and there is no good human cell line model for evaluation of the toxicity of amyloid peptides. Here we studied the effect of amyloid beta 1-40 and 1-42 on undifferentiated and differentiated human neuroblastoma cell line SH-SY5Y.

Results Undifferentiated cell culture was too diverse and unstable to reveal a toxic effect of amyloid beta peptides quantitatively. Differentiated cells established more neuron-like phenotype and were more identical and stable in culture suggesting potential susceptibility to amyloid beta as a neurotoxic agent. Amyloid peptides are prone to form different aggregates with diverse toxic properties, in current study, monomeric amyloid beta 1-40 and 1-42 were applied to the cells. Viability test WST-1 and propidium iodide (PI) uptake tests showed that undifferentiated cells are not susceptible to amyloid beta, however, differentiated cells showed reduced viability and increased PI uptake in case of amyloid beta 1-42, but not in case of amyloid beta 1-40.