FEATURED RESEARCH SESSIONS
F4-01
ADVANCES IN NUTRITION AND DEMENTIA RESEARCH

F4-01-01 HABITUAL COFFEE AND TEA CONSUMPTION, GENETIC VARIATION AND COGNITIVE ABILITY IN THE UK BIOBANK

Marilyn C. Cornelis, *Northwestern University, Chicago, IL, USA. Contact e-mail: marilyn.cornelis@northwestern.edu*

Background: Coffee and tea are important sources of caffeine, the most commonly ingested behaviorally active substance in the world. Evidence points to the premise that caffeine may benefit cognition. However, factors that contribute to variation in caffeine metabolism may interact with caffeine intake and modify its physiological effects. **Methods:** The UK Biobank includes 500,000+ persons aged 37-73 years recruited in 2006-2010. Participants provided biological samples and completed touchscreen questionnaires regarding sociodemographic factors, medical history, lifestyle, and diet. Usual coffee and tea intake was self-reported in cups/d. Between 100,217 and 471,715 participants with data also completed at least one of seven self-administered cognitive functioning tests using the touchscreen system (2006-2010): prospective memory (PM), pairs matching (Pairs), fluid intelligence (FI), and reaction time (RT), or on home computers (2014): symbol digit substitution (SDS), Trail Making Test A (TrailA) and B (TrailB). Multivariate regressions were used to examine the association between coffee and tea consumption [each modeled as 0 (ref), <1, 1, 2-3 or 4+ cups/d] with cognition test scores, adjusting for sociodemographic, lifestyle and dietary factors. We examined beverage interactions with a genetic caffeine-metabolism score (CMS) derived from variants in *CYP1A2* and *AHR*. **Results:** Coffee consumption was associated with better performance on FI, RT, Pairs, TrailB, and PM (P-trend <0.004). Consuming predominately decaffeinated coffee (compared to no coffee) was associated with better performance on all tests (P<0.0003). Tea consumption was associated with poor performance on all tests (P<0.0001). Significant CMS×coffee interactions were observed for FI, RT, Pairs, TrailB and PM (P<0.006). The better performance on these tests with coffee consumption was greatest among those with a lower CMS (slower caffeine metabolism). CMS×decaf-coffee interactions were observed for FI, RT and Pairs (P<0.02), with patterns similar to those for CMS×coffee. No statistically significant CMS×tea interactions were observed. **Conclusions:** Coffee consumption was associated with better cognitive ability. The stronger associations observed among those with a lower CMS suggests that caffeine may partly underlie the observed association. Tea consumption was associated with poor cognitive ability and warrants further investigation.

F4-01-02 LEAFY GREEN VEGETABLE CONSUMPTION IS ASSOCIATED WITH REDUCED BRAIN AD NEUROPATHOLOGY

Martha Clare Morris[1], Julie A. Schneider[1], Sarah Booth[2], Thomas Holland[3], Puja Agarwal[4], Yamin Wang[4], *[1]Rush University Medical Center, Chicago, IL, USA; [2]Tufts University, Boston, MA, USA; [3]Rush University, Chicago, IL, USA; [4]Rush University, Chicago, IL, USA. Contact e-mail: Martha_Morris@rush.edu*

Background: Previous studies found strong associations of leafy green vegetable consumption and slower cognitive decline with age. Leafy green vegetables are rich sources of lutein, folate, β-carotene, vitamin K, vitamin E, kaempferol and nitrate, all of which have been found to be associated with slower cognitive decline. In this study, we investigated potential mechanisms for these associations in human brain. **Methods:** The study was conducted in 445 deceased participants of the Rush Memory and Aging Project, a clinical-neuropathologic cohort study in Chicago; at enrollment participants are dementia free. Participants completed at least one valid food frequency questionnaire (FFQ) containing 138 food items including three on leafy green vegetables. Energy-adjusted daily intakes of specified nutrients were computed from all food items. Post-mortem brains were studied for dementia pathologies and summary measures were computed based on published criteria: NIA-Reagan score (low, intermediate, high AD pathology), Braak stage (neurofibrillary tangle stage I – VI), CERAD score (neuritic plaque severity), Lewy bodies, and macro- and micro-infarcts. Primary analyses used averaged dietary intakes from valid FFQs collected over the study follow-up. Linear and logistic regression models were used to assess the cross-sectional associations of the dietary variables with brain neuropathologies. **Results:** In separate models adjusted for age at death, sex, and education, persons in the top quartile of leafy green vegetable consumption (mean, 1.1 servings per day) compared with those in the lowest quartile (mean, 0.12 servings/d) had lower Braak stage (b= -0.44, SE=.16, p=.005), lower NIA-Reagan scores (less AD pathology) (b= -0.24, SE=.09, p=.01), and reduced odds of macro-infarcts (OR=0.48, 95% CI: 0.25, 0.93). No associations were observed between leafy greens and other neuropathologies. In separate adjusted models of the nutrients, inverse associations were observed for lutein and Braak and CERAD scores; vitamin K and Braak score; folate and NIA-Reagan and Lewy bodies; β-carotene and CERAD score and Lewy bodies; and vitamin E and NIA-Reagan and CERAD scores. **Conclusions:** Consumption of 1 or more servings per day of green leafy vegetables is associated with less AD brain neuropathology and macro infarcts. Leafy greens contain a number of nutrients that may provide neuroprotection through different mechanisms.

F4-01-03 A BIOMARKER-BASED NUTRITIONAL RISK INDEX EXPLAINS THE HETEROGENEITY IN RATES OF COGNITIVE DECLINE IN THE MULTIDOMAIN ALZHEIMER PREVENTION TRIAL (MAPT)

Gene L. Bowman[1], Hiroko Dodge[2], Sophie Guyonnet[3], Nina Zhou[4], Juliana Donohue[1], Aline Bichel[1], Jeroen Schmitt[5], Claudie Hooper[6], Tamas Barfai[7], Sandrine Andrieu[8], Bruno Vellas[8], *[1]Nestle Institute of Health Sciences, Lausanne, Switzerland; [2]Oregon Health & Science University, Portland, OR, USA; [3]University of Toulouse III, Toulouse, France; [4]University of Michigan, Ann Arbor, MI, USA; [5]Nestle Research Center, Lausanne, Switzerland; [6]Gerontopole, Centre Hospitalier Universitaire, Toulouse, France; [7]Stockholm University, Stockholm, Sweden; [8]Centre Hospitalier Universitaire Toulouse, Toulouse, France. Contact e-mail: drgenebowman@gmail.com*

Background: Nutritional status and nutrient interaction are underappreciated in the design and interpretation of clinical nutrition trials. Nutritional biomarkers are objective measures of diet and metabolism readily available to the brain. We created a nutritional risk index (NRI) to test the hypothesis that nutritional status and nutrient interaction explain the heterogeneity in rates of cognitive decline in the MAPT. **Methods:** Erythrocyte omega 3 fatty acids measured by GC-FID, plasma homocysteine by enzymatic assay and serum

25-hydroxyvitamin D by electrochemiluminescence in samples from a subset of participants from each trial arm (n = 780). The cut-offs for each were based on existing literature. NRI scores ranged from 0 (all 3 optimum) to 3 (all 3 suboptimum). The cognitive composite Z scores collected over 3 years in the parent MAPT were fit with linear mixed-effects models. **Results:** Mean age was 75 (4.5), 67% were women, mean MMSE was 28 (1.6) and 20.7% carried an *APOE4* allele. Over half of the population presented with nutritional risk (57.1% with NRI = 1) and 31.6% with NRI = 2. In adjusted mixed models, each unit increase in the NRI was associated with an annual incremental increase in rates of cognitive decline compared to those without nutritional risk (NRI = 0) (e.g., NRI = 1 (β = -0.04, p = 0.0325); NRI = 2 (β = -0.08, $p <$ 0.0001); NRI = 3 (β = -0.10, p = 0.0017). Subjects with NRI = 0 appreciated a 0.03 annual unit increase in their cognitive composite Z score over 3 years. Further controlling for *APOE4,* trial arm, baseline cognitive state and their interactions with time did not materially change the results. **Conclusions:** This biomarker-based Nutritional Risk Index that includes omega 3 fatty acids, vitamin D and homocysteine explains the heterogeneity observed in rates of cognitive decline in older non-demented adults with subjective memory concerns. Whether reducing nutritional risk by optimizing these nutritional biomarkers can slow cognitive decline will require formal clinical trial testing. The prudent deployment of nutritional biomarkers will advance clinical trials and deepen our understanding of nutrition and brain health.

F4-01-04 APOE GENOTYPE INFLUENCES BRAIN TO BLOOD GLUCOSE RATIOS AFTER HIGH FAT FEEDING

Angela J. Hanson[1], Kelly C. Stewart[1], Deepa Subramaniyan[1], Suzanne Craft[2], William A. Banks[3], *[1]University of Washington, Seattle, WA, USA; [2]Wake Forest School of Medicine, Winston-Salem, NC, USA; [3]Geriatric Research Education and Clinical Center, Veterans Affairs Puget Sound Health Care System and Division of Gerontology and Geriatric Medicine, Department of Medicine, University of Washington School of Medicine, Seattle, WA, USA. Contact e-mail: hansonaj@uw.edu*

Background: Glucose hypometabolism is a feature of Alzheimer's disease (AD), and occurs earlier in APOE E4 (E4+) individuals. Post-prandial glucose metabolism differs by E4 status; however, little is known about how this influences brain glucose. We examined the relationship between blood and cerebrospinal fluid (CSF) glucose in an ongoing meal intervention in E4+ and E4- adults. **Methods:** Healthy older adults (n=13, 54% E4+) ingested a 700 calorie high fat meal (HFM) or high carbohydrate meal (HCM) in a random crossover design. Each meal was 20% protein; HCM was 25% total fat (5% saturated), 55% carb, glycemic index < 55 and HFM was 50% total fat (25% saturated), 30% carb, glycemic index >70. Blood samples were taken at 7 time points up to 4 hours, and CSF was collected at 4h. Data were analyzed using t tests and Pearson correlation. **Results:** CSF glucose was higher after HCM compared to HFM (63.1 ± 5.8 vs 61.6 ± 4.8 mg/dl, p=0.029). For the group, CSF glucose did not significantly correlate with blood glucose at any of the 7 time points; highest correlation was noted with 2h blood glucose. There was a trend toward higher 2h blood glucose after HCM, but the CSF:blood ratio did not differ by meal (Table). When stratified by E4, findings did not differ for HCM. For HFM, the E4+ group had higher 2h blood glucose (103.1 ± 9.6 vs 90.3 ± 9, p=0.03) but lower CSF:blood ratios (0.59 ± 0.04 vs 0.7 ± 0.04, p=0.0006). **Conclusions:** In this intervention, 4h CSF glucose was higher after high carb compared to high fat feeding, and for both meals CSF glucose correlated stronger with 2h blood glucose. Despite a higher blood glucose after HFM, the E4+ group showed an 11 percentage point lower CSF:blood glucose ratio than the E4- group. Whether this reflects decreased transport or increased utilization is unknown. In summary, meals with varying macronutrients can acutely affect CSF glucose, and the relationship between blood and CSF glucose differs by E4 status after high fat feeding.

	HIGH FAT MEAL (HFM)			HIGH CARB MEAL (HCM)		
	CSF glu	2h blood glu	Ratio	CSF glu	2h blood glu	Ratio
Group (n=13)	61.6 ± 4.8*	97.2 ± 11.1	0.64 ±0.1	63.1 ±5.8*	109.2 ± 19.6	0.61 ±0.09
E4 Neg (n=6)	62.7 ±3.4	90.3 ±9 $	0.7 ± 0.04 %	65.2 ±5.1	112 ±26	0.64 ±0.09
E4 Pos(n=7)	60.7 ±5.8	103.1 ±9.6 $	0.59 ± 0.04 %	61.3 ±6.1	106.9 ± 13.8	0.58 ±0.09

* HCM > HFM, paired t test p=0.029, $ E4+ > E4- for HFM, p=0.03, % E4- > E4- for HFM, p=0.0006

FEATURED RESEARCH SESSIONS
F4-02
NEW APPROACHES TO THE TREATMENT OF AGITATION ASSOCIATED WITH NEUROCOGNITIVE DISORDERS

F4-02-01 ALGORITHMIC APPROACH TO THE MANAGEMENT OF AGITATION AND AGGRESSION IN ALZHEIMER'S DISEASE

Sanjeev Kumar[1,2], Amruta Shanbhag[1,2], Simon Davies[1,2], Donna Kim[1,2], Philip Gerretsen[1,2], Ariel Graff-Guerrero[1,2], Sarah Colman[1,2], Saima Awan[1], Jyll Simmons[1], Amer M. Burhan[3], Bruce G. Pollock[1,2], Benoit H. Mulsant[1,2], Tarek K. Rajji[1,2], *[1]Centre for Addiction and Mental Health, Toronto, ON, Canada; [2]University of Toronto, Toronto, ON, Canada; [3]Western University, London, ON, Canada. Contact e-mail: sanjeev.kumar@camh.ca*

Background: Agitation and aggression affect more than 80% of patients with Alzheimer's disease (AD) at some point in their illness. Concerns have been raised about the inappropriate psychotropic use (e.g. polypharmacy), which may be associated with serious adverse effects in these patients. We designed and implemented a measurement-based algorithm, an integrated care pathway (ICP) that consists of four key components: (1) medical/ psychiatric work up; (2) caregiver education; (3) non-pharmacological interventions; and (4) a sequential pharmacological algorithm with clear decision points guided by standardized assessments. The aim of this study was to assess the effectiveness of ICP in treating agitation and to compare the ICP with usual care. **Methods:** Patients diagnosed with Dementia of AD or mixed AD+ vascular type with clinically significant agitation admitted to geriatric psychiatry inpatient unit from year 2010-2017 were enrolled. Effectiveness of the ICP was assessed using Cohen Mansfield Agitation Inventory – Frequency (CMAI-F), and Neuropsychiatric Inventory Questionnaire (NPI-Q) scores at entry and exit. We examined outcomes of polypharmacy, length of stay, and use of emergency seclusion/restraints.