(baseline CSDD score ≥ 18) were selected and compared (n = 6 for each group), differences were more definite. The main difference was in the 'cyclic functions' category. Significant differences were not observed among secondary outcome measures. The number of treatment-related adverse-events (AE) did not differ between groups (p=0.83) and no serious treatment-related AE were observed.

Conclusion: The use of escitalopram was well tolerated in depressive dementia patients, and it also reduced depressive symptoms faster that placebo in subjects with definite major depression. Future studies focusing on subjects with more severe levels of depression, and with more statistical power, will be needed.

PT560

A comparative study of serum Tau protein and Aß levels on intestinal endotoxemia among Alzheimer's disease rats and in Chinese sample of Alzheimer's disease patients and healthy controls

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Abstract

Objective: Early our animal experiments study showed that AD rats occurs intestinal endotoxemia (IETM), and with the increasing of endotoxin, the Tau protein and Aβ increased and promote the generation of AD. Study on the change of endotoxin Tau protein and Aβ levels on intestinal endotoxemia on Alzheimer's disease rats and in Chinese sample of Alzheimer's disease patients and healthy controls.

Methods: The AD model of wistar rats were produced by injecting D-galactose and $AlCl_3$ for 90 days. From January 2014 to January 2015, 40 subjects were selected from Hospitals and Nursing Homes at Taiyuan City and Perking, and control group were from communities. Neurocognitive function was detected by neuropsychological tests with the Mini mental state examination (MMSE) and Alzheimer's disease assessment scale cognitive subscale (ADAS-cog); LPS level was detected by CE TAL; TNFα and Tau protein and Aβ levels were tested by ELISA.

Results: Compared with the control group, the AD rats group had longer latency (P<0.05) and more error times (P<0.05) in Morris water maze test, and LPS, TNF-α and Tau protein and Aβ levels were increased (P<0.05). MMSE score in the patients with AD were significantly lower than the healthy elderly (P<0.01), ADAS-Cog score in patients with AD were significantly higher than the healthy elderly (P <0.001); AD patients' and healthy controls LPS, TNF-α, Tau protein and Aβ were significantly higher than the healthy elderly (P<0.01).

Conclusion: AD rats and patients with AD and healthy controls were all accompanied intestinal endotoxemia and that may be a new risk factors in the development in the process of happen of AD, Tau protein and Aβ role is unique, and is also proved a powerful evidence of Alzheimer's disease.

PT561

Study on intestinal endotoxemia on learning memory ability and hippocampal gene expression of apoptosis of brain cell in Alzheimer's disease rats

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Abstract

Objective: Recently studies have demonstrated that inflammatory reaction and neurotoxic effect caused by activated microglia which induced by hippocampal gene expression of apoptosis of brain cell deposition plays an important role in the development of AD.

To investigate the effect of intestinal endotoxemia (IETM) on learning and memory ability in rats with Alzheimer's disease (AD) and its possible mechanisms.

Methods: The AD model of wistar rats were produced by injecting D-galactose and $AlCl_3$ intraperitoneally for 90 days. Subsequently, learning and memory ability of the rats were evaluated by Morris water maze; the level of lipopolysaccharide (LPS) and tumor necrosis factor-α (TNF_α), IL-1_β, IL-10, TNF_α, NO were determined by ELISA; the apoptosis of brain cell were detected by TUNEL.

Results: The learning and memory ability of the rats were observed by Morris water maze. The results indicated that compared with the normal control, the learning and memory ability of model rats and AD rats is markedly decreased; LPS and IL-1_β, IL-10, TNF_α, NO in blood in AD rats were increased (P<0.05); indicated that compared with the normal control, the incidence rate of the brain cell apoptosis of model rats and AD rats is markedly increased (P<0.01).

Conclusions: The rat model of Alzheimer's disease is accompanied IETM and that apoptosis of hippocampus of brain cell may plays an important role in the development of AD.

Key words: Alzheimer's disease; Intestinal endotoxemia; LPS; TNF-α; apoptosis of brain cell

PT562

Alzheimer disease therapeutics candidate, SAK3 improves the cognitive functions through inhibition of amyloid beta accumulation in APP23 mice.

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Abstract

As Alzheimer disease therapeutics candidate, we have developed SAK3 (Ethyl 2',3'-dyhydro-8-methyl-2',4-dioxo-2-peperidinospiro[2-cyclopentene-1,3'-imidazo[1,2-a]-pyridine]-3-carboxylates) (PCT/JP2013/051388). SAK3 stimulates T-type voltage-gated Ca^{2+} channels (T-VGCC) in mouse cortical slices (Moriguchi et al., J Neurochem 2012;121:44–53). We also reported that SAK3 stimulates acetylcholine release and promotes long-term potentiation in mouse hippocampus (Neuroscience 2014 abstract 265.21). We here tested whether SAK3 reduced amyliod beta (1–42) accumulation in Alzheimer model (APP23) mice. APP23 mice aged 6 and 9 months were treated for two or three months with SAK3 (0.5mg/kg, p.o.) and measured amyliod beta (1–42) levels in both soluble and insoluble fractions from APP23 mouse cortex. The chronic administration significantly reduced the amyliod beta (1–42) levels. Consistent with the reduced amyliod beta (1–42) levels, the numbers of amyloid plaques assessed by thioflavin staining were significantly reduced by the chronic SAK3 treatment. Furthermore, the cognition assessed by novel object recognition task was improved by the chronic administration. Using LC/MS/MS system, we established high sensitivity quantification system in blood to obtain proof-of-concept of SAK3 safety in human. Taken together, the novel T-type calcium channel stimulator SAK3 restored cognition ability in APP23 mice and reduced the amyliod beta (1–42) accumulation/

aggregation. However, further extensive studies are required to elucidate the underlying mechanism.

PT563

Prenatal nicotine exposure impairs the proliferation of neuronal progenitors, leading to fewer glutamatergic neurons in the medial prefrontal cortex

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Abstract

Cigarette smoking during pregnancy is associated with various disabilities in the offspring such as attention deficit/hyperactivity disorder, learning disabilities, and persistent anxiety. We have reported that nicotine exposure in female mice during pregnancy, in particular from embryonic day 14 (E14) to postnatal day 0 (P0), induces long-lasting behavioral deficits in offspring. However, the mechanism by which prenatal nicotine exposure (PNE) affects neurodevelopment, resulting in behavioral deficits, has remained unclear. Here, we report that PNE disrupted the proliferation of neuronal progenitors, leading to a decrease in the progenitor pool in the ventricular and subventricular zones. In addition, using a cumulative 5-bromo-2'-deoxyuridine labeling assay, we evaluated the rate of cell cycle progression causing the impairment of neuronal progenitor proliferation, and uncovered anomalous cell cycle kinetics in mice with PNE. Accordingly, the density of glutamatergic neurons in the medial prefrontal cortex (medial PFC) was reduced, implying glutamatergic dysregulation. Mice with PNE exhibited behavioral impairments in attentional function and behavioral flexibility in adulthood, and the deficits were ameliorated by microinjection of D-cycloserine into the PFC. Collectively, our findings suggest that PNE affects the proliferation and maturation of progenitor cells to glutamatergic neuron during neurodevelopment in the medial PFC, which may be associated with cognitive deficits in the offspring.

PT564

Involvement of astrocyte-neuron lactate shuttle dysfunction in the cognitive impairment in diabetic mice

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Abstract

Diabetes mellitus is a risk factor for cognitive dysfunction. Several investigations have pointed that hippocampus is the key brain region in diabetic cognitive impairment. However, there are no effective curatives for diabetic cognitive impairment. Since recent reports suggested that the hippocampal astrocyte-neuron-lactate-shuttle (ANLS) is essential for the memory formation, the present study was then designed to investigate the role of ANLS in the cognitive impairment of streptozotocin-induced diabetic mice. Diabetic mice exhibit cognitive impairment in the novel object recognition test and reduced long-term potentiation (LTP) of synaptic transmission in hippocampus. These behavioral and electrophysiological changes are improved by L-lactate. We observed that inhibition of l-lactate synthesis by lactate dehydrogenase (LDH) inhibitor isosafrole caused cognitive dysfunction and reduced hippocampal LTP formation in non-diabetic, but not diabetic mice. Therefore, it is possible that diabetic cognitive dysfunction might be due to the reduced l-lactate supply in the hippocampus. We also observed that the expression of LDH5 was decreased in the hippocampus of diabetic mice as compared with non-diabetic mice. The expression of monocarboxylate transporter (MCT) that transport l-lactate, especially MCT1 and MCT4 isoform, was also decreased in the hippocampus of diabetic mice. These results indicated that the production and supply of l-lactate is attenuated in the hippocampus of diabetic mice. Since l-lactate is synthesized and released from the astrocytes, the expression of glial fibriary acidic protein (GFAP) in the hippocampus was examined. GFAP-immunoreactivity was increased in diabetic mice than non-diabetic mice, indicating that the function of hippocampal astrocytes might be changed. Inhibition of astroglial l-lactate production by pharmacological inhibition of MCT or glycogen phosphorylase caused the cognitive dysfunction in non-diabetic, but not diabetic mice. Therefore, it is possible that the cognitive impairment in diabetic mice is due to the dysfunction of the ANLS in the hippocampus.

PT565

Prenatal nicotine exposure impairs adolescent mouse hippocampal function

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Abstract

It is not clear how prenatal nicotine exposure (PNE) may cause cognitive impairment in offspring. In this study, we investigated whether the exposure to nicotine (0.2 mg/mL in drinking water with 2 % sucrose) during E14-P0 impaired hippocampus-dependent learning and memory in adolescence. In the hippocampal CA1 region, the induction and maintenance of *N*-methyl-D-aspartate (NMDA) receptor dependent long-term potentiation (LTP) was diminished by PNE, whereas the paired-pulse facilitation was not affected. Behaviorally, PNE impaired contextual- but not tone-dependent fear memory in 7- to 8-week-old mice. Both impairments were attenuated by the repeated co-treatment with methyllycaconitine (5 mg/kg s.c.), a nicotinic alpha 7 receptor antagonist. The results suggest that the nicotinic alpha 7 receptor dependent plasticity during embryonic period may be required for NMDA receptor-related long-term memory formation, and that PNE may disrupt this form of plasticity.