Alzheimer's disease. Nal tau deposition in normal aging and pathological process. PET THK-5351 enables sensitive and selective detection. In some cognitively normal individuals, THK retention is higher and more extensive in Alzheimer's disease. Patients with higher THK retention in the fusiform gyrus, inferior temporal and parietal cortices than healthy control subjects. Subjects with mild cognitive impairment showed a reference region. We compared the intensity and decline rates of FITC signal at each piece of the mask. The discrepancy transforms into the uniformity index (UI) and AAC. The UI was higher in cortex than simple diffusion. The AAC was higher in the artery-dominant piece. FITC-dextran moves into artery pieces faster than vein pieces and the difference is assumed to reflect the amount of PVD. In aged and AD mice, the UIs are relatively steady and the AAC is significantly decreased compared with normal mouse. These results indicate that PVD is impaired in AD.

PT572 Advances in the Development of Tau PET Radiotracers and Their Clinical Applications Kazuhiro Yanai 1, Ryuichi Harada 1 and Nobuyuki Okamura 1,2 1 Department of Pharmacology, Tohoku University School of Medicine, Sendai, Japan 2 Department of Pharmacology, Tohoku Medical and Pharmaceutical University, Sendai, Japan

Abstract Objective: Recent progress in the development of tau-selective PET tracers enabled non-invasive visualization of neurofibrillary pathology in the human brain. The amount and spatial distribution of tau tracer binding in the brain is closely associated with neurodegeneration and cognitive symptom of dementia. Therefore, tau PET imaging is expected to be useful for tracking disease progression, assessing disease severity, and accurately predicting dementia prognosis. The purpose of this study was to assess the clinical usefulness of THK tau PET tracers.

Methods: Subjects with Alzheimer’s disease, mild cognitive impairment and healthy controls (Number of each group is more than 10) underwent [18F]THK-5351 and [11C]PiB PET scans. Standard uptake value ratios between 50–60 minutes post injection for THK-5351 was calculated using the cerebellar cortex as a reference region.

Results: Subjects with mild cognitive impairment showed higher THK retention in the fusiform gyrus, inferior temporal and parietal cortices than healthy control subjects. Patients with Alzheimer’s disease showed higher and more extensive neocortical THK retention than subjects with mild cognitive impairment. In some cognitively normal individuals, THK retention was mildly elevated in the inferior temporal area. THK retention in the parahippocampal and fusiform gyrus, inferior temporal and parietal cortices was correlated with clinical severity of dementia.

Conclusion: THK-5351 enables sensitive and selective detection of neurofibrillary pathology in Alzheimer’s disease. Tau PET imaging with this tracer could be employed to study longitudinal tau deposition in normal aging and pathological process of Alzheimer’s disease.

PT573 The effects of intestinal endotoxemia on APP, PS1 and BACE expression in Alzheimer’s disease Bai Han1, Hejun Li1, Xizheng Shan2, Qin Sun3, Fan Wu1 Kezhan Liu1, Litao Ma1,2 1Shanxi Medical University, China, 2The General Hospital of The Chinese Armed Police Forces (CAPF) China, 3The Shanxi Provincial Children’s Hospital, China

Abstract Objective: Early our animal experiments study showed that AD rats occurs intestinal endotoxemia (IETM), and with the increasing of endotoxin, the APP, PS1, BACE mRNA increased and promote the generation of $A_{\beta}$. The aim of this study was to observe the occurrence of IETM in AD patients and to investigate the effect of intestinal endotoxemia in AD, provide evidence for the prevention and treatment of AD.

Methods According to the inclusion and the exclusion criteria, choose AD patients and healthy elderly, evaluate cognition by the Mini mental state examination (MMSE) and Alzheimer’s disease assessment scale cognitive subscale (ADAS-cog), detect the serum LPS, TNF-$\alpha$ and $A_{\beta}$ level by ELISA, detect APP, PS1 and BACE mRNA expression by real-time PCR. All the data were analyzed by SPSS 17.0.

Results 1. The AD group and the control group showed no significant differences in sex ($\chi^2=0.312, P=0.576$), age ($t=0.243, P=0.809$) and education level ($u=735.000, P=0.682$).
2. The MMSE score of AD group was significantly lower than the control group ($u=0.000, P<0.001$), the ADAS-cog score was significantly higher than that in control group ($u=0.000, P<0.001$), the differences were statistically significant.
3. The LPS ($u=0.000, P<0.001$), TNF-$\alpha$ ($t=6.175, P<0.001$), $A_{\beta}$ ($u=13.000, P<0.001$) levels were significantly higher than the control group, the differences were statistically significant.
4. The APP ($u=16.000, P<0.001$), PS1 ($u=24.000, P<0.001$) and BACE ($u=60.000, P<0.001$) mRNA expression levels in AD group were significantly higher than the control group, the differences were statistically significant.
5. The LPS level was highly related to the $A_{\beta}$ level ($r=0.894$), The LPS level was moderately related to the APP ($r=0.563$), BACE ($r=0.486$) mRNA expression. The correlation between LPS level and PS1 mRNA expression was not significant.

Conclusion: This study preliminary confirmed that AD patients occurs IETM, and IETM could upregulate the expression of APP, the key enzyme BACE by induce inflammatory cytokines, then promote $A_{\beta}$ generation, lead to the development of AD.

Key Words Alzheimer’s disease; intestinal endotoxemia; endotoxin; $\beta$ amyloid protein; presenilin

PT574 The increased serum lipopolysaccharides was associated with the TNFa and formation of $\beta$ amyloid protein in Alzheimer’s disease patients of Chinese Bai Han1, Hejun Li1, Xizheng Shan2, Qin Sun3, Fan Wu1 Kezhan Liu1, Hongxin Wang4 1Shanxi Medical University, China, 2The General Hospital of The Chinese Armed Police Forces (CAPF) China, 3The Shanxi Provincial Children’s Hospital, China, 4Peking An Ding Hospital, China

Abstract Objective: A growing body of studies has demonstrated bidirectional interplay between the brain and the gut microbiota. Endotoxemia produced by gut microbiota may have an effect on neurodegenerative diseases. However, it is unclear how changes of endotoxia are linked to the AD pathophysiology associated to their brain cognitive functions. Therefore the aim of our study was to define the existing correlation between endotoxia and AD.
Methods: Cognitive functions of 79 patients were assessed via Mini Mental Status Examination (MMSE) and Alzheimer’s Disease Assessment Scale Cognitive subscale (ADAS-cog). 40 healthy controls (HC) and 39 patients with AD. Levels of serum lipopolysaccharides (LPS), tumor necrosis factor-alpha (TNF-α) and β amyloid protein (Aβ) in plasma were determined by enzyme linked immunosorbent assay (ELISA). mRNA expressions in leukocytes of amyloid protein precursor(APP), presenilin1 (PS1) and β-site APP-cleaving enzyme 1 (BACE1) were determined using real-time PCR.

Results: Serum LPS level in patients with AD were significantly higher than that of healthy controls. Proinflammatory analysis showed that serum TNF-α level in patients with AD was prominently elevated in comparison to HC. And the results on the related markers about the formation of Aβ deposition revealed that serum Aβ level and mRNA manifestation levels of APP, PS1, and BACE1 in AD group were significantly higher than that of healthy controls. Correlation analysis showed that the LPS level was significantly positively related to the serum TNF-α level and Aβ levels, and APP and BACE1 mRNA expressions in AD patients, while only positively correlated with the Aβ level (r=0.827, p<0.001) and TNF-α level (r=0.780, p<0.001) in plasma, but no correlation with mRNA expressions of APP, PS1, and BACE1 (p>0.05).

Conclusion: AD patients have the increase of endotoxemia and endotoxicemia may upregulate the expression of APP and BACE1 by activating inflammation response with the representation of the elevated TNF-α level in blood.

Keywords: Microbiota-gut-brain axis; endotoxemia; Alzheimer’s disease; β-amyloid protein; presenilin

PT575
Citalopram Ameliorates Synaptic Plasticity Deficits in Different Cognition-associated Brain Regions Induced by Social Isolation in Middle-Aged Rats
Wei-Gang Gong, School of Medicine, Southeast University, China

Abstract
Our previous experiments demonstrated that social isolation (SI) caused AD-like tau hyperphosphorylation and spatial memory deficits in middle-aged rats. However, the underlying mechanisms of SI-induced spatial memory deficits remains elusive. Middle-aged rats (10 months) were group or isolation reared for 8 weeks. Following the initial four-week period of rearing, citalopram (10 mg/kg i.p.) was administered for 28 days. Then, pathophysiological changes were assessed by performing behavioral, biochemical and pathological analyses. We found that SI could cause cognitive dysfunction and decrease synaptic protein (synaptophysin or PSD93) expression in different brain regions associated with cognition, such as the prefrontal cortex, dorsal hippocampus, ventral hippocampus, amygdala and caudal putamen, but not in the entorhinal cortex or posterior cingulate. Citalopram could significantly improve learning and memory and partially restore synaptophysin or PSD93 expression in the prefrontal cortex, hippocampus and amygdala in SI rats. Moreover, SI decreased the number of dendritic spines in the prefrontal cortex, dorsal hippocampus and ventral hippocampus, which could be reversed by citalopram. Furthermore, SI reduced the levels of BDNF, serine-473-phosphorylated Akt (active form) and serine-9-phosphorylated GSK-3β (inactive form) with no significant changes in the levels of total GSK-3β and Akt in the dorsal hippocampus, but not in the posterior cingulate. Our results suggest that decreased synaptic plasticity in cognition-associated regions might contribute to SI-induced cognitive deficits, and citalopram could ameliorate these deficits by promoting synaptic plasticity mainly in the prefrontal cortex, dorsal hippocampus and ventral hippocampus. The BDNF/Akt/GSK-3β pathway plays an important role in regulating synaptic plasticity in SI rats.

Keywords: Social Isolation · Citalopram · Alzheimer’s disease · Synaptic Plasticity · Spatial Memory

PT576
Fluvoxamine alleviates ER stress via induction of Sigma-1 receptor.
Takashi Kudo, Osaka University, Japan

Abstract
We have recently demonstrated that induction of sigma 1 receptor (Sig-1R) expression is caused by endoplasmic reticulum (ER) stress through the PERK pathway, which is one of the cell’s responses to ER stress. In addition, it has been demonstrated that cell death signal transmission can be suppressed by up-regulation of Sig-1R. Fluvoxamine (Flv) is a selective serotonin reuptake inhibitor (SSRI) that it is known to have a high affinity for Sig-1R. In the present study, we have shown that treatment of neuroblastoma cells with Flv induces Sig-1R by directly increasing ATF4 translational regulation without any involvement of PERK pathway. The Flv-mediated induction of Sig-1R prevents neuronal cell death by ER stress. Moreover the ER stress resistance by Flv results in reduction of infarction area due to focal cerebral ischemia in mice. This study shows that Flv, frequently used in clinical practice, has the property of alleviating ER stress suggesting that it can be used as a feasible therapy for cerebral diseases caused by ER stress.

PT577
Distribution of Human Umbilical Cord Blood-derived Mesenchymal Stem Cells (hUCB-MSCs) in the Alzheimer’s Disease Transgenic Mouse after a Single Intravenous Injection

Abstract
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Sang Eon Park1,2,3,4, Na Kyung Lee1,2,3,4, Jeongmin Lee1,2,3,4, Jung Won Hwang1,2,3,4, Soo Jin Choi5, Hyeri Huang6, Brian Hyung7, Jong Wook Chang8,9, and Duk L. Na1,2,3,4

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