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Poster Abstracts

BON01

Macular Pigment and Visual Function in Patients with Glaucoma

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Purpose: Recent studies have shown that macular pigment (MP) is significantly lower in glaucoma patients. In our study, we used the Heidelberg Spectralis dual-wavelength autofluorescence (AF) technology to study the relationship between MP and visual function in this population.

Methods: This cross-sectional study included 85 glaucoma patients and 22 controls. All subjects had standard automated perimetry (SAP) and retinal nerve fiber layer (RNFL) thickness measurements. Intake of macular carotenoids was estimated using a dietary screener. The association between MP volume and glaucoma was investigated using linear regression models accounting for potential confounding factors.

Results: Glaucoma subjects had significantly worse SAP mean deviation (MD) and lower RNFL thickness in the study eye compared to control subjects ($P < 0.001$ for both). MP (volume) was statistically comparable between groups ($P = 0.436$). In the univariable model, diagnosis of glaucoma was not associated with MP volume ($R2 = 1.22\%$; $P = 0.257$). Dietary carotenoid intake was positively and significantly related to MP in the univariable ($P = 0.022$) and multivariable ($P = 0.020$) models.

Conclusions: Our results challenge previous studies that reported that glaucoma is associated with low MP. Dietary habits were found to be the main predictor of MP in this sample. Further research is merited to better understand the relationship between glaucoma, MP and visual performance in these patients.

Disclosures: The authors have no disclosures.

BON02

Inhibition of mTOR Pathway to Prevent Photoreceptor Cell Damage and The Role of Resveratrol

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Purpose: mTOR is a cytoplasmic kinase that regulates cell growth and metabolism in response to mitogens, hormones including insulin and cytokines. But later in life, when growth has been completed, mTOR drives cellular and organismal aging by acquiring pro-inflammatory and signal resistant characteristics. mTOR pathway also takes part in retinal degenerative diseases.

Methods: 10 patients with mid stage Retinitis Pigmentosa (RP) were treated by intravitreal Rapamycin and oral Metformin plus Resveratrol for 6 months. 10 other RP patients were given placebo. The average age of the patients was 28. After 1 year, change in visual acuity and visual fields (VF) was recorded.

Results: Difference in change in visual acuity did not reach a significant statistical result between the 2 groups whilst the visual fields were either protected or slightly improved in the Treatment group. The difference in Mean Deviation before and after 1 year follow up between the 2 groups was statistically significant. ($P \geq 0.001$) VF deteriorated in the placebo group, but was preserved in the Treatment group.

Conclusions: Inhibition of mTOR maintains cellular proteostasis and attenuates oxidative stress by reducing misfolded protein synthesis and augmenting autophagy to remove misfolded proteins .The combination of Rapamycin, Metformin and Resveratrol may help to stabilize VF loss in hereditary retinal diseases. Prior studies with administration of Resveratrol are associated significant increases in the proportion of circulating Treg cells defined as $CD3^+$, $CD4^+$, $CD25^+$, and $CD127^{dim/neg}$ lymphocytes. The results obtained in this study also confirm the synergistic effects of Resveratrol.

BON03

Macular pigment and glare geometry

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Purpose: In a number of past studies we and others have shown that MP density reduces glare disability and discomfort when using centrally-fixated stimuli with light scatter that obscures foveal targets (e.g., from a surrounding annulus). Light entering the anterior segment, however, can also spread well outside the macula in what is often described as halos and starbursts. Clinically, this is referred to as positive dysphotopsia and tends to affect patients who have undergone procedures that affect the anterior media, such as laser corrections and cataract surgery. Given the spatial distribution of MP, which filters mostly in and around the fovea, we tested whether MP density is related to these glare halos and peripheral spokes.

Methods: 43 young healthy subjects (age = 17-21) were assessed. MP density was measured with customized HFP. Iris color was determined based on comparison to an extended photographic comparison set. Halos and spokes were determined by using a bright xenon point source combined with centering calipers and an iris diaphragm.

Results: MP density was not related to either halos or starbursts, nor was the relation moderated by iris color.

Conclusions: Most of the effects of MP on glare appear to be local to the macula and linked to filtering in the central retina. Light spread arising from the anterior media and extending outside of filtering within the macula is not affected by such filtering. This study focused on young healthy subjects. If the macular carotenoids lead to a clearer lens in the elderly (as past studies suggest), however, we may have found a different result in an older sample (via less anterior scatter).

BON04

Macular pigment does not screen the retina from ultraviolet B radiation

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Purpose: It has long been known that a small portion of ultraviolet-A (UV, 315-400 nm) penetrates the cornea and crystalline lens. UV transmission to the retina appears to be unique to the young and some older pseudophakes. It has also been postulated that the macular pigments screen the young retina from this highly actinic light. In this study, we determine the variation in UV perception in a relatively homogenous sample of young adults and assess putative screening by the macular pigments.

Methods: 42 subjects were tested (19, sd = 1.3). Absolute thresholds to UV light were collected. A relative narrowband (full waveband = 305-325 nm) LED was used with a max = 315 nm (UVTOP310, QPhotonics LLC, Ann Arbor, MI). An additional interference filter centered on the peak wavelength was used to eliminate any extraneous light and this was confirmed using a spectral radiometer (ILT950, Peabody, MA). Macular pigment optical density (MPOD, measured using heterochromatic flicker photometry) and iris color (using a standardized color scale) were also assessed as potential covariates.

Results: All of the subjects could detect UV light at 315 nm but individual variation was large (over a factor of 40) despite the subjects all being nearly the same age. Higher MPOD, and darker irides were not related to UV sensitivity in this young sample.

Conclusions: It has often been assumed that humans are blind to light outside the "visible spectrum" ranging from around 400-700 nm. All of the subjects in our study, however, easily perceived light in the UVB range (315 nm). MP (or iridial pigment) did not alter these thresholds. The large individual differences in UV reaching the retina of younger individuals suggests equally significant vulnerability to the actinic effects of this highly energetic light. Subjects reported that the light appeared violet/blue suggesting it was photopigment absorbance in the beta band that mediated detection (not longer-wave fluorescence within the retina).

BON05

Skin carotenoid index and its correlation with macular pigment in Japanese subjects

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Purpose: To investigate skin carotenoid (SC) indices and quantitative correlations between SC indices and macular pigment (MP).

Methods: SC indices were measured in 811 subjects (498 men, 314 women, 6-98 years old, mean; 69.7±14.1[SD]) using reflection spectroscopy (RS, Veggie Meter, Longevity Link Corporation, US). MP levels were measured in 152 eyes using Spectralis MultiColor (Heidelberg Engineering, Germany).

Results: The SC indices showed a normal distribution ranging from 32 to 892, and features a large halfwidth (mean; 342.9±145.1). Indices for women were significantly higher than for men (mean; 389 vs 314, p=0.000). Subjects taking lutein supplements had higher SC indices compared to non-supplementing subjects (mean of 416 vs mean of 322, p=0.000). Non-smokers, past smokers and current smokers had decreasing SC indices in this order (p=0.000, ANOVA with Bonferroni). No significant correlation existed between SC indices and age. A weak correlation existed between SC indices and MP optical density at 0.9° (R=0.209, p=0.010) or the total MP amount within 8.98° eccentricity (R=0.241, p=0.003). Multiple regression analyses revealed that both the total MP amount in the 1.99° to 8.98°range and the absence of age-related maculopathy (ARM) correlated significantly with a high SC index.

Conclusions: Women, non-smokers, and lutein supplementation were identified as contributing factors for high SC indices. SC indices correlated with MP and ARM.

Disclosures: Werner Gellermann and Mohsen Sharifzadeh are employees of Longevity Link Corporation, Salt Lake City, UT, United States of America.

BON06

Compensation for the influence of cataract on the measurement of macular pigment optical density by autofluorescence imaging

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Purpose: To develop a method of compensation for the influence of cataract on the measurement of macular pigment optical density (MPOD) by autofluorescence imaging.

Methods: MPOD values at four different eccentricities were measured by the MPOD module of the Spectralis MultiColor device (Spectralis-MP, Heidelberg) before and after cataract surgery in 100 eyes. Multiple regression analyses were performed using the change of MPOD value at each eccentricity as the independent factor and age, cataract grade, and quality of autofluorescence image as dependent factors. Regression equations at various eccentricities were obtained. The compensated values using the regression equation were further evaluated in 27 healthy subjects in comparison to MPOD measured by heterochromatic photometry (HFP).

Results: Regression equation was composed of age, grade of cataract, and standard deviation (SD) ratio of MPOD. For example, the increase rate of MPOD at 0.51° eccentricity after surgery = 0.14 + 1.71×SD ratio + 0.27×cataract stage + 0.01×age (p=0.000). The compensated MPOD was obtained

by the following calculation; MPOD = original value x the increase rate. The compensated values showed good correlation with values obtained by HFP in subjects aged more than 40 years.

Conclusions: We obtained useful regression equations to estimate the increase rate of measurement values after surgery. MPOD measurement in the subjects aged more than 40 years should be compensated using the present equations.

Disclosures: None.

BON07

Macular pigment formation in premature infants evaluated by fundus reflectometry

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Purpose: To demonstrate the presence of macular pigment in the retina of premature infants and to examine its changes with age.

Methods: The participants included 40 premature infants. Infants who had received laser photocoagulation for retinopathy of prematurity (ROP) were excluded. Macular pigment optical density (MPOD) was measured by fundus reflectometry using RetCam3®, a digital fundus camera. The reflection imaging was performed at the examination for ROP screening. The imaging time points were from a post-menstrual age (PMA) of 29 weeks 0 days to 46 weeks 5 days.

Results: The MPOD levels could be obtained from 39 premature infants. The levels at the first measurement ranged from 0 to 0.18 (mean 0.076, S.D 0.044). The earliest time, when a non-vanishing MPOD level was obtained, was at a PMA of 33 weeks and 2 days, and that level was 0.05. The initial examination MPOD levels showed a moderate correlation with age (R^2=0.32, $p<0.00017$). The mean MPOD levels measured each week during the follow-up period showed a very strong correlation with age (R^2=0.91, $p<0.0001$). A regression line of MPOD = 0.0069 x age - 0.1783 was derived, where age is counted in PMA days. There was a strong correlation between right and left eyes over the range of all MPOD levels (R^2=0.73, $p<0.0001$).

Conclusions: The MPOD levels of premature infants were for the first time measured in living eyes. Macular pigment increased linearly with age.

Disclosures: We have no conflicts of interest.

BON08

Metabolomic profiling reveals metabolites correlating with α-tocopherol concentrations in the frontal cortex of human infant brain

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Purpose: α-Tocopherol (αT) is essential for the developing brain but it may have other roles beyond antioxidative function. Metabolomic profiling in pediatric brain tissues with varied αT concentrations would be a useful tool to investigate the roles of αT in neural development.

Methods: Brain tissues from the frontal cortex were acquired from 29 infants (age 111 ± 74 d) who had no brain and/or systemic pathologies at death. Total αT concentrations were measured by high performance liquid chromatography coupled with fluorescence detection. Metabolomic profiling was performed on gas chromatography coupled with mass spectrometry (GC/MS) and liquid chromatography coupled with mass spectrometry (LC/MS). Pearson's partial correlation analysis (univariate analysis) adjusting for age, sex, and race, and partial-least squares discrimination analysis (multivariate analysis) were performed to identify metabolites that correlate with total αT concentrations.

Results: Total αT ranged from 6.28 to 43.50 μmol/g brain tissue. Among 402 metabolites detected by GC/MS or LC/MS, 32 metabolites were identified to be correlated with total αT concentrations

by both univariate ($p < 0.05$) and multivariate analyses. They included antioxidative metabolites (ascorbate, dehydroascorbate, homocarnosine), amino acid metabolites, derivatives of cholesterol, phospholipids, arachidonic acid, and other fatty acids.

Conclusions: αT may have essential roles in the developing brain beyond its antioxidative function. Our future analysis of αT stereoisomers in brain samples from these same subjects may find novel roles in neural tissue of different αT stereoisomers during infancy.

Disclosures: Abbott Nutrition.

BON09

Brain fat-soluble nutrient pattern is associated with cognitive functioning in older adults with no dementia

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Purpose: Brain is rich in fat-soluble nutrients that are individually related to cognitive health but their synergistic effects remain to be identified. The objective is to characterize brain fat-soluble nutrient patterns (FSNPs) and evaluate their relationship to cognitive function.

Methods: Brain samples from the frontal (FC) and temporal cortices (TC) were obtained from 47 centenarian decedents. Subjects underwent cognitive tests every six months and tests from the time point closest to death were used to calculate cognitive domain scores. Carotenoids, retinoids, tocopherols, and fatty acids (FAs) were quantified using established protocols and averaged from FC and TC. FSNPs were identified separately in subjects with ($n = 24$) and without ($n = 23$) dementia using principal component analysis. The relationship between FSNPs and cognitive domain scores was evaluated by Pearson's correlation with an adjustment for sex, education, diabetes, and hypertension.

Results: Among non-demented subjects, a FSNP characterized by high levels of carotenoids, saturated FAs, n-3 polyunsaturated FAs, and low levels of retinoids, monounsaturated FAs, n-6 polyunsaturated FAs, trans-FAs was significantly ($p < 0.05$) related to memory ($r = 0.57$), executive function ($r = 0.57$), language ($r = 0.70$), global cognition ($r = 0.62$), and activities of daily living ($r = 0.55$). No consistent relationship was observed in demented subjects.

Conclusions: Brain FSNP is related to cognitive functioning in older adults with no dementia. Our future analyses on neuropathology and brain metabolomics may explain such relationship observed. Findings from this study provide a basis for developing dietary patterns aimed at prevention of cognitive impairment.

BON010

The relation between retinol, serum carotenoids, Vitamin D and cognitive function in community dwelling older adults

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Purpose: The neural efficiency hypothesis predicts a unique role for lutein (L) and zeaxanthin (Z) in neural and cognitive function; however, the physical amount of L+Z in brain is relatively low. Past research suggests that L uniquely predicts cognitive function in the oldest older adults (e.g., centenarians). The purpose of this study was to compare the relation between serum L+Z and cognitive function to other antioxidant nutrients that exist in higher concentration in the brain, in a community-dwelling sample of older adults.

Methods: 59 community dwelling older adults ($M=73.03\pm7.41$ years) were tested. Retinol, L, Z, α-tocopherol, β-carotene, β-cryptoxanthin and α-carotene were measured via high-performance liquid chromatography. Plasma 25-OH-D3 was measured on a subset of participants ($n=26$) using derivatization with PTAD and liquid chromatography / mass spectrometry. Cognitive

function was measured using the CNS Vital Signs test battery.

Results: L, 25-OH-D and retinol were significantly correlated with cognitive function, across multiple domains. General linear modeling and comparison of β weights suggests a unique role for L in cognitive function across multiple domains when compared against other serum nutrients.

Conclusions: L likely serves a unique role in neural efficiency, even compared to nutrients that are found in brain in higher concentration.

Disclosures: Research funding was provided by Abbott Nutrition. Authors MK and SE are employees of Abbott Nutrition. During a portion of the data collection period, author LRH was an employee of Abbott Nutrition. LRH is now solely employed by the University of Georgia. Author LRH has received honoraria for educational presentations by Abbott Nutrition within the last 12-months.

BON011

Macular Pigment and Vision Function Among Older Women in the Second Carotenoids in Age-Related Eye Disease Study (CAREDS2), an ancillary study of the Women's Health Initiative

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Purpose: Macular pigment (MP) is thought to protect against ocular pathology and enhance vision performance, but evidence about the degree to which MP is associated with vision in older people is limited to short term trials. We evaluated the association between MP and measures of vision function in post-menopausal women.

Methods: The analysis includes 386 women in CAREDS2 with MP optical density (MPOD) measured at baseline (2001-2004) and follow-up (2016-January 2018). Log photopic contrast sensitivity (CS) was measured using a Pelli-Robson chart, and best corrected visual acuity (BCVA; letters read) was assessed in each eye using the standardized ETDRS protocol as modified for the AREDS trial. MPOD at 0.5 degrees from the foveal center was measured using heterochromatic flicker photometry. Associations between MPOD and vision in the best eye were evaluated using ordinal logistic (log CS) or linear (letters read) regression models.

Results: Participants were on average 80.3 years of age (standard deviation [SD]=5.4). MPOD increased between baseline and follow-up from a mean of 0.38 (SD=0.19) to 0.53 (SD=0.29). Higher MP at follow-up was associated with better CS (odds ratio=3.1, 95% confidence interval=1.5, 6.2) and the association was strengthened when adjusting for age and having an intraocular lens. For BCVA, higher MPOD was associated with more letters read in cross-sectional analyses (baseline: age-adjusted β=2.9, p=0.01; follow-up: age-adjusted β=2.6, p=0.01) while the longitudinal association was not significant (baseline MPOD with follow-up letters read: β=2.2, p=0.12).

Conclusions: Preliminary analyses in older women in the CAREDS2 study indicate higher MP at follow-up was associated with better CS and possibly BCVA.

BON012

Redox switching of anti-oxidants and the significance for protein aggregation

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Purpose: Anti-oxidants can become harmful and switch into acting as pro-oxidants. We report on a pilot study into the characterisation of the conditions which promote this 'redox switching' in common anti-oxidants.

Methods: Proteins were exposed to oxidants and subsequent aggregation or its inhibition by anti-oxidants was monitored by photospectrophotometry. Three different anti-oxidants were investigated at a range of concentrations and pHs – punicagalin, beta-carotene and epigallocatechin gallate (EGCG). The target protein used was lysozyme in the range 1-5% w/v.

Results: Punicagalin was found to rapidly inhibit aggregation of oxidized lysozyme within the concentration range of 9.21-92.1 uM and the pH range 5-10, but this was not observed with EGCG or beta carotene. At low pH, increased aggregation was observed in the presence of EGCG.

Conclusions: Preliminary data indicates that the polyphenolic anti-oxidant punicagalin can inhibit protein aggregation whereas EGCG may promote it at low pH. Further studies will be carried out to confirm these observations as knowledge of the redox switch points for many anti-oxidants may have significance for therapeutic and health strategies.

BON013

The relationship between retinal quantitative autofluorescence and macular pigment optical density in the Northern Ireland Cohort for the Longitudinal study of Ageing (NICOLA)

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Purpose: Quantitative Autofluorescence (qAF) provides a density map of lipofuscin in the retina and is a biomarker of photo-oxidative damage. Therefore we investigated the relationship between qAF, age and MPOD in healthy subjects in a pilot subsample of NICOLA participants.

Methods: qAF images were obtained within the multi-modal retinal imaging component of the NICOLA study using a confocal scanning laser ophthalmoscope (SLO) equipped with an internal fluorescent reference to account for variable laser power and detector sensitivity (Heidelberg Engineering, Germany). qAF images from 60 subjects with no retinal disease and gradable qAF images were analysed using Spectralis qAF software (Heidelberg Engineering, Germany) with a Delori pattern. qAF was calculated as average qAF of the eight middle segments for each image (qAF8) and log transformed to approximately conform to normality. MPOD sum volume within a plateau of 80 centred on the fovea was also calculated using the SLO. The relationship between log(qAF8) and log(MPOD) was evaluated using generalised estimating equations (GEE), corrected for age and sex.

Results: Subjects were aged 62.7±8.4SD (range 48-81) with 48% males. The GEE model showed that log(qAF8) increased with age (β=0.007, p=<0.001) while no association with sex was found. log(MPOD) was found not to be related to qAF8 (β=-0.009, p=0.94).

Conclusions: The results suggest that while qAF increases with age, it is not related to MPOD.

BON014

Macular Pigment Optical Density alterations in Diabetes

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Purpose: To assess the alterations of macular pigment optical density (MPOD) in patients with self-reported diabetes mellitis (PwDM) in a subset of the Northern Ireland Cohort for the Longitudinal Study of Aging (NICOLA).

Methods: MPOD data were obtained from double-wavelength autofluorescence images captured using Heidelberg Spectralis HRA+OCT MultiColor device, as part of the NICOLA health assessment. All participants with self-reported diabetes are included in this analysis. A control group with no evidence of retinal disease or DM was used for comparison. MPOD sum volume within a plateau of 8o centred on the fovea was computed and log transformed to conform approximately to normality. The means for both groups were compared using generalized estimating equations (GEEs) to enable data from both eyes to be used, corrected for age.

Results: A subsample of 643 individuals were included, 299 PwDM and 344 controls. PwDM were 66.6 ± 10.56 years compared to controls 62.9 ± 7.32 years. GEE analysis showed that people with diabetes have reduced logMPOD when adjusted for age (β=-0.265 p<0.001).

Conclusions: Our data suggest that diabetes causes significant reduction in MPOD in PwDM compared to healthy controls which is in keeping with previous literature.

Disclosures: None of the authors had no proprietary interest and no conflicts of interest.

BON015

Zeaxanthin Moderates the Relationship Between Right Hemisphere Precuneus Volume and Immediate Memory in Healthy Older Adults

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Purpose: To characterize the relationship between macular carotenoids and facets of intelligence

to understand healthy brain aging. We hypothesize that peripheral zeaxanthin status moderates the relationship between right hemisphere precuneus volume (RHPV) and immediate memory (IM) performance.

Methods: A moderation analysis was conducted to examine the relationship between RHPV, zeaxanthin status, and IM performance. Covariates included age, sex, education, socio-economic status, and body mass index. All data were collected from healthy individuals aged 65-75 (N = 97).

Results: RHPV ($t(88) = 2.74$, $p < .01$) and zeaxanthin status ($t(88) = 2.36$, $p < .05$) explained the variance in IM performance ($R2 = .23$, $F(8, 88) = 3.33$, $p < .01$). The interaction term was also significant ($t(88) = -2.22$, $p < .05$). Conditional effects indicate that low zeaxanthin status influences the relationship between RHPV and IM ($t(88) = 2.67$, $p < .01$). Average ($t(88) = 1.89$, $p < .05$) and high ($t(88) = -0.288$, $p > .05$) zeaxanthin status do not.

Conclusions: The interaction shows a "rescuing" effect of zeaxanthin status on IM. When RHPV is large, IM does not differ between individuals with low, average, and high zeaxanthin status. However, as RHPV decreases, individuals with low zeaxanthin levels show a significant decrease in IM whereas those with high zeaxanthin levels do not. Our findings suggest that increasing zeaxanthin status may attenuate age-related decline in markers of IM in healthy older adults.

Disclosures: This work was supported by a grant from Abbott Nutrition throught the Center for Nutrition, Learning, and Memory at the University of Illinois at Urbana-Champaign (ANGC1205; PI: AB)

BON016

Nutritional, Cognitive and Biomarker Patterns of Healthy Brain Aging

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Purpose: To discover nutrient biomarker patterns associated with healthy brain aging.

Methods: Hierarchical clustering analysis identified multivariate relationships among a large set of variables in 124 older adults (age 65-75). Measurements were obtained for 60 nutrients from serum, 75 variables reflecting cognitive abilities and intelligence, 80 neuroinflammatory markers, 8 brain metabolites using Magnetic Resonance Spectroscopy, 200 voxel-based morphometry brain regions and connectivity matrices from resting-state fMRI.

Results: One cluster is associated with healthy brain aging, which shows a pattern with higher intake of carotenoids, fatty acids and B-vitamins shows; higher executive function scores, tests of memory and decision-making; less brain inflammation (i.e. beta-amyloid) and increased neuronal health (i.e. apolipoprotein and bone-derived neurotrophic growth factor); more gray matter volume and larger hippocampi; and enhanced functional connectivity. Another HCA cluster shows patterns of cognitive and brain decline more typical of cognitive aging, with cortical thinning and decreased intelligence scores, and this pattern is associated with lower serum levels of fatty acids, carotenoids and B-vitamins.

Conclusions: The reported findings provide evidence that nutrition plays an important role in healthy brain aging and motivate future research to investigate the efficacy of specific nutritional profiles to promote cognitive performance in the aging brain.

Disclosures: This work was support by the Center of Nutrition, Learning and Memory at the University of Illinois, which received funding support from Abbott Nutrition.

BON017

Absorption and Delivery of Synthetic VLC-PUFAs to Mouse Retina

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Purpose: Very long chain-polyunsaturated fatty acids, VLC-PUFAs ($C \geq 24$) are a special class of non-dietary fatty acids identified and bio-synthesized only in retina in the presence of ELOVL4 enzyme, whose deficiency is observed in AMD and Stargardt-3(STGD3) diseases. We hypothesize that supplementation with exogenous VLC-PUFAs could serve as an effective treatment strategy, but until now there has been no known method for producing them in sufficient quantities required for supplementation studies. We therefore chemically synthesized VLC-PUFAs to study their absorption and delivery to the retina.

Methods: We confirmed the synthesis of 32:6 (n-3) from DHA ethyl ester using NMR, LC-MS and GC-MS. To measure uptake of orally administered VLC-PUFAs in WT mice, synthetic 32:6, n-3 (250mg/kg/day) was gavage fed. At 0, 2, 4, 8 and 24h time points, mice (n=4) were sacrificed to collect serum, red blood cells (RBCs), brain, liver, and retina. All tissues were analyzed for LC- and VLC-PUFAs using standardized methods.

Results: At baseline, no VLC-PUFAs were detectable in serum, but we observed 32:6 (n-3) in serum 2h after gavage feeding (~2% of total fatty acids). Retinal 32:6, n-3 levels increased significantly to 50% above baseline within 8h and none were detected in liver, brain or RBCs at any time points.

Conclusions: This study shows that chemically synthesized VLC-PUFA are present in the serum soon after oral administration and can be specifically delivered to the retina. Further supplementation studies in mouse models for STGD3 and AMD will provide insight into the potential value of exogenously administered VLC-PUFAs for the treatment of retinal degenerative diseases associated with abnormally low VLC-PUFA levels.

Disclosures: No commercial relationships

BON018

How we see macular pigment: Computational simulation of Haidinger‘s brushes

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Purpose: Macular pigments are bound to ganglion cell axons of the Henle fibre layer that emanate outwards from the centre of the macula like spokes on a wheel. The preferential absorption of linearly polarized blue light by the macular pigments results in an entoptic phenomenon called Haidinger's brushes. Previous computational models have assisted in understanding the behaviour of these subjective phenomena, but have been limited in their application. Our objective was to develop a new model that more accurately accounted for known variables that affect the perception of Haidinger's brushes

Methods: A computational model was created that built on previous models and added known determinants of the form and behaviour of Haidinger's brushes.

Results: The model generated both static and animated simulations of Haidinger's brushes that could be quantified by their density, contrast and radial/circumferential extent. Measured physiological parameters were used to demonstrate the dependency of Haidinger's brushes on macular pigment density, macular pigment distribution and ocular retardation.

Conclusions: Our new computational model shows that variations in macular pigment density and distribution, as well as ocular retardation, can explain the reported variations in the perception of Haidinger's brushes. The implication is that an individual's perception of Haidinger's brushes can provide information about both the density and distribution of macular pigments in their eyes.

Disclosures: Shelby E Temple is director at Azul Optics Ltd Gary P Misson is associated with Optical Diagnostics Ltd

BON019

Evaluation of synergies in the antioxidant effect of phytoene, phytofluene and lycopene in Caenorhabditis elegans

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Purpose: In a previous study it was observed that the treatment with phytoene (PT), phytofluene (PTF) and lycopene (LYC) was accompanied by significant increases ($P \leq 0.05$) in the survival rates of Caenorhabditis elegans subjected to oxidative stress [1]. This study is aimed at evaluating possible synergistic effects.

Methods: Age-synchronized worms were grown in NGM plates (as control media) or NGM plates with the different doses of each carotenoid [1] or their combination. The combination tested were C1

(lycopene (0.05 μg/mL) + phytoene (0.05 μg/mL) + phytofluene (0.1 μg/mL)), C2 (lycopene (0.05 μg/mL) + phytoene (0.05 μg/mL)), C3 (lycopene (0.05 μg/mL) + phytofluene (0.1 μg/mL)), and C4 (phytoene (0.05 μg/mL) + phytofluene (0.1 μg/mL)). Worms were incubated at 20 °C during 7 days in the different conditions. Afterwards, an acute oxidative stress was applied with hydrogen peroxide (2 mM). After 5 h, survival was analyzed in each fed condition.

Results: The C3 combination (lycopene + phytofluene) exhibited a marked synergistic effect. The theoretical percentage of survival (calculated as the sum of the survival obtained with the individual carotenoids [1]) for this combination (17.0%) was statistically lower ($P \leq 0.05$) than the experimental percentage of survival for this combination (28.5%).

Conclusions: The combination of lycopene and phytofluene tested exhibit a synergistic effect.

Disclosures: AJMM is a member of the advisory board of Israeli Biotechnology Research Ltd.

BON020

Bioaccessibility of Phytoene and Phytofluene from Tomato Powders and Effect of the Addition of Sunflower Oil

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Purpose: To assess the bioaccessibility of phytoene (PT) and phytofluene (PTF) from two types of tomato powders and the pulp of a common and a cherry tomato. The effect of adding oil was also assessed. PT and PTF are carotenoids that are acquiring a growing interest for the possible relationship between their consumption and human health.

Methods: Bioaccessibility in percentage (BA) and potentially absorbable amounts were determined by applying an in vitro digestion protocol.

Results: The levels of PT and PTF in the more concentrated powder (7.5 and 3.1 mg/g respectively) were up to 1000 times higher than that in the tomatoes. PT was more bioaccessible than PTF in all samples. BA of PT in the powders ranged between 27.4 and 29.6% and that of PTF from 16.4 to 21.3%. BA of PT and PTF from the powders was lower as compared to the tomato fruits and increased markedly when sunflower oil was added. However, the best source of potentially absorbable PT (2 mg/g) and PTF (0.5 mg/g) was by far the powder with higher levels of them.

Conclusions: Despite the lower carotenoid BA of the powders in comparison with the tomato pulps, their bioaccessible content is much higher. Both the higher concentration of PT and PTF in the powders and the reduction of the particle sizes compared to the pulps may contribute to this. Adding sunflower oil to the samples can increase the carotenoid BA, and hence their bioavailability in the samples.

Disclosures: This study was funded by Israeli Biotechnology Research Ltd. AJMM is a member of its advisory board.

BON21

Macular Pigment is associated with early cognitive decline in the Northern Ireland Cohort for Longitudinal Aging Study (NICOLA)- a population-based study of older adults

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Purpose: To explore associations between macular pigment and personal, lifestyle, cognitive and retinal health factors in a population based study of older adults in Northern Ireland.

Methods: Macular pigment optical density (MPOD) was measured with the two-wavelength autofluorescence method using a modified Heidelberg Retinal Angiograph (Spectralis; Heidelberg Engineering Co., Heidelberg, Germany) as part of the NICOLA study health assessment. Participants also underwent multi-modal retinal imaging which was graded for common ocular conditions including age-related macular degeneration, glaucoma, diabetic retinopathy and vascular occlusions. Detailed information on medical history, lifestyle, social circumstances and education were collected within the computer-assisted home interview and health assessment. The health assessment also included the Mini-Mental State Exam (MMSE) and the Montreal Cognitive Assessment (MoCA). Confounder

adjusted multivariate analysis was used to investigate the determinants of MPOD (0.23° radius) in this population and in particular the associations with cognitive ability.

Results: Images of sufficient quality for analysis were available in at least one eye in 1,421 participants with no signs of retinal disease. Participants ranged in age from 35-92, 702 were female (49%) (mean age 61 yrs SD=8.2) and 719 male (mean age 64yrs SD=8.3). MPOD was significantly associated in the multi-variate analysis with BMI (β=-0.030 p=0.032), non-smoking (β=0.037 p=0.027), Multiple deprivation score (β=-0.093, p=0.019) and MoCA score (β=0.023, p=0.024).

Conclusions: In this population based cohort MPOS was associated with signs of early cognitive decline (MoCA score), supporting the importance of dietary carotenoid intake for the maintenance of cognition in later life.

Disclosures: We are extremely grateful to all the participants of NICOLA, and the whole NICOLA team, which includes nursing staff, research scientists, clerical staff, computer and laboratory technicians, managers and receptionists. Atlantic Philanthropies, ESRC, HSC Research and Development, UKCRC and Queen's University Belfast provide core financial support for NICOLA. The authors alone are responsible for the interpretation of the data and any views or opinions presented are solely those of the author and do not necessarily represent those of the NICOLA team.

BON22

"Turn and face the strange Ch-ch-changes" - Cognitive, visual and nutritional deficiencies in mild cognitive impairment

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Purpose: To compare cognitive, visual and nutritional outcomes of individuals with mild cognitive impairment (MCI) to age-matched controls.

Methods: Cross-sectional study comparing MCI (n=19) to control (n=60) subjects. Sensitive and validated diagnostic tools were used to assess global cognition, comprehension, executive function, episodic memory (visual stimuli) and reaction time. Visual function measurements included best-corrected visual acuity and contrast sensitivity (CS). Nutritional status was assessed by questionnaire, macular pigment (MP) and skin carotenoid score (SCS).

Results: MCIs (mean±SD age 74.16±6.29; 68.4% female) performed statistically significantly poorer ($p<0.005$) in all cognitive assessments when compared to controls (mean±SD age 69.40±4.07; 63.3% female). Visual function (CS at 2.4 cpd) was significantly worse in MCIs compared to controls ($p = 0.016$). Nutritional status (questionnaire and SCS) was lower in MCIs than controls. MP volume was statistically comparable between both groups (MCIs: 6052±2894, controls: 5342±2090, p=0.411).

Conclusions: This study confirms that subjects with clinically confirmed MCI exhibit significant deficiencies in cognitive and visual function. This is an important discovery, demonstrating a clear loss of function in MCI patients, which may be explained by nutritional deficiencies. Further research will test if nutritional optimisation can enhance loss of cognitive and visual function in these patients.

BON023

Global Biofortification of Maize Grain with Higher Levels of Xanthophylls and Total Carotenoids

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Purpose: In Africa, dark orange maize grain color is effectively differentiating high ProVA varieties from yellow or white varieties with little carotenoids. There is interest in using orange color to differentiate high xanthophyll corn grain varieties in the developed world.

Methods: Using genetic and genomic approaches we have identified genes in the carotenoid and isoprenoid pathways, and carotenoid degradation enzymes that are associated with maize grain color and levels of carotenoids. We are using various food science approaches to develop food products with higher levels of xanthophylls.

Results: The identified genes include dxs2, psy, lycE, zep1, ccd1. We have started gene specific marker assisted selection programs for darker orange color, and higher levels of xanthophylls and total carotenoids in maize grain. We associated the hydroxylase4 gene with levels of beta-cryptoxanthin, a proVA carotenoid with other nutritional properties. We have made tortillas from orange maize with higher levels of xanthophylls. We have included white, yellow and orange maize in the feed of laying hens, and eggs yolks with 3x-4x the amount of zeaxanthin were produced from orange corn diet over the yellow corn diet.

Conclusions: We have identified genes, breeding strategies, and food science approaches to create mechanisms for providing consumers with products with higher levels of lutein and zeaxanthin in highly bioavailable food contexts.

Disclosures: Some of this research is supported by NutraMaize, LLC, a startup company with Torbert Rocheford Co-Founder and CTO, and Evan Rocheford Co-Founder and CEO NutraMaize has received Small Business Innovation and Science and Technology Transfer grants from the US Dept of Agriculture and the US National Science Foundation to support some of this research.

BON024

Lutein and zeaxanthin status markers (serum and macular pigment) and their dietary intake in Spanish subjects aged 45-65 years

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Purpose: Assessment of serum lutein (Lut.) and zeaxanthin (Zeax.) concentrations and the macular pigment optical density (MPOD) in subjects aged 45-65 y. This study is part of a project to assess dietary intake effect on the MPOD and relations between intake, status and visual function.

Methods: 150 volunteers will be included in a cross-sectional study, here results of 97 (38 men). Criteria: cholesterolemia (<250mg/dl), BMI (<30kg/m^2), mixed diet, no dietary supplements intake, drugs/foods to lower cholesterol, chronic diseases. Lut. and zeax. in blood and faeces by HPLC. Dietary intake by three 24 h recalls and a carotenoid database and software (Beltrán et al., 2012; Estévez-Santiago et al., 2013). MPOD by heterochromic flicker photometry (Olmedilla-Alonso et al., 2014).

Results: Serum concentrations as mean±SD (median): Lut. 18.5 ± 8.8 (16.6); Zeax. 4.0 ± 2.5 (3.4) (μg/dl); lut.+zeax./chol.+triglycerides (μg/mg) 18.5 ± 8.8 (16.6). Dietary intake (μg/day): Lut. 1068 ± 1263 (601), Zeax. 93 ± 119 (49). MPOD (density units) (n = 193) 0.326 ± 0.150 (0.335). No differences between sexes, except serum zeax., HDL-chol. Significant correlations (Spearman's ρ, p value): MPOD – Serum: Lut. 0.179 (0.013), zeax. 0.261 (0.000), Lut.+Zeax. 0.202 (0.005), Lut.+Zeax./chol.+trigl. 0.179 (0.013). MPOD - Dietary intake: zeax. 0.224 (0.002).

Conclusions: Lut. and zeax. serum and diet concentrations and MPOD data contribute to the establishment of normal /reference ranges for subjects aged 45-65 y, target population for an improvement in vision quality through dietary means.

Disclosures: The authors have no conflict of interest

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BON025

How to analyze effects of potentially neuroactive compounds on the blood-brain barrier? – Porcine brain capillary endothelial cells as a versatile in vitro model

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Purpose: Any neuroactive compound, either a drug to treat neurological diseases or a neurotoxin influencing neuronal function, need to cross the blood-brain barrier (BBB) to act directly on neuronal cells. Therefore, the analysis of any biological effect on the BBB is of high interest. This poster illustrates the diagnostic potential of a model utilizing primary porcine brain capillary endothelial cells (PBCEC) to mimic the BBB. This two-compartment model system allows reliable transfer and transport studies across the BBB.

Methods: Primary porcine brain capillary endothelial cells (PBCEC) are seeded on Transwell® two compartment filter inserts. The upper (apical) compartment of the filter system represents the "blood"-side and the lower (basolateral) compartment the "brain"-side. As markers of the barrier integrity the transendothelial electrical resistance (TEER) and the electrical capacitance are monitored with a cellZscope® impedance spectrometer. Furthermore, the permeability of 14C sucrose is analyzed by scintillation counting. The transfer of the compounds of interest from apical to basolateral or vice versa are quantified by LC MS/MS.

Results: The PBCEC model enables investigations of the effect of bioactive compounds on brain endothelial cells, BBB and membrane integrity as well as the determination of transfer rates and permeation or active transport across the BBB.

Conclusions: The presented model is a versatile tool to study effects of various biological active compounds on the BBB. High TEER and low 14C sucrose permeability of PBCEC combined with sensitive LC-MS/MS quantitation of the applied compounds enable reliable transfer and transport studies across the BBB.

Disclosures: The authors declare no competing.

BON 026

Zeaxanthin-biofortified popcorn: stability of carotenoids following microwave popping

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Purpose: Popcorn is a potentially good source of dietary zeaxanthin. Because popcorn kernels require high internal pressure and temperature to pop, carotenoids are likely to suffer significant degradation during the popping process. This trial investigated the impact of microwave popping on carotenoid stability of zeaxanthin-biofortified popcorn immediately, and up to two weeks after popping.

Methods: Kernels of zeaxanthin-biofortified and standard popcorn were popped in a microwave oven (1000 w) for 4 minutes. Carotenoid profiles were assessed by HPLC prior to, immediately after popping, and over a two week storage period at ambient temperature (23°C).

Results: Carotenoid concentrations in zeaxanthin-biofortified and standard popcorn significantly declined immediately following popping. Popping was associated with an immediate 55% reduction in zeaxanthin, followed by a further 12% decline in the first 4 hours. After this point, rate of zeaxanthin degradation slowed, with only a further 10% loss over the remaining 2 week storage period.

Conclusions: Microwaving popcorn can cause significant reduction in carotenoid content immediately after popping, but also in the 4 hours after popping. This indicates that in order to maintain an enhanced zeaxanthin concentration in popped popcorn, initial zeaxanthin concentration in unpopped kernels should be as high as possible to offset this loss, and consumption should occur soon after popping to avoid further degradation of zeaxanthin.

BON 027

Glaucoma as a protein misfolding disease: an investigation of its metastable proteome

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Purpose: Glaucoma is a major cause of irreversible blindness worldwide characterised by the progressive degeneration of the optic nerve. Although a successful clinical treatment involves lowering of intraocular pressure, it does not necessarily stop the progression of the disease, which ultimately leads to the destruction of retinal ganglion cells (RGCs). The precise mechanism by which irreversible destruction of RGCs occurs is unclear. Evidence suggests that glaucoma shares similar mechanisms to Alzheimer's disease (AD), which is a neurodegenerative disease widely believed to be caused by the abnormal aggregation of Amyloid-beta in the brain. In this study, we further explore this link of shared mechanisms of pathology between these two diseases; to propose progressive protein aggregation in vulnerable eye tissues that leads to destruction of RGCs.

Methods: Recent studies from Primary Open Angle Glaucoma patients have indicated genetic mutations in three genes - myocilin (MYOC), optineurin (OPTN), and TANK-binding kinase 1 (TBK1) resulting in a pathological state that are most likely caused due to gain of function. This gain-of-function facilitates the toxic accumulation of Myocilin into amyloid-containing aggregates. By analysing the tissue specific information for gene expression from The Ocular Tissue Database and Gene Expression Omnibus, in normal vs. glaucomatous eye, we shed some insights into the nature of the metastable proteome in glaucoma in comparison to AD.

Results: We propose the idea that one of the underlying causes of glaucoma could potentially be protein aggregation driven by a metastable proteome, similar as in the case of Alzheimer's disease.

Conclusions: Both Glaucoma and AD are multifactorial in nature, with some degree of correlation attributed to epidemiological, genetic and immunohistochemical data. We propose that therapeutic approaches designed to maintain protein homeostasis in Alzheimer's disease could potentially be extended to Glaucoma and vice versa.

BON 028

Standardizing how we report macular pigment using the Heidelberg Spectralis

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Purpose: It is essential to have a valid, accurate, and reliable measurement of macular pigment (MP). Also, how we report MP data (e.g. eccentricities, spatial profiles, total volume etc.) will influence the interpretation of the results. Here we describe and introduce MP volume (MPV) as an appropriate value for reporting MP.

Methods: Pooled data from previous studies including 303 subjects were used: 151 normal subjects; 119 subjects with age-related macular degeneration; 19 subjects with mild cognitive impairment; 14 subjects with Alzheimer's disease. MPV and MP optical density (MPOD at 0.23, 0.47, 0.98, and 1.76°) were measured using the Heidelberg Spectralis HRA+OCT MultiColor. Demographics, health parameters and lutein (L) and zeaxanthin (Z) dietary intake and serum concentrations were evaluated.

Results: The mean MPV was 5,056 (95% CI: 4,798-5,322); range: 166-15,005. MPV was positively and significantly related to MPOD at all eccentricities ($r=0.698$ to 0.899, $p<0.001$), with the strongest agreement at 1.76° ($r=0.899$). Significant relationships were identified with serum concentrations of L and Z ($r=0.414$ and $r=0.343$) and BMI ($r=-0.209$) ($p<0.001$, for all).

Conclusions: Although MPV was strongly correlated to MPOD at all eccentricities, the agreement improved with increasing eccentricity. This study confirms that MPV is related to known predictors of MP. The Spectralis provides an objective assessment of MP, and MPV represents a reliable evaluation of the MP profile.

BON 029

Visual function is compromised in patients with vitreous floaters

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Purpose: Vitreous floaters can have a negative impact on visual function and quality of life. This

study compares visual function in patients with vitreous floaters (VF) to control subjects free of vitreoretinal disease.

Methods: 61 subjects with confirmed VF (cases) and 53 subjects free of vitreoretinal disease (controls) were examined using the Advanced Vision and Optometric Tests (AVOT) system. The following thresholds of visual function were assessed: photopic and mesopic visual acuity (VA) and contrast sensitivity (CS), and cone and rod sensitivity. Macular pigment optical density (MPOD) was measured using the Heidelberg Spectralis HRA + OCT Multicolour. Demographic and lifestyle data were collected for all participants.

Results: Cases were significantly older than the controls (mean±SD age: 57±12 vs 45±10 years; $p<0.001$), but sex, smoking status and BMI were comparable ($p>0.05$). After adjusting for age, photopic and mesopic VA and CS, and cone sensitivity were significantly worse for cases compared to controls ($p<0.05$). Similarly, MPOD for all eccentricities and macular pigment volume (MPV) was lower in cases compared to controls ($p<0.05$, for all except MPOD at 0.23°).

Conclusions: Patients with VF exhibited significantly worse visual function than control subjects. The Floater Intervention Study (FLIES) will now investigate if supplementation with micronutrients (VitroCap®) reduces visual disturbances and/or enhances visual function in these patients.

BON 030

The effect of oral supplementation with L-lysine, hesperidin, proanthocyanidins, vitamin C and zinc on the subjective assessment of the quality of vision in patients with vitreous floaters

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Purpose: Vitreous floaters (VF) are known to reduce the quality of vision and life. VF-formation is the result of glycation processes and oxidative stress. In this study the quality of vision in patients with VF and the effect of oral supplementation with a combination of micronutrients was investigated.

Methods: 463 patients with VF were included (334 women,129 men). The mean±SD age was 61.1 ± 14.5 years. Questionnaires for the assessment of quality of vision were applied at baseline and after 3 months of a daily supplementation with L-lysine (125mg), hesperidin (60 mg), proanthocyanidins (23.75mg), vitamin C (40mg) and zinc (5mg). Analysis was performed according sex and age-ranged groups using chi^2 test or Fisher's exact test.

Results: 90% of the patients reported visual disturbances. They were mild in 27%, moderate in 28%, highly disturbing in 28% and extremely disturbing in 7% at baseline. Statistically significant improvement was found after supplementation (90.6 % of patients; $p<0.001$). Patients reported 25.9% small, 27.6% moderate, 28.4% significant and 8.7% a very substantial improvement. There were no differences between sexes. The effect on vision quality was higher in younger age groups of women and men (19-29, 30-39 and 40-49 years) than in elderly groups (50 years and above; $p<0.001$).

Conclusions: The subjectively perceived improvement of vision quality appears to be greater in younger patients. The finding merits a placebo-controlled trial in VF-patients.

BON 031

The physics of using the Heidelberg Spectralis dual-wavelength autofluorescence method for the measurement of macular pigment volume

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Purpose: To describe the methodology used by the Heidelberg Spectralis HRA+OCT MultiColor device for the measurement of macular pigment (MP), in order to serve as a reference regarding the concepts of macular pigment optical density (MPOD) and macular pigment volume (MPV).

Methods: The Spectralis uses a confocal scanning laser ophthalmoscope [cSLO] platform to provide blue (487 nm) and green (514 nm) laser diodes. Since macular pigment is yellow, it absorbs its op-

posite primary colour (blue) four times greater than the green wavelength. By the comparison of light intensities after fluorescence from the Retinal Pigment Epithelium (RPE) using the two wavelengths, we can measure the MPOD at any eccentricity, as defined by the Beer-Lambert law.

Results: Optical Density refers to the amount of light intensity that can pass through some material, which is calculated as a log-ratio of both outgoing light intensities from the RPE. In the presence of any level of any MP, the intensity of blue light exiting the eye should be lower than that of the green light. The Beer-Lambert law defines the log-ratio of both exiting light intensities to be MPOD (MPOD = ⟦Log⟧_10 ((Intentiy of Green Light)/(Intensity of Blue Light))). The numerical integration of all MPOD values within a given area is known as MPV.

Conclusions: Using this relevant terminology, we can deepen our knowledge of MP, and using proven mathematical techniques, expand the current boundaries of MP research.

BON 032

Composite skin carotenoid concentration is related to macular pigment volume: The Pharmanex BioPhotonic Scanner

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Purpose: Carotenoids are a group of phytonutrients that play an important role in human health via their antioxidant properties. Gold standard carotenoid assessment includes in vitro (e.g. HPLC analysis of biological samples) and in vivo (e.g. macular pigment via Resonant Raman Spectroscopy, Autofluorescence and Heterochromatic Flicker Photometry). This work compares a non-invasive skin carotenoid score (SCS) to macular pigment volume (MPV) measurements.

Methods: Demographic, lifestyle and health variables from 79 subjects recruited at the Nutrition Research Centre Ireland (NRCI) were used for this investigation. SCS was measured using the Pharmanex BioPhotonic Scanner. MPV was measured using the Heidelberg Spectralis HRA+OCT Multicolour.

Results: SCS was positively and significantly correlated to years of education ($r=0.382$, $p<0.005$) and MPV ($r=0.339$, $p<0.005$). SCS was negatively and significantly correlated to BMI ($r=-0.358$, $p<0.005$). Age and smoking status was not significantly correlated to SCS ($p>0.05$).

Conclusions: The SCS is advantageous when estimating total carotenoid levels as it is easy to use, quick, and cost effective. Although, it measures the total tissue concentrations of carotenoids, our research shows it correlates well as an indicator of MPV.

Disclosures: The authors report no conflict of interest.

BON 033

Novel biochemical process to produce zooplankton rich in nutrients of interest using a land-based zero water-exchange integrated multi-trophic recirculating system (ZWE-IMTRS): Herena Trophic Reactor (HTR)

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Purpose: Carotenoids such as astaxanthin and fatty acids such as EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) are used in food supplements and promoted to improve health. The current means of production of astaxanthin (using algae H. pluvialis) is very expensive, and the overexploitation of fish and krill to obtain EPA and DHA represents major concern for the food web. Our aim was to design a system capable of producing these nutrients in an economically feasible and environmentally friendly way.

Methods: We have developed a process to produce zooplankton rich in metabolites of interest using microalgae as sole feed source. This process consists of the continuous cultivation of microalgae, whose biomass is continuously supplied to a zooplankton culture as feed. In this way, the zooplankton grows whilst bio-encapsulating the nutrients obtained from microalgae, and in some cases converting these nutrients into more valuable metabolites. Closing the cycle, microalgae use the zooplankton wastes as nutrients for their growth.

Periodically, the zooplankton is harvested and the nutrients extracted.

Results: Our process yields zooplankton rich in carotenoids and fatty acids of interest. The process works in biochemical equilibrium, with no wastes build-up, making its operation continuous and stable over time. It requires only inorganic nutrients, sunlight and carbonic acid from the atmosphere.

Conclusions: We are currently evaluating the feasibility of the process for commercialization, with positive results thus far. If this is successful, the reactor can be used to produce valuable nutrients for human consumption, and in a way that is environmentally friendly.

BON 034

Food for Thought: The Memory Intervention with Nutrition for Dementia (re-MIND) Study

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Purpose: We have shown that patients with Alzheimer's disease (AD) exhibit significant deficiencies in xanthophyll carotenoid concentrations in diet, serum and retina compared to controls. Also, our interventional studies identified benefits for patients with AD that were supplemented with the xanthophyll carotenoids plus fish oil over an 18-month period; with carers reporting subjective improvements in their day-to-day function, sight, and mood. We are now preparing to test this discovery in a larger study entitled "Memory Intervention with Nutrition for Dementia" (re-MIND).

Methods: We have prepared a double-blind, placebo-controlled, clinical trial for 120 patients with mild to moderate AD who will be followed for 24 months. 80 AD patients will consume the active ingredient daily containing: 10mg lutein, 10mg meso-zeaxanthin, 2mg zeaxanthin, 1g fish oil and 15mg vitamin E. 40 AD patients will consume placebo daily. Our primary outcome measure is disease progression assessed by MMSE. Our secondary outcome measures include: quality of life (QOL) assessed using the QOL-AD scale, functional ability assessed using the dementia severity rating scale (DSRS), and clinical collateral. Biochemical assessment of xanthophyll carotenoids, omega-3 and vitamin E will also be assessed.

Results: We have developed a recruitment strategy with local memory clinics to identify patients with mild to moderate AD for the trial. Recruitment will begin in August 2018 and we aim to complete all testing by December 2020, with reports to be completed by June 2021.

Conclusions: Given that our preliminary report suggests positive outcomes for patients with AD who consumed a combination of xanthophyll carotenoids plus fish oil, this new study (re-MIND) is required to confirm this important observation.

Speakers Abstracts

Dementia of the Eye- Alzheimer's-linked Amyloid beta proteins provide new insights into retinal degeneration

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Purpose: Age-related Macular Degeneration (AMD) is the most common cause of irreversible blindness in the developed world for which there is no effective treatment. Advanced stages of the disease manifests as two broadly-defined phenotypes; geographic atrophy or neovascular AMD. The disease has a complex aetiology underlying a mixture of genetic and non-genetic/environmental risk factors that are still incompletely understood. Adding to this complexity is the Alzheimer's-associated Amyloid beta (Aβ) family of misfolding proteins which accumulate in aged and AMD retinas. The deposition of Aβ within pathogenic deposits under the retina and its dysregulation in plasma of AMD patients offers the possibility of studying degenerative changes in the retina from a new perspective.

Methods: We developed a mouse model of Aβ-induced retinal degeneration in order to study its effects in the living retina. We then exploited a cell culture model to determine its effects at single-cell resolution.

Results: Sub-retinally injected human oligomeric Aβ aggregated in murine eyes in a manner consistent with amyloid deposition in donor tissues, and caused progressive retinal degeneration. Two weeks after treatment, Aβ injected eyes showed features similar to neovascular AMD. However, overall retinal function remained unaffected as non-invasive OCT and ERG scans revealed this damage to be highly localised. Studies at single-cell resolution revealed that Aβ was internalised by RPE cells to accumulate within late endosomes and lysosomes. The activity of the lysosomal proteolytic enzyme cathepsin B was upregulated in response to lysosomal Aβ cargos. However, Aβ persisted after cathepsin B activity had returned to baseline levels suggesting a potential new mechanism through which Aβ can accumulate within RPE lysosomes over time. The ability to degrade POS cargos were also diminished in RPE with lysosomal Aβ, revealing an altogether novel cellular mechanism through which Aβ can contribute to AMD.

Conclusions: Our findings reveal a novel disease-causing pathway in the senescent retina. They also shed light on how impaired cargo-handling processes including poor responses to the accumulation of aggregate-prone/high-molecular-weight molecules within lysosomes underpin related pathophysiologies such as Alzheimer's disease. As an unhealthy diet and metabolic disorders are associated with increased Aβ pathology in the eye and brain, our results provide further evidence of shared pathophysiology in these tissues.

Nutrition for the ageing brain: The impact of polyphenols on cognitive health

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Purpose: Accumulating evidence suggests that diet and lifestyle can play an important role in delaying the onset or halting the progression of age-related health disorders and to improve cognitive function. A growing number of dietary intervention studies in humans and animals and in particular those using polyphenols, have been proposed to exert a multiplicity of neuroprotective actions within the brain, including a potential to protect neurons against injury induced by neurotoxins, an ability to suppress neuroinflammation and a potential to promote memory, learning, and cognitive functions. This presentation will summarise the latest evidence related to the neuroprotective effect of polyphenols and their underlying molecular mechanisms.

Methods: Investigation of the neuroprotective effect of polyphenols was carried out in neuronal and astroglial primary cell cultures, in young and aged animal, and in randomized clinical trials in adult and older adults. Underpinning molecular mechanisms were investigated using cellular and molecular biology techniques, along with functional magnetic resonance imaging and flow mediated dilation.

Results: Polyphenols' effects appear to be underpinned by two common processes. First, they are capable of interactions with critical protein and lipid kinase signalling cascades in the brain, leading to an inhibition of apoptosis triggered by neurotoxic species and to a promotion of neuronal survival and synaptic plasticity. Second, they induce beneficial effects on the vascular system, leading to changes in cerebrovascular blood flow capable of causing enhance vascularisation and neurogenesis, two events important in the maintenance of cognitive performances.

Conclusions: Altogether, these processes act to maintain brain homeostasis and play important roles in neuronal stress adaptation and thus polyphenols might have the potential to prevent the progression of neurodegenerative pathologies.

Disclosures: No financial or competing interest to disclose.

Carotenoid Bioavailability – Knowns and Unknowns

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Purpose: While a good amount of data exists regarding carotenoid intake, many factors influencing their bioavailability are still poorly understood. This is important, as factors influencing their absorption, distribution, metabolism and excretion (ADME), resulting in inter-individual differences regarding plasma and tissue levels, are presumably also related to alterations regarding their health benefits.

Methods: In this overview presentation, it is aimed to highlight the present state of knowledge but also the gaps of knowledge regarding the bioavailability of these promising phytochemicals.

Results: Absorption of these highly lipophilic secondary plant compounds from the diet is rather low, around 5-30%, depending among other on successful incorporation into mixed micelles prior to their cellular uptake in the small intestine. Several dietary factors that hamper this step and inhibit bioaccessibility have been suggested and studied, including the amount of dietary lipids, which may foster solubilisation, the amount of dietary fibre, which may inhibit their transfer to mixed micelles, and high amounts of divalent minerals, which may precipitate bile salts and fatty acids required for micellization. However, the influence of other dietary factors such as proteins has not been systematically investigated, and aspects such as carotenoid location within cells of the plant food matrix have only recently been scrutinized. Also food processing may be a double edged sword, fostering maceration and release of carotenoids, but also risking their degradation. In addition to these dietary factors, an array of host factors can influence carotenoid bioavailability. Especially genetic factors such as single nucleotide polymorphisms (SNPs), influencing e.g. the activity of carotenoid transporters such as SRBI or CD36, cleavage enzymes such as beta-carotene-oxygenases (BCO1/2), or carotenoid associations with apolipoproteins for further biodistribution have been related to carotenoid absorption or accumulation in target tissues, including the macula. Also the influence of the colon regarding potential metabolism or absorption is virtually unknown.

Conclusions: Factors influencing ADME are crucial aspects in sight of the potential bioactivity of carotenoids and their metabolites, potentially interacting on many aspects of cellular metabolism, such as transcription factors and nuclear receptors such as RAR/RXR.

Disclosures: No conflict of interest.

Nutritional Cognitive Neuroscience

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Purpose: Nutritional cognitive neuroscience is an emerging interdisciplinary field of research that seeks to understand nutrition's impact on cognition and brain health across the life span. Research in this burgeoning field demonstrates that many aspects of nutrition—from entire diets to specific nutrients—affect brain structure and function, and therefore have profound implications for understanding the nature of healthy brain aging. The aim of this talk is to examine recent advances in nutritional cognitive

neuroscience, with an emphasis on methods that enable discovery of nutrient biomarkers that predict healthy brain aging.

Methods: We propose an integrative framework that calls for the synthesis of research in nutritional epidemiology and cognitive neuroscience, incorporating: (i) methods for the precise characterization of nutritional health based on the analysis of nutrient biomarker patterns (NBPs), along with (ii) modern indices of brain health derived from high-resolution magnetic resonance imaging (MRI).

Conclusions: By integrating cutting-edge techniques from nutritional epidemiology and cognitive neuroscience, nutritional cognitive neuroscience will continue to advance our understanding of the beneficial effects of nutrition on the aging brain and establish effective nutritional interventions to promote healthy brain aging.

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Age-dependent decline of MPOD in rhesus monkeys fed controlled diets.

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Purpose: To quantify macular pigment optical density (MPOD) across the lifespan, and to compare the spatial profile of MPOD with quantitative fundus autofluorescence (qFAF) images in rhesus monkeys fed a life-long controlled healthy diet.

Methods: MPOD was measured by two-wavelength reflectometry from rhesus monkeys (2-25yrs; n=60) fed a life-long standard laboratory diet. Peak MPOD was estimated from horizontal and vertical profiles through the fovea. MPOD volume was calculated in the superior, inferior, nasal, and temporal quadrants within the central 1 mm, and all regions were summed to determine MPOD total volume. Quantitative FAF images were collected using the Heidelberg Spectralis and mean grey value (MGV) was measured in the same regions as MPOD using ImageJ. MPOD and qFAF images were coregistered using I2K retina. Retinal tissue from select animals was analyzed using confocal Raman imaging.

Results: All 60 monkeys exhibited a central peak of MPOD, and 31 showed secondary peaks approximately 0.3 mm from the center. Both peak MPOD and total volume decreased significantly with age (r=-0.54, r=-0.53 respectively) at a rate of -0.002 and -0.001 per year, respectively. Total MPOD volume was significantly lower in the superior quadrant than all other regions. Animals were stratified into those with high (n=13, above 0.020) or low (n=47, below 0.020) MPOD total volume. Eight of the high MPOD group exhibited a ring of visibly reduced FAF at approximately 0.3 mm eccentricity, consistent with the location of the secondary MPOD peaks. In contrast, only three reduced FAF rings were detected in the low MPOD animals, and each of these animals was over 20 years of age. QFAF increased significantly in all regions with age. In young animals (≤16 years, N=35), there was a significant correlation between qFAF and both MPOD peak and volume within the central 1 mm (r=-0.36, r=-0.43), but no significant correlation between central MPOD and qFAF measured in regions outside the central 1 mm. In old animals (≥16, N=25), there were no significant correlations between MPOD and qFAF. When all animals are included, MPOD peak and volume were negatively correlated with qFAF in all regions. Confocal Raman imaging confirmed a single macular pigment peak in both flatmounted 4-mm macular punches and horizontal tissue sections.

Conclusions: MPOD decreased across the lifespan in rhesus monkeys fed a standard laboratory diet and a similar rate of decline was observed in animals with both high and low MPOD. FAF increased throughout the lifespan in the same animals, confirming previously reported data. These data make possible the comparison of in vivo measurements of MPOD and qFAF correlated with biochemical measurements and molecular mapping of lutein/zeaxanthin and sources of autofluorescence in retinal tissue. This data also will provide the foundation for examining the genetic and biochemical basis for differences in MPOD levels and spatial distribution in populations of nonhuman primates fed a controlled diet.

Xanthophyll carotenoids and cognitive function in healthy older adults: insights from a longitudinal population ageing study

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Purpose: There is considerable interest in the role of the xanthophyll carotenoids in brain function during both development and senescence. Investigations of lutein (L) and zeaxanthin (Z) concentrations in the primate and human brain are complemented by studies of the potential role of these dietary pigments in cognitive function and neurodegenerative disease. The purpose of this presentation is to review and discuss evidence for an association between the xanthophyll carotenoids and cognitive function in healthy older adults and implications for the epidemiology of cognitive impairment and dementia.

Methods: Data from The Irish Longitudinal Study of Ageing (TILDA) will be presented. TILDA is a population study of community dwelling adults aged 50 and older in Ireland. Multiple waves of data have been collected, allowing modeling of patterns of change in cognitive performance over time. L and Z were measured in blood plasma at baseline and cognitive performance was assessed with a battery of tests at multiple waves.

Results: Plasma L and Z show small, but robust independent associations with cognitive performance. Preliminary results suggest that these effects persist over time; however, carotenoid concentrations did not predict a change in cognitive function across multiple waves, independently of other risk factors.

Conclusions: Xanthophyll carotenoids are positively associated with cognitive function in older adults and may contribute to a reduction in risk of cognitive impairment in concert with other lifestyle factors.

Mechanisms of transport and delivery of vitamin A & carotenoids to the eye

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Purpose: Vision of vertebrates depends on the delivery of vitamin A (retinol) to the retina where it is converted to 11-cis-retinaldehyde, the chromophore for rhodopsin. The retinol is delivered to the eye from the blood where it is bound to plasma retinol-binding protein. We will briefly review the mechanisms involved in uptake of vitamin A in the eye. In contrast, carotenoids are transported in blood in lipoproteins. In primates, the the xanthophylls, lutein and zeaxanthin, are dietary carotenoids that selectively accumulate in the macula of the eye providing protection against age-related macular degeneration (AMD). To reach the macula, carotenoids cross the retinal pigment epithelium (RPE). In plasma, xanthophylls and β-carotene mostly associate with high-density lipoprotein (HDL) and low-density lipoprotein (LDL), respectively. HDL binds to cells via a scavenger receptor class B1 (SR-B1)-dependent mechanism while LDL binds via the LDL receptor (LDLR).

Methods: Using an in-vitro, human RPE cell model (ARPE-19), we studied the mechanisms of carotenoid uptake into the RPE by evaluating kinetics of cell uptake when carotenoids were delivered in micelles, serum or isolated LDL or HDL.

Results: For lutein and β-carotene, LDL delivery resulted in the highest rates and extents of uptake. In contrast, HDL was more effective in delivering zeaxanthin and meso-zeaxanthin leading to the highest rates and extents of uptake of all four carotenoids. Inhibition or knockdown of SR-B1 suppressed zeaxanthin delivery from micelles, lipoproteins, and from isolated HDL. Results show a selective HDL-mediated uptake of zeaxanthin and meso-zeaxanthin via SRB1 and a LDL-mediated uptake of lutein and β-carotene.

Conclusions: The results demonstrate a plausible mechanism for the selective accumulation of zeaxanthin > lutein and xanthophylls over β-carotene in the macula.

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Macular pigment and biology upstream to age-related macular degeneration (AMD): a view from eye pathology

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AMD pathobiology was irreversibly changed by the recent discovery of extracellular deposits in the subretinal space, between the photoreceptors and RPE, called subretinal drusenoid deposits (SDD). SDD strikingly mirror the topography of rod photoreceptors - is there is an equivalent process related to foveal cones? We propose that AMD's pathognomonic lesion - soft drusen and basal linear deposit (BLinD, a diffusely distributed form of the same material) - is the leading candidate. Epidemiologic, clinical, and histologic data suggest these deposits are thickest under the fovea. Strong evidence (histochemistry, ultrastructure, direct assay, gene expression, cell culture, longitudinal clinical imaging) supports the idea that the retinal pigment epithelium (RPE) constitutively secretes large apolipoprotein B,E-containing lipoproteins, which are the dominant ultrastructural component of soft drusen. Further, because fatty acids in these lipoproteins are dominated by linoleate rather than docosahexaenoate, we seek within neurosensory retina cellular relationships and dietary factors that can explain the topography of soft drusen and BLinD in older adults. The delivery of xanthophyll pigments to highly evolved and numerous Müller cells in the human fovea, through RPE, is one strong candidate. Evolution of neuroglial relations and xanthophyll delivery, underlying exquisite human foveal vision came with a price, i.e., soft drusen and sequela, long after reproductive years.

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Genomic Approaches Revealing the Action of Foods on Brain Function and Disease

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Purpose: The mechanisms by which foods affects the brain are highly complex, and its understanding requires the use of approaches with the capacity to integrate many signals and events occurring in a multitude of systems. It is crucial to understand how signals from peripheral organs and brain interact to regulate cognitive function under the regulatory action of foods, and how the effects of foods are saved to confer resistance or vulnerability to neurological and psychiatric disorders.

Methods: We utilize modern molecular biology procedures including RNA sequencing to determine how omega-3 fatty acids, flavonoids, and sugars affect the program of genes of molecules important for synaptic plasticity and cognitive function.

Results: We have found that foods influence long-term brain plasticity by building an "epigenetic memory" (Tyagi, E., et al., Neurobiol Dis, 2015. 73). Early life exposure to the omega 3 fatty acid DHA promotes long-term protection against the detriments of adult exposure to a western diet, and confers resistance to neurological challenges (Agrawal, R., et al., J Cereb Blood Flow Metab, 2015). To investigate mechanisms involved with the action of diet-induced metabolic disorder on brain, we use an animal model of fructose consumption (major cause of metabolic syndrome). Fructose disrupts hippocampal mitochondria bioenergetics and predisposes the brain to cognitive dysfunction. Using a systems nutrigenomics approach, we found that fructose promotes selective transcriptomic and epigenomic alterations in the hypothalamus (central control of metabolism) and hippocampus (critical for cognitive functions) regions of the brain, engaging cell metabolism, communication, inflammation, immune response, neuronal signaling, and cognition (Meng, Q., et al., EBioMedicine, 2016. 7). These alterations converge with genes conferring genetic risks of neurological disorders, metabolic and neuropsychiatric disorders in human genome-wide association studies. Diet affects multiple levels of brain and body physiology resulting in metabolic imprinting of the genome that determines long-lasting resilience to neurological disorders.

Conclusions: Foods signals are saved as epigenetic alterations across body and brain, and can modulate homeostasis and disease. Findings are significant on the context of the contemporary epidemic of metabolic disorders and health risk posed to resilience to neurological disorders.

Understanding Alzheimer's as a Disease of Chronic Oxidative Stress

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Purpose: Alzheimer's disease is characterized pathologically by two principal hallmark lesions, the senile plaque and the neurofibrillary tangle. Since the identification of each over 100 years ago, the major protein components have been elucidated. This has led in turn to the elaboration of metabolic cascades involving amyloid- production in the case of the senile plaque, and phosphorylated-tau protein in the case of the neurofibrillary tangle.

Methods/Results: The pathogenesis and histogenesis of each have been the source of extensive investigation and some controversy in recent years, as both cascades have been implicated in the pathogenesis of Alzheimer's disease, relied upon in the diagnostic criteria for Alzheimer's disease at autopsy, and targeted for therapeutic intervention. With the accumulation of data and expansion of knowledge of the molecular biology of Alzheimer's disease, it appears that the enthusiasm for successful intervention has been premature. Our efforts have focused on metal and mitochondria abnormalities as a window to the disease. Results highlight homeostatic balance as essential to understanding the slow progression of chronic diseases that have their roots in mid-life.

Conclusions: We will detail the discovery and characterization of the major pathological lesions, their associated molecular biology, their relationship to clinical disease, and potential fundamental errors in understanding that may be leading scientific investigators in unintended directions.

Disclosures: George Perry is a board member, advisor, or owns equity in the following companies: Neurotez Inc., Phoenix Biotechnology Inc., Neurotrope Inc., and InvestAcure.

Rising atmospheric CO2 tends to lower carotenoid levels in plants: Can the global decline in dietary carotenoids affect human vision and memory?

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Purpose: Photosynthetic tissues in higher plants and human retina share the need for xanthophylls (oxygen containing carotenoids) to reduce damage caused by light-induced oxidative stress. While plants synthesize carotenoids de novo, humans must rely on their dietary intake. Randomized double-blind clinical trials showed that increasing dietary intake of xanthophylls improves vision and memory in humans. Conversely, a global decline in carotenoid levels in plants could be detrimental to human health. Elevated atmospheric CO2 levels (eCO2) have been shown to lower the nutritional plant quality by decreasing the levels of essential minerals, including zinc. We sought to investigate the impact of eCO2 on plant carotenoids.

Methods: We compiled and analyzed data on carotenoids from published studies covering 308 paired observations at ambient and elevated CO2 in 25 plant varieties, and reviewed some of the physiological mechanisms by which eCO2 affects carotenoids.

Results: eCO2 decreases carotenoid levels in plants by -20% (95% confidence interval, -38% to -2%). While the action of eCO2 on plant carotenoids is not well understood, it appears that plant demands for xanthophylls can decline in mesophyll and guard cells under eCO2.

Conclusions: Rising CO2 levels are likely to lower plant carotenoid concentrations. This can decrease the global dietary intake of carotenoids, including xanthophylls (e.g. zeaxanthin), which would be detrimental to vision and memory functions in humans.

A Decade of Research on Lutein and Cognition

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Purpose: In 2008 it was first reported that supplementation with a dietary level of lutein resulted in cognitive improvements in older adults (1). Since then, evidence has accumulated to support a role for lutein in cognitive function not only in older adults, but throughout the lifespan. The purpose of this lecture is to review the past decade of research evaluating lutein and cognitive function.

Methods: Literature was searched using MEDLINE®, Commonwealth Agricultural Bureau, and Cochrane Central databases for all published studies that examined lutein/zeaxanthin and cognitive outcomes.

Results: Data supporting a role for lutein in cognitive function include cross-sectional relationships between lutein concentrations and neurotransmitters in pediatric brain tissue (2) and pre-mortem measures of cognition in centenarians (3). Several research groups have reported significant associations between macular pigment density, a non-invasive measure of lutein embedded in neural tissue (4), and cognitive measures in various populations and ages (5). Among the dietary carotenoids, lutein is selectively taken up into neural tissue (3). In part, this may be due to the presence of a specific binding protein (6) which provides biological rationale for its importance. However, little is known regarding the mechanisms by which lutein functions in brain tissue. Gene expression data in rhesus monkeys suggest that lutein levels in the brain are related to genes related to carotenoid and fatty acid metabolism as well as the immune response (7). Furthermore, subcellular accumulation of lutein in mitochondrial lutein was found to be inversely related to DHA oxidation products in non human primate brains (8), supporting the hypothesis that lutein may be associated with antioxidant functions in the brain.

Conclusions: Future research directions include an understanding of factors involved in lutein uptake into neural tissue as well as further characterization of the relationships between lutein and other nutrients of interest to cognitive health.

Understanding the role of nutrition in lifespan brain development

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Purpose: Recent research from our laboratory and others suggests that dietary xanthophyll supplementation can improve neurological health and cognitive function in adult participants, and that relations exist between central nervous system xanthophyll status and cognitive function in preadolescent children. The purpose of this presentation is to address these relationships in two ways: 1) on the intervention side, to discuss whether or not xanthophylls predict more variance in cognitive function than other nutrients found in higher concentrations in the diet and brain, across the lifespan; and 2) on the application side, to determine barriers to recommending dietary change and nutritional supplementation among healthcare providers, including response rates, patient literacy and autonomy, provider support of autonomy, and tracking cognitive improvements from infancy through older adulthood.

Methods: Data from a variety of studies conducted in the Human Biofactors and Vision Sciences Laboratory will be presented. Male and female participants ranged in age from 3-months of age to 99 years of age and were assessed using a variety of methods.

Results: Serum lutein and zeaxanthin concentrations predicted a variety of cognitive functions better than other carotenoids measured, as well as the majority of the fat-soluble vitamins measured. These results suggest that targeted xanthophyll supplementation and increasing xanthophyll-rich food intake could uniquely promote cognitive development. Healthcare provider attitudes toward recommending dietary change and nutritional supplementation are, however, currently poor.

Conclusions: Lutein and zeaxanthin account for the dominant proportion of variance in cognitive function among other dietary carotenoids and fat soluble vitamins tested in our study populations. Understanding barriers to dietary change and healthcare provider recommendations, including health literacy, health autonomy and provider support of autonomy, is necessary.

Disclosures: Abbott Nutrition funded a portion of the data collection. DSM Nutritional Products

supplied dietary supplements. Author LRH has received speaking fees from Abbott Nutrition within the last 12-months. During a portion of the data collection, LRH was employed by Abbott Nutrition. For the past three years, author LRH has been employed solely by the University of Georgia and continues to be employed by the University of Georgia on a full-time basis.

The Power of Contrast Sensitivity and Nutritional Intervention in Primary Eye Care

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Purpose: This paper discusses the proper use of visual acuity measurement and its limitations in assessing a patient's ability to perform daily activities. It demonstrates that Contrast Sensitivity (CS) testing, when measured at intermediate spatial frequencies, is a powerful tool useful in providing unique and important information for both patients with healthy eyes and those with ocular pathology. The results of CS testing enable the practitioner to provide more accurate guidance regarding nutritional intervention with macular carotenoids as shown in recent research, and for other interventions as indicated.

Methods: The proper methods for measuring CS are described with a comparison of sine wave gratings and letter charts. The Harris Contrast Test for measuring CS with an electronic device is discussed and compared to the Pelli-Robson Chart for assessing letter CS. Normal letter CS threshold ranges are presented for patients with no ocular pathology with a suggested action diagram. The effect of ocular disease on letter CS is also detailed with suggestions for appropriate action with monitoring or referring a cataract patient. New research showing the positive effect of nutrition on visual performance in patients with early Age-Related Macular Degeneration is also reviewed.

Results: Case illustrations show that the techniques presented for measuring CS provide a powerful tool for proper assessment and appropriate management of patients with impaired CS in the clinic setting. The practical application of nutritional intervention utilizing the latest research findings is demonstrated for patients with no apparent ocular pathology and for those with ocular disease.

Conclusions: Eye Care Practitioners cannot effectively help a patient unless they truly understand the patient's visual world. This requires the use of both visual acuity testing and accurate CS measurements at intermediate spatial frequencies for the best patient care.

Disclosure: The speaker has served as a consultant for MacuHealth, LLC and for M&S Technologies.

COST Action EUROCAROTEN: European network to advance carotenoid research and applications in agro-food and health

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Carotenoids appeared very early in life's history on Earth. They were present in cyanobacteria, one of the first inhabitants of our planet, were they are thought to contribute to light harvesting and photoprotection. During the evolution of life, the structures and functions of carotenoids have diversified to a great extent. They are considered as versatile secondary metabolites that play key roles in photosynthesis, protection against oxidation, communication within and between species and so on. Interestingly, they are metabolized into a series of metabolites like norisoprenoids, retinoids, strigolactones, among others, which also play numerous key roles in Nature. To date, more than 700 carotenoids have been identified in organisms living in the most disparate organisms, although very few (10-20) are being studied thoroughly. There is therefore a great potential of expanding research and applications in the carotenoid field.

In this context, an European network of laboratories and companies has been set up through the financial support of COST (European Cooperation in Science and Technology, http://www.cost.eu/). The main goal of the COST Action EUROCAROTEN ("European network to advance carotenoid research and applications in agro-food and health", www.eurocaroten.eu) is to advance carotenoid research and applications in agro-food and health through networking tools that facilitate the sharing of knowledge, and infrastructures and synergistic interactions. To date over 100 scientists and technicians from 35 countries are taking part in the Action.

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Development of Improved Animal Models to Study the Ocular Benefits of Carotenoid and Lipid Supplementation

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Purpose: There is growing clinical evidence that supplementation with carotenoids and various lipids can improve visual performance in humans, but animal model development to delve into the underlying biochemical and biophysical mechanisms has lagged due to inadequate delivery of these dietary factors into the retina in a reproducible and verifiable manner. We have therefore initiated a long-term project to optimize carotenoid and lipid uptake into the mouse retina through transgenic and nutriceutical approaches in order to elucidate the mechanisms by which these nutrients can enhance performance of the vertebrae eye.

Methods: In order to optimize carotenoid uptake into the mouse retina, we knocked out the carotenoid cleavage enzymes BCO1 and/or BCO2 and then fed the mice a diet supplemented with DSM ActiLease beadlets containing lutein, zeaxanthin, β-carotene, or placebo. We then compared visual performance by OptoMotry, a validated technique to assess visual acuity and contrast sensitivity in rodents. In order to study function of retina-specific very long chain polyunsaturated fatty acids (VLC-PUFAs), we initiated a collaboration with the University of Utah chemistry department to synthesize these rare lipids for gavage feeding to mice.

Results: Wild type mice never had detectable carotenoids in their retinas, but knocking out BCO enzymes shut down the mouse's highly active carotenoid cleavage pathways and allowed reproducible uptake of carotenoids into their retinas. Especially in the case of lutein and zeaxanthin in BCO2 knockout mice, we could document significant improvements of visual acuity and contrast sensitivity. When we fed wild type mice synthetic VLC-PUFAs, we could detect selective uptake into the retina within 6 hours. After further optimization of VLC-PUFA feeding protocols, we will perform comparable OptoMotry studies.

Conclusions: Transgenic "macular pigment mice" and feeding protocols for carotenoids and synthetic VLC-PUFAs have been successfully developed and optimized to objectively demonstrate that nutritional supplementation can enhance visual performance of the vertebrate retina. These novel laboratory models can be used by researchers to probe the biochemical and biophysical mechanisms underlying these important physiological effects.

Eating for Eye Health: An award-winning community cookery project to engage older people with research on diet and lifestyle for eye health

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Purpose: To investigate perspectives of older people regarding nutrition and diet for eye health and to identify suitable interventional approach(es) which could serve to increase sense of agency and/or self-efficacy in this context.

Methods: Focus group, individual interviews and pilot community cookery intervention. Participants were recruited via NIHR Moorfields Biomedical Research Centre, London, UK.

Results: 12 participants aged 60-75 years were recruited for the focus group. 100% of focus group participants indicated an interest in diet for eye health and reported that they ate fruits or vegetables rich in carotenoids at least once per week (mean: twice a week, range: 1-6 times per week). 8 out of 12 participants from the focus group (in addition to 2 further participants) attended a community cookery day at Central Street Cookery School, St Luke's Community Centre, London, UK. All participants reported increased confidence levels in cooking for eye health after the cookery session, and 8 out of 10 participants reported a confidence level of 7 or above with regard to cooking for themselves with the recipes provided.

Conclusions: Community cookery has potential as a methodology to engage patients with nutritional advice for eye health and to increase self-efficacy in the context of sight-threatening retinal disease.

Fair-Weather Friends: Lipid Mediators in Retinal Parainflammation

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Purpose: Astrocytes and related macroglia play critical non-cell autonomous roles in the central nervous system (CNS), involving either parainflammatory neurotoxic or homeostatic effects. Yet, the regulation of these activities, and nature of potential pro-survival cues has remained unclear. We have utilized models of retinal injury to characterize a novel neuroprotective signal secreted by astrocytes.

Methods: We developed in vitro and in vivo assays to model astrocyte-neuron interactions in homeostatic, and metabolic and oxidative injury contexts. Using these platforms biochemical and metabolomic methods were used to characterize a secreted neuroprotective signal. This work was followed by validation studies in acute and chronic neurodegeneration models.

Results: Surprisingly, small lipid mediators of the lipoxin family were identified as key component of this protective signal, rather than a conventional peptide neurotrophic factor. The lipoxins, LXA4 and LXB4, are derived from polyunsaturated fatty acids (PUFAs), and act locally to potently dampen inflammation, but they have not been linked to direct neuronal actions. We discovered that LXA4 and LXB4 are synthesized in the healthy inner retina, but are decreased following injury. Each is sufficient to produce neuroprotection in retinal and cortical neurons, in association with mitochondrial stabilization. Conversely, inhibition of key lipoxin pathway components exacerbates injury. LXA4 signaling has been much more extensively investigated than LXB4. Yet, LXB4 is unexpectedly more potent in this protective role. We demonstrated that LXB4 neuroprotection is independent of established lipoxin signaling, and that therapeutic LXB4 treatment is efficacious in a chronic 15-week model of glaucomatous neuropathy.

Conclusions: Together these results identify a new paracrine mechanism that can coordinate neuronal survival and inflammation in the retina and CNS.

Disclosures: the author has applied for a patent on the discussed topic.

The Macular Carotenoids and Visual Performance: A 2018 Update

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Purpose: The purpose of this lecture has several facets: 1) To define visual performance, 2) To provide a framework within which different macular carotenoid properties mediate different aspects of visual performance, and 3) To provide a review of the relatively brief history of research on macular carotenoids and visual performance, with an emphasis on recent findings.

Methods: Macular carotenoid status in the eye (macular pigment optical density [MPOD]) has been shown in several studies to confer visual performance benefits. For example, temporal processing speed, contrast sensitivity, vision in dim lighting conditions, and several aspects of vision impacted by glare have all been found to be related to and / or enhanced by higher MPOD. This review lecture will draw from the results of several studies, for which methods will be described in adequate detail, so as to promote a thorough understanding of how these effects appear to work.

Results: Results of previous studies of the relationship between macular carotenoid status and visual performance enhancement will be described and characterized within the framework noted above.

Conclusions: Although they appear to serve a significant function of retinal protection against oxidative stress and short-wavelength light exposure, lutein, zeaxanthin, and mesozeaxanthin do not exist in the eye to protect against age-related eye disease. Their purpose, rather, is to promote good visual performance. The basis of this claim is twofold: 1) Age-related disease manifests well after the reproductive cycle, and therefore the ability to accumulate these carotenoids in the retina would not be selected for based on protection against, e.g., AMD, and 2) There now exists a wealth of data that serve to substantiate a significant role for macular carotenoids in good visual performance.

Disclosures: James M. Stringham serves as a consultant / speaker for Abbott Nutrition, MacuHealth, and VizionEdge.

Retinal Carotenoids and Childhood Cognitive Function and Achievement

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Purpose: Identification of foods and nutrients that promote childhood cognitive function has the potential to have a lasting impact on children's long-term cognitive well-being. Lutein and zeaxanthin are plant pigments known to preferentially accumulate in neural tissue. Greater retinal accumulation of these carotenoids has been shown to provide neuroprotective effects on cognition during later adulthood. However, research examining the relationship between retinal carotenoids and cognitive function during childhood remains limited. This work aimed to elucidate the relationship between retinal carotenoids and children's ability for cognitive function and achievement.

Methods: Children between 7-10 years of age underwent a modified heterochromatic flicker photometry procedure to assess macular pigment optical density (MPOD). Attentional control and relational memory were assessed using a modified flanker and spatial reconstruction tasks, respectively, Children also completed standardized academic achievement tests.

Results: Findings from this work suggest that preadolescent children with higher MPOD exhibit greater academic achievement. Further, MPOD was positively associated with greater ability for hippocampal-dependent relational memory as well as behavioral and neurolectric measures of attentional control.

Conclusions: This work revealed that the benefits of superior MPOD status for cognitive function are evident as early as childhood. Given that childhood signifies a critical period for cognitive development accompanied by rapid carotenoid accumulation in brain, additional research is needed to characterize the importance of dietary intake of carotenoids for cognitive function during childhood. Ongoing work is examining the impact of daily lutein intake on changes in MPOD and cognitive function.

Disclosures: Support for this work was presented by Abbott Nutrition via the Center for Nutrition, Learning, and Memory at the University of Illinois at Urbana-Champaign.

Determination of intestinal β-carotene bioconversion in humans by a new single-sample plasma isotope ratio method

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Purpose: The conversion of provitamin A carotenoids to retinol is determined traditionally by an area-under-the-curve method calculated from 0 – 8 h after absorption. To facilitate the estimation of provitamin A carotenoid bioconversion in large intervention studies or in children, when repeated blood sampling is not feasible, a simpler yet accurate method of bioconversion is needed.

Methods: Intestinal bioconversion of absorbed β-carotene was calculated at 2, 4, 6, 8, 10, 12 and 24 h after dosing as a plasma isotope ratio (IR method). The IR method was compared to a) the traditional AUC method or b) an adjusted AUC method (AUC-adj) that estimates the β-carotene chylomicron fraction using the integrated areas under the plasma isotope response curves.

Results: Intestinal bioconversion of β-carotene can be estimated based on analysis of a single plasma sample collected 6 h from the ratio of retinyl esters to retinyl esters plus β-carotene. Plasma isotope ratio predictions of bioconversion ranged from 50 – 93% (mean 76%) for 45 healthy young adults with low vitamin A stores. Results were the same as predictions made by a traditional area-under-the-curve method calculated from 0 – 8 h or a modified area-under-the-curve method calculated from 0 – 12 h.

Conclusions: The modified method may provide better estimates of bioconversion between 8 and 24 h after ingestion of a carotenoid dose when stable isotopes cannot be used due to cost or logistics. The plasma isotope ratio method will facilitate estimation of provitamin A carotenoid bioconversion in large intervention studies and children, as it requires only one blood sample and no isolation of triglyceride-rich lipoproteins.

Nutritional intervention to enhance cognitive function and prevent Alzheimer's disease: a summary of studies from Waterford

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Purpose: The exact triggers for the neurodegeneration in Alzheimer's disease (AD) remain unknown, but are likely to occur as a result of a cascade of events that lead to alteration in cell structure and function within the brain. A growing body of scientific evidence suggests that enrichment of certain nutritional compounds in the brain may enhance cognitive function and reduce the risk of AD. The Waterford studies have investigated the impact of supplemental xanthophyll carotenoids on cognitive function across different stages of cognitive abilities (i.e. from cognitively healthy individuals to patients with AD).

Methods: Our work on cognitively healthy individuals examined the impact of meso-zeaxanthin, lutein, and zeaxanthin (MZ:L:Z) (10:10:2 mg/day plus sunflower oil – Formulation 1) on cognitive function in a 12-month placebo-controlled trial (CREST). Our work on patients with AD compared the xanthophyll carotenoid status in diet, serum and retina (i.e. macular pigment) to controls (CARDS). CARDS interventional work examined the impact of Formulation 1 to a formulation containing MZ:L:Z (10:10:2 mg/day plus 1g of fish oil containing 430mg docohexaenoic acid [DHA] and 90mg eicopentaenoic acid [EPA]) (Formulation 2). Outcomes assessed included serum carotenoid response at 6 months and quality of life at 18 months (via nurse and carer reports). Blood carotenoid response was measured in all trials by HPLC. Omega-3 fatty acids were profiled by direct infusion mass spectrometry.

Results: In CREST, individuals in the active group exhibited statistically significant improvements in episodic memory when compared to the placebo group (paired associated learning [PAL] memory score [rANOVA, $p=0.009$]; PAL errors [rANOVA, $p=0.017$]). In CARDS, serum xanthophyll carotenoid concentrations and macular pigment were significantly lower in subjects with AD compared to controls ($p < 0.05$, for all). Following supplementation, increases in serum xanthophyll carotenoid concentrations were significantly greater for Formulation 2 compared to Formulation 1 ($p<0.05$), and progression of AD was less for this group ($p=0.003$), with carers reporting functional benefits in everyday activities, sight and mood.

Conclusions: Our work to date confirms improvements in cognitive function with supplemental xanthophyll carotenoids in cognitively healthy individuals, and our preliminary work in AD suggests positive outcomes for patients who consumed a combination of xanthophyll carotenoids plus fish oil. We are currently conducting a larger trial (reMIND) to examine the impact of xanthophyll carotenoid plus fish oil supplementation on disease progression and quality of life in AD patients.

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