Background: Alzheimer’s disease (AD) is an incurable and progressive neurodegenerative disorder. Diagnosis of Alzheimer’s disease (AD) through amyloid positron emission tomography (PET) is expensive, has limited availability, and exposes subjects to radiation. Thus, we sought to develop a non-toxic nanoparticle to visualize amyloid plaques for diagnosis of AD by a more affordable, more accessible, and non-radioactive method, magnetic resonance imaging (MRI).

Methods: An iron oxide core was coated by a layer of curcumin through hydrogen-bonding and was encapsulated by polyethylene glycol-polyactic acid (PEG-PLA) co-block polymer and polyvinylpyrrolidone (PVP) by a multi-inlet vortex mixer (MIVM). Curcumin conjugated magnetic nanoparticles (Cur-MNPs) were characterized by Fourier transform infrared spectroscopy (FTIR), thermal gravimetric analysis (TGA), X-ray photoelectron spectroscopy (XPS) and Time-of-flight secondary ion mass spectrometry (ToF-SIMS). The nanoparticles were tested for cytotoxicity on Madin-Darby canine kidney (MDCK) and differentiated human neuroblastoma cells (SH-SY5Y). The apparent permeability coefficient was determined using an in vitro blood brain barrier model. On serial brain sections of Tg2576 mice, ex vivo amyloid plaque staining by Cur-MNPs was compared with staining with Thioflavin T and by curcumin.

Results: The mean diameter of iron oxide nanoparticles in suspension was $\approx 80$ nm. Characterization of Cur-MNPs showed that the polymeric coating was on the outer layer, while curcumin was attached to the iron oxide. Cur-MNPs were not cytotoxic to either MDCK or SH-SY5Y cells. The apparent permeability coefficient (Papp) was $2.3 \pm 0.72 \times 10^{-5}$ cm/s, based on an in vitro blood brain barrier model. Cur-MNPs exhibited the same ex vivo amyloid plaque binding and specificity as curcumin or Thioflavin. Conclusions: Our novel iron oxide nanoparticle formulation demonstrated amyloid plaque detection ability on AD Tg2576 mice brain sections. It displayed no cytotoxicity on cultured cells. The formulation can be further investigated for diagnosis of AD.

Figure 1. a) Hydrodynamic size of Cur-MNPs at different stage - red line: freshly-made; blue line: 24 hours after dialysis. b) Transmission electron microscopy (TEM) image of Cur-MNPS, the core mean particle size $\sim 9$ nm.

Figure 2. Histochemically stained $A\beta$ plaques on serial brain sections of Tg2576 mice Both top and bottom images were viewed by confocal microscopy. Top images were bright view and bottom images were fluorescence signal from stained chemical (from left to right stained by thioflavin T, curcumin or Cur-MNPs). It proved that Cur-MNPs have same $A\beta$ plaque binding as thioflavin T or curcumin.

O1-12-02 AMYLOID BURDEN, CORTICAL THICKNESS, AND COGNITIVE FUNCTION IN THE WISCONSIN REGISTRY FOR ALZHEIMER’S PREVENTION

Benjamin Matthew Doherty 1, Jennifer M. Oh 1, Stephanie A. Schultz 2, Rebecca L. Kosciuk 3, N. Maritza Dowling 4, Todd E. Barnhart 5, Dhanabal Murali 6, Catherine L. Gallagher 1, Cynthia M. Carlsson 2, Barbara B. Bendlin 1, Asenath LaRue 3, Bruce P. Hermann 4, Howard A. Rowley 1, Sanjay Ashiana 2, Mark A. Sager 7, Brad T. Christian 2, Sterling C. Johnson 8, Ozioma C. Okonkwo 9, 1 Wisconsin Alzheimer’s Disease Research Center, Madison, Wisconsin, United States; 2University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, United States; 3University of Wisconsin - Madison, Madison, Wisconsin, United States; 4University of Wisconsin-Madison, Middleton, Wisconsin, United States; 5UW, Madison, Wisconsin, United States; 6UW Section of Geriatrics/Gerontology, Madison, Wisconsin, United States; 7University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, United States; 8VA GRECC, Madison, Wisconsin, United States; 9University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, United States. Contact e-mail: ben.m.doherty@gmail.com

Background: The preclinical stage of Alzheimer’s disease is characterized by gradual accumulation of amyloid-β ($A\beta$), in the absence of detectable clinical symptoms. Existing investigations on the influence of early $A\beta$ accumulation on cognitive function and brain morphometric measures have been primarily conducted in older cognitively-normal (CN) individuals. This study investigated the associations between $A\beta$ burden, cortical thickness, and cognition in younger CN individuals.

Methods: Participants were 109 cognitively normal (CN) late-middle-aged adults (age range, 46.93-71.26 years) enrolled in the Wisconsin Registry for Alzheimer’s Prevention. All participants underwent PiB-PET (Siemens HR+) and anatomical T1 MR (GE 3.0T) imaging. They also completed a comprehensive cognitive exam within 6.60±5.97 months of the PiB-PET scan. The cognitive test scores mapped onto six cognitive factors: Immediate Memory, Verbal Learning & Memory, Working Memory, Speed & Flexibility, Visuospatial Ability, and Verbal Ability. Participants were classified as $A\beta$ positive ($A\beta+$) or $A\beta$ negative ($A\beta-$) based on visual rating of PiB DVR maps. Cortical thicknesses of AD-vulnerable ROIs were obtained from MR images using FreeSurfer. Analyses of covariance, adjusted for relevant covariates, were used to investigate group differences in cortical thickness and cognitive factor scores. Finally, covariate-adjusted multiple regression models, which included age*$A\beta$ rating interactions, were used to investigate whether age-related cortical thinning and cognitive decline is more pronounced in $A\beta+$ individuals.

Results: Compared to the $A\beta-$ group, the $A\beta+$ group exhibited significant cortical thinning of the entorhinal cortex ($p=0.017$). Secondary analyses revealed significant negative correlations between co-localized $A\beta$ burden and cortical thickness in both the entorhinal cortex ($p=0.005$) and amygdala ($p=0.025$). The $A\beta+$ group also tended to have more pronounced age-related cortical thinning in the parahippocampal gyrus ($p=0.058$). With respect to cognition, compared to the $A\beta-$ group, the $A\beta+$ group had lower, but nonsignificant, test scores on all cognitive measures, and significantly greater age-associated cognitive decline on measures of Speed & Flexibility ($p=0.034$), Verbal Ability ($p=0.058$), and Visuospatial Ability ($p=0.089$).

Conclusions: Our findings suggest that early $A\beta$ aggregation has deleterious effects on brain structure and cognitive function, even in midlife; and that the temporal lag between $A\beta$ deposition and the inception of neurodegenerative/cognitive changes might be narrower than currently thought.

O1-12-03 THAL AMYLOID PHASE: CLINICOPATHOLOGIC AND PiB-PET IMPLICATIONS OF AD PATHOPHYSIOLOGY

Melissa Erin Murray 1, Neill R. Graff-Radford 2, Amanda M. Liesinger 3, Ashley D. Cannon 1, Bhupendra Rawal 1, Ronald Carl Petersen 1, Clifford R. Jack 4, Kejal Kantarci 5, Owen A. Ross 6, Ranjan Duara 7, Val J. Lowe 8, Dennis W. Dickson 1, 1 Mayo Clinic, Jacksonville, Florida, United States; 2Mayo Clinic Jacksonville, Jacksonville, Florida, United States; 3Mayo Clinic, Rochester, Minnesota, United States; 4Wien Center for...