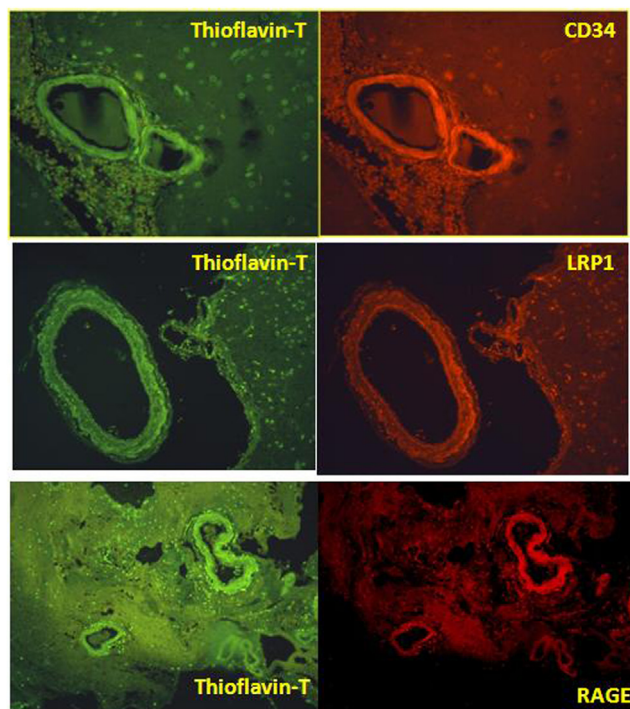


Background: The spontaneous intracerebral hemorrhage (ICH) need to receive surgical treatment is the most serious and least treatable form of stroke. We aim to investigate the prevalence of cerebral amyloid angiopathy (CAA) in Chinese patients with spontaneous intracerebral hemorrhage (ICH), who received surgical treatment. Further, to explore the connection between low-density lipoprotein receptor related protein-1 (LRP1) and receptor for advanced glycation end products (RAGE), the main receptors for amyloid-beta peptide (A β) clearance. **Methods:** Surgical samples of 46 ICH patients from 2010 to 2011 of Nanjing Medical University Affiliated Brain Hospital were enrolled, which included 27 male patients and 19 female patients. The average age was 56 ± 16 yo. The co-expression of A β , RAGE and LRP1 protein in the samples were detected by immunohistochemical fluorescence and semi-quantitative analysed. **Results:** Among 46 cases, 8 patients (17.39%) are diagnosis as CAA by Pathology. The ratio between male and female patients reaches 27: 19 and the positive CAA is 5: 3. Based on the age of onset, patients can be divided into five parts, that is 0% of these patients of younger than 40 years have been confirmed CAA, 10% of the 40 to 49 group, 9.1% of the 50 to 59 group, 23.08% of the 60 to 69 group, the age greater than 70 years old reaching 27.27%. The abnormal proportion of LRP1 protein in patients with ICH achieves the same amount as that of CAA, while there is no unusual expression in non-CAA patients. LRP1 expression is reduced to about 23.03% and RAGE expression is increased to about 32.45%. **Conclusions:** CAA is one of the major reasons leading to the disease of ICH. The abnormal expression of CAA-related immune-angiogenic factors RAGE and LRP1 protein prompts CAA to result in the inflammatory damage which plays a vital role in the ICH pathogenesis.



P2-230 WITHDRAWN

P2-231 PULSE PRESSURE AND ATHEROSCLEROSIS, ARTERIOLOSCLEROSIS AND CORTICAL MICROINFARCTS IN INDIVIDUALS WITH CLINICAL ALZHEIMER'S DISEASE

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Background: Pulse pressure (PP), calculated as systolic (SBP) minus diastolic blood pressure (DBP), is generally considered a surrogate marker of arterial stiffness. Few studies have examined changes in PP and BP before death or the association between sustained elevated PP and cerebrovascular pathology in clinical Alzheimer's Disease (AD). Understanding cerebrovascular disease is important because it may increase the risk of AD diagnosis, earlier disease onset, or faster cognitive decline. **Methods:** Data from the Uniform Data Set (UDS) were used to study 237 patients with an AD diagnosis at their last visit before death, autopsy data, and ≥ 2 BP measures in the three years before death. Linear and logistic regression were used to estimate the: (1) average and annual change in PP, SBP, and DBP three years before death; (2) average PP, SBP, and DBP just before death; and (3) association between sustained elevated PP (> 70 mmHg over ≥ 2 visits three years before death) and atherosclerosis, arteriolosclerosis, and cortical microinfarcts at autopsy. All models used Generalized Estimating Equations to account for clustering by Center. Descriptive Aims 1 and 2 were examined using unadjusted analyses; Aim 3 models controlled for death age, demographics, comorbidities, and medication use, and restricted to those with normal (≤ 140 mmHg) SBP one year before death. **Results:** Three years preceding autopsy, the average PP, SBP, and DBP (annual change) was 57 mmHg (-3.3 mmHg/year), 129 mmHg (-1.8 mmHg/year), and 71 mmHg (-1.4 mmHg/year), respectively. The 3-year decline in PP was greater but not significantly different ($p=0.15$) for those with sustained elevated PP (-12.6 mmHg/year) compared to those with sustained lower PP (-2.1 mmHg/year). The average PP, SBP, and DBP in the year before death were 53 mmHg, 125 mmHg, and 70 mmHg, respectively. Results from the multivariable analysis, restricting to those with normal SBP, suggest an association between sustained elevated PP and arteriolosclerosis (OR: 2.01; 95% CI: 0.86-4.66) and cortical microinfarcts (OR: 3.19, 95% CI: 1.07-9.49). **Conclusions:** Our study suggests that sustained elevated PP is associated with arteriolosclerosis and cortical microinfarcts among clinical AD patients with normal SBP. Based on these findings, our future analyses will examine whether elevated PP is associated with rate of cognitive decline in AD.

P2-232 CEREBROVASCULAR DISEASE AND HIGHER PREVALENCE OF DEMENTIA IN INDIVIDUALS WITH FEWER YEARS OF EDUCATION: A NEUROPATHOLOGICAL STUDY

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Background: Dementia is more frequent in low educated individuals probably due to low cognitive reserve. However, educational level is linked to several other features that have impact on the risk or protective factors for dementia. Low educational level may be associated with inappropriate medical care for disorders that predispose to cerebrovascular disease. **Methods:** Brains of deceased individuals aged 50 years or over were collected when a reliable informant signed a written consent form to donate the brain and to provide information through a comprehensive interview about the deceased. From April 2004 to November 2012, a total of 745 cases (380 women) have completed interview and pathological examinations. Educational level (years of schooling) ranged from 0 to 19 years [mean 3.9 (± 3.5)]. Socioeconomic status (SES) was classified into 5 levels. Neuropathological examination was performed according to standard protocols using immunohistochemistry. Cerebrovascular disease was classified as present when infarcts, arteriolosclerosis or both were detected in the neuropathological examination. **Results:** Cerebrovascular disease was present in

205 cases (27.5%; 99 arteriolosclerosis, 65 infarcts and 41 cases both). Multivariate analysis using logistic regression showed that cerebrovascular disease was more frequent in individual with higher age ($p=0.011$; Exp (B)= 1.561; 95% CI 1.106-2.202), less years of schooling ($p=0.035$; Exp (B) = 0.690; 95% CI 0.488-0.975) and lower SES ($p=0.034$; Exp (B)= 0.662; 95% CI 0.453-0.969). **Conclusions:** Higher prevalence of dementia in low educated individuals may be not only due to low cognitive reserve, but also to the increased burden of cerebrovascular disease.

P2-233

ASSESSMENT OF CEREBRAL VASOREACTIVITY USING ULTRASOUND TECHNIQUES IN ALZHEIMER'S DISEASE

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Background: Alzheimer's Disease (AD) is the most important cause of neurodegenerative dementia and its main pathological hallmarks include neuritic plaques and neurofibrillary tangles, involved in the beta amyloid cascade. Nevertheless, changes in cerebral hemodynamic might play a role in the cognitive decline. The aims of this study were to assess in AD subjects the cerebral vasomotor reactivity and to evaluate the possible correlation between this reactivity and the cognitive deficit. **Methods:** Thirty-six subjects (mean age \pm SD, 68.58 ± 6.16 years) were consecutively enrolled. We recruited twenty-five subjects affected by AD, matched for age and education to eleven healthy control. Subjects with a Mini Mental State Evaluation (MMSE) score less than 15, cerebrovascular disease history, severe leucoencephalopathy and carotid stenoses major than 40% were excluded. All the subjects underwent MRI imaging, Neuropsychological evaluation and Carotid Duplex Ultrasonography. Cerebral vasomotor reactivity was assessed using the transcranial Doppler-based breath-holding index test (BHI). **Results:** Both Cerebral blood flow velocity at the steady-state (CBFV) and BHI values were significantly lower in AD subject than in healthy control (46.34 ± 7.61 cm/s vs 55.1 ± 8.09 cm/s, $p=0.007$; 0.99 ± 0.26 vs 1.21 ± 0.24 , $p=0.031$). Furthermore, we found a correlation between CBFV value and MMSE score ($p=0.003$, $r=0.654$; Spearman's correlation), but no correlation between BHI value and MMSE score. No significant relationship was found between White Matter Lesions on MRI and both CBFV and BHI values. However, the AD subjects with carotid stenoses had a lower CBFV and BHI values than those without carotid stenoses (43.12 ± 7.56 cm/s vs 48.68 ± 7.07 cm/s, $p=0.008$; 0.9 ± 0.23 vs 1.06 ± 0.27 , $p=0.04$; respectively). Considering the correlation between each neuropsychological test and the cerebrovascular reactivity indices, we only found a significant correlation with the Digit Span test score (CBFV: $r=0.542$, $p=0.046$; BHI: $r=0.525$, $p=0.05$; Spearman's correlation). **Conclusions:** Our study suggests that AD subjects have changes in both dynamics and structure of their cerebral blood flow circulation. In particular, the CBFV reduction is correlated with the severity of the cognitive decline, suggesting that it can influence the cognitive decline in AD subjects.

P2-234

THE BRAIN AGING: BETWEEN BETA-AMYLOID OLIGOMERS AND INDIVIDUAL VARIABILITY OF ALZHEIMER'S DISEASE-TYPE LESIONS

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Background: The formation of neurofibrillary tangles (NFTs), senile plaques (SPs) and the synaptic loss in both cognitively intact individuals and patients with Alzheimer's disease (AD) characterize the neuropathology of brain aging. Following various observations, there is a differential cortical vulnerability to the degenerative process in extreme aging. In very old individuals the distribution and severity of the AD-type lesions could be different compared to younger persons. It is well known that in normal aging

NFTs are usually restricted to the hippocampus, and clinical signs of dementia appear when the temporal neocortex is involved. The A β oligomer toxicity has been postulated in absence of major A β -plaques correlation with the clinical severity. **Methods:** With immunohistological methods the distribution of A β -oligomers, amyloid plaques and NFTs has been studied in the hippocampal formation and the temporal neocortex as well as in the frontal and occipital cortical areas, in 74 cases (43 to 104 years old). A parallel evolution in the presence and the severity of A β -oligomers and plaques has been observed in all the studied areas. **Results:** A parallel evolution in the presence and the severity of A β -oligomers and plaques has been observed in all the studied areas. Moreover, in aging brain the microvascular pathology progresses, including amyloid angiopathy. **Conclusions:** The anatomical inter-individual variability, mainly of the entorhinal cortex, is very important and could be related to functional reserve at the onset of cognitive decline. Microvascular changes, including amyloid angiopathy, increase with age.

P2-235

VISUAL REPRODUCTION ON THE WECHSLER MEMORY SCALE-REVISED AS A PREDICTOR OF ALZHEIMER'S DISEASE IN JAPANESE PEOPLE WITH MILD COGNITIVE IMPAIRMENT

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Background: Immediate and delayed Visual Reproduction (VR) subtest scores (VR-I and VR-II, respectively) in the Japanese version of the Wechsler Memory Scale-Revised (WMS-R-J) have been reported to be significantly higher in healthy Japanese subjects than in age-matched healthy American subjects. Although nonverbal episodic memory tests, such as the VR subtests of the WMS-R, have been recommended to be included in the diagnostic criteria for mild cognitive impairment (MCI), the characteristics of VR in Japanese patients with MCI have not been clarified. **Methods:** We evaluated the VR scores of WMS-R-J in 27 patients with MCI out of 144 enrolled Japanese participants (MMSE score ≥ 24). We then compared these scores with those of subjects without dementia (ND) or patients with Alzheimer's disease (AD). We compared the VR scores of patients with MCI who converted to AD within 2 years with those of non-converted patients. **Results:** The mean baseline MMSE score of patients with MCI was 27.6. The annual conversion rate of MCI to AD was 18.8% during 3.4 ± 1.7 years. Mean VR-I and VR-II baseline scores for MCI patients were 33.3 ± 5.6 and 20.5 ± 14.0 , respectively. Mean VR-II scores for converters ($n = 10$) and non-converters ($n = 13$) were 7.2 ± 8.7 and 29.8 ± 9.3 , respectively, and sensitivity and specificity for conversion prediction by VR-II were 90% and 84.6%, respectively. Multiple logistic regression analysis using age, sex, and educational years as additional independent variables revealed that VR-II, VR-II/I, and hypoperfusion of the precuneus in SPECT were significantly useful for predicting conversion. The difference in Z-scores of the mean VR-II between converters and non-converters was 2.28, which was higher than that previously reported in the USA. **Conclusions:** Our results indicate that VR of WMS-R-J in Japanese patients with MCI is potentially sensitive and useful for predicting conversion to AD within 2 years. Our results also indicate that visual memory may vary according to the racial or educational background in each country, and suggest that these factors should be closely monitored when comparing non-verbal cognitive functions.

P2-236

THE MCI INDEX: RISK ASSESSMENT OF COGNITIVE DECLINE

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