

THE 2015 AGEING SUMMIT



ABSTRACTS

**10th-12th February
London, UK**

EuroSciCon

This event will look at current scientific research and thinking regarding the ageing process. With discussions ranging from discovery of biomarkers and assay development to the immunology of ageing, this event promises to be packed with discussion and debate and is an ideal opportunity to discover what is new in the field.

This event has [CPD accreditation](#)

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Day 1, Session 1: Cellular Level Research

Invited Speakers Abstracts

The extracellular metabolome in senescence and oral cancer

[Professor Ken Parkinson](#), Queen Mary, University of London, UK

Cellular senescence can contribute to ageing in animal models and is defined as a permanent cell cycle arrest; it is associated with a number of secreted proteins known as the senescence-associated secretory phenotype, which can spread senescence throughout cell populations and promote cancer. The metabolism of senescent cells is also altered; the transfer of energy metabolites can increase oxidative phosphorylation in neighbouring cells and lipid peroxidation can drive parts of the inflammasome. We have conducted an unbiased screen of senescent cell extracellular metabolites and identified several molecules that may be candidates for the detection of senescent cells in humans.

Chronic Inflammation, Proteases and Extracellular Matrix Degradation in Extrinsic Aging

[Professor David Granville](#), Department of Pathology & Laboratory Medicine, University of British Columbia, Director, GEM Facility, Centre for Heart Lung Innovation, St. Paul's Hospital Co-Director, CIHR STIHR IMPACT Program, Founder and CSO, viDA Therapeutics, Inc. Vancouver, BC, Canada

The skin represents an ideal model organ for aging research. Its accessibility allows for the study of intrinsic and extrinsic/environmental factors that contribute to the complex phenomenon of aging, chronic injury, inflammation and repair. Among all the environmental factors, UV irradiation is the most influential in premature aging of the skin, causing ~80% of the morphological, structural and biochemical changes collectively termed photoaging. Protease-mediated extracellular matrix (ECM) degradation is a hallmark of most age-related, chronic inflammatory disorders. Our research suggests that the serine protease, granzyme B, may be an important contributor to age-related skin degeneration and disease.

Age-related Changes in Mitochondria Complex-I Activity in Brain: PET Study with [18F]BCPP-EF in Monkey

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Age-related changes in mitochondria complex-I (MC-I) activity have been suggested in postmortem brain, however few data have been reported in the living brain. We recently developed a novel PET probe, [18F]BCPP-EF, and reported that this PET probe could accurately detect the ischemic-induced neuronal damage without any disturbances by neuroinflammation caused by activated microglia. We recently confirmed the lowered MC-I activity in the living brains of aged monkeys compared with those of young ones, and also demonstrated that aged monkeys with lower MC-I activity showed higher amyloid- β deposition measured with [11C]PIB and higher neuroinflammation determined with [11C]DPA-713.

Hormones and Aging

[Dr Cheryl Anne Frye](#), Professor of Neuroscience, Department of Chemistry & Biochemistry, Institute of Arctic Biology, University of Alaska- Fairbanks, USA

There are sex/gender differences in hormones and aging for cognitive processes. A question is the role of neurosteroids, cholesterol-based hormones that are produced de novo in the brain, in aging. Neurosteroids are synthesized in response to environmental and social challenges to regulate homeostasis. Data obtained from animal models, and clinical conditions, suggest that aging may be associated with a reduced capacity for the brain to produce androstane (male-typical) and pregnane (female-typical) neurosteroids, which has consequences beyond reproduction to cognition and affect. Additionally, recent studies relevant for cognitive effects of cholesterol inhibitors and "chemobrain," in addition to neurosteroid mechanisms will be discussed.

Longevity and beta-2 microglobulin

[Professor. Bernard Cheung](#), Sun Chieh Yeh Heart Foundation Professor in Cardiovascular Therapeutics, Department of Medicine, University of Hong Kong

Beta-2 microglobulin (B2M) is present in all nucleated cells. B2M level in the highest quartile confers a 20-fold risk of death. It is a powerful predictor of all-cause mortality because of its correlation with risk factors such as hypertension and dyslipidaemia, and common causes of death such as malignancies. Moreover, B2M is related to arterial stiffness and atherosclerosis, as well as chronic kidney disease.

Ageing induced defects of the thermosensor plasma membrane can downregulate the expression of stress protein molecular chaperones

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Ageing (and important diseases) are known to be associated with abnormally low stress (or heat shock) protein (HSP) levels and characteristic membrane defects. The present study aims to establish a mechanism for the possible interconnection between specific changes of lipid composition, fluidity- and microdomain organization of plasma membrane and the simultaneously altered (dysregulated) expression of HSPs during ageing. Exposure of cells to fever stress, non-proteotoxic membrane fluidizers or non-proteotoxic drug candidates which interact specifically with certain membrane domains, all can upregulate the expression of heat shock proteins. Monitoring the surface membrane microdomains by confocal- and ultrasensitive single molecular microscopy we established a relationship between specific distribution of lipid nanostructure ("rafts") and the concomitant changes in the level, profile and cellular distribution of HSPs. A comparative lipidomics study explored key lipid molecular species with the potential to activate of HSP signalling pathways. Drug candidates, capable to refine HSP profile by targeting specific membrane microdomains, - with considerable therapeutic benefit -, will also be discussed.

A subpopulation of HSPs is membrane associated: via their specific lipid interactions these HSPs can control major attributes of the membranes like fluidity or curvature. The membrane microdomain associated HSPs can also participate in the orchestration of distinct raft-associated signalling platforms: thus, membrane association of HSPs can refine hsp gene expression in the ageing cells.

Immune cells: their part in brain ageing

[Dr Jennifer Pocock](#), Senior Lecturer and Principal Investigator, Department of Neuroinflammation, University College London Institute of Neurology, London, UK

Immune cells of the brain (microglia), and the periphery (macrophages) protect the body from infection, by producing reactive oxygen and nitrogen species which kill invading pathogens, aid repair, by producing neurotrophic factors and promote regeneration, by removing apoptotic debris and synapse stripping within the processes of memory formation. Microglia and macrophages are highly plastic, and can change phenotype in response to cues from their local environment as well as from more distant signals. With ageing, the plasticity of these cells may be compromised and their ability to promote repair and regeneration diminished. My talk will address some of the problems of microglial and macrophage responses within the ageing brain.

Oral Presentation Abstracts

PROTECTION AGAINST AGE-RELATED HEARING LOSS BY OVER-EXPRESSION OF X-LINKED INHIBITOR OF APOPTOSIS PROTEIN IN C57BL/6J MICE

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Apoptosis of cochlear cells plays a significant role in age-related hearing loss or presbycusis. In this study, we evaluated whether over-expression of the anti-apoptotic protein known as X-linked Inhibitor of Apoptosis Protein (XIAP) delays the development of presbycusis. We compared the age-related hearing loss between transgenic (TG) mice that over-express human XIAP tagged with 6-myc (Myc-XIAP) on a pure C57BL/6J genetic background with wild-type (WT) littermates by measuring auditory brainstem responses.

The result showed that TG mice developed hearing loss considerably slower than WT littermates, primarily within the high-frequency range. The average total loss of hair cells was significantly less in TG mice than WT littermates. The protective effect of XIAP over-expression was also clearly demonstrated by delayed and reduced degeneration in both afferent and efferent cochlear innervations. These results suggest that XIAP over-expression reduces age-related hearing loss and hair cell death in the cochlea.

Several other interesting facts related to cochlear aging were obtained. Firstly, the results suggest that the age-related degeneration of cochlear neurites may be independent of hair cells, opposite to what is expected in the traditional view. Secondly, although the level of Myc-XIAP in the ear remained constant at 2 and 14 months, there was a marked increase in the amount of endogenous XIAP over this period in the cochlea (but not the brain) in both genotypes.

RAISING AWARENESS OF AGEING AND DENTAL CARE

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The United States geriatric population is living longer and the trend is expected to increase in the decades to come. By 2029 more than 20 percent of the total U.S. population will be over the age of 65 (Colby & Ortman, 2014). According to the U.S. Administration on Aging, the population of Americans older than 65 years is expected to double to 71 million by 2040. The population over 85 years old is also expected to increase to 9.6 million by 2030 (US Census Bureau, 2010). As people live longer and retain more natural teeth, the complexity of the geriatrics populations treatment increases (American Dental Association, n.d.). The lower rates of edentulism and an ageing population mean that older people will feature more prominently in dental services (Hartfort, 2009). Changes in the population has been documented but what is not well understood is the pattern of dental expenditures of the aging population and its effect on rising healthcare costs and access to treatment. The need to increase awareness and research to better understand the correlation between ageing and dental care is needed. The knowledge gained can help plan access to dental care and help alleviate dental expenditures in the ageing population.

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PHOSPHODIESTERASE 1 REGULATION IS A KEY MECHANISM IN VASCULAR AGEING

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Introduction and aims: Reduced nitric oxide – cyclic guanosine monophosphate (cGMP) signaling is observed in age-related vascular disease. We hypothesise that this disturbed signaling involves effects of genomic instability, a primary causal factor in ageing, on vascular smooth muscle cells (VSMC), and that the underlying mechanism plays a role in human age-related vascular disease.

To test our hypothesis we first explored the effect of genomic instability in mice on cGMP-induced vasodilator function and key enzymes of this signaling pathway. Subsequently, we explored the role of cellular senescence on the cGMP pathway in primary cultures of human arterial VSMC. Finally, we used genetic association studies in human cohorts to explore if there is a role of genetic variants in PDE genes on age-related human vascular disease: blood pressure (BP), Pulse pressure (PP), pulse wave velocity (PWV) and carotid intima media thickness (cIMT).

Methods and results: Organ bath studies on thoracic aortas from *Ercc1^{d/-}* and wild-type (WT) mice were performed. Relaxation concentration-response curves (CRCs) were constructed to sodium nitroprusside (SNP) to test cGMP-mediated responses. To investigate the involvement of increased activity of PDE enzyme in VSMC dysfunction, segments were preincubated with sildenafil or vinpocetine. To test for differences in cGMP-dependent protein kinase 1 α (PKG1) responsiveness, CRCs to 8-Br-PET-cGMP were constructed. In addition, sGC expression and activity, PKG expression and PDE activity were tested in mouse tissue and in young vs. senescent human VSMC. Aortic rings of *Ercc1^{d/-}* showed 43% reduced SNP responses, which was normalised by sildenafil and vinpocetin. PDE1C levels were increased in lung and aorta. cGMP hydrolysis by PDE in lungs was higher in *Ercc1^{d/-}*. No differences in activity or levels of PKG or sGC were observed in *Ercc1^{d/-}* mice vs. WT. Senescent human VSMC showed elevated *PDE1A* and *PDE1C* and *PDE5* mRNA levels (by 11.6, 9 and 2.3 fold respectively), which associated with markers of cellular senescence. Human genetic studies revealed significant associations of *PDE1A* single nucleotide polymorphisms with diastolic blood pressure (β = 0.28, p = 2.47x10⁻⁵) and carotid intima media thickness (β = -0.0061, p = 2.89x10⁻⁵) after Bonferroni correction.

Conclusions: Genomic instability and *in vitro* VSMC aging lead to increased PDE1, decreasing cGMP signaling. *PDE1A* gene variations are associated with increased diastolic blood pressure and carotid intima media thickness. These results suggest that PDE1 plays a pivotal role in human age-related vascular disease, which might involve VMSC senescence and genomic instability.

AGING, CHRONIC KIDNEY DISEASE AND HOME SUPPORT: AN EXPLORATORY STUDY

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Background: Home support (HS) services provide personal assistance with activities of daily living and help prevent or delay the need for long-term institutional-based services. There is limited information about HS use in chronic kidney disease (CKD) that is known to be common among older people and is often accompanied by several comorbid conditions and functional limitations. This study explores HS use among CKD patients in British Columbia (BC), Canada.

Methods: Clinical data from BC Renal Agency and BC Transplant (kidney transplants) on 15,110 CKD patients (mean age=69.0±15.2) was linked with the BC Ministry of Health Discharge Abstracts Database and Home and Community Care data for fiscal year 2009/10 for a cross-sectional study. Patients were grouped into 'non-end-stage renal disease (non-ESRD) CKD' (65%) and ESRD CKD (35%) based on the type of care they received during the fiscal year. The ESRD CKD were further divided into 'dependent dialysis only' (in-center and community hemodialysis (HD), 12%), 'independent dialysis only' (home HD and peritoneal dialysis, 4%), 'transplants and transitions ending with a transplant' ('transplant' group, 13%) and 'other transitions' (capturing transitions between different types of care excluding transplantation, 6%). Transitions involving 'non-ESRD CKD' made up 72% of 'other transitions' group. Logistic regression was used to explore factors that are associated with publicly subsidized HS use among CKD patients in BC.

Results: Of the CKD patients, 'non-ESRD CKD' group was the oldest (mean age=72.7±13.5) and had the highest proportion of females (47%). The 'transplant' group was the youngest (mean age=54.2±13.5) and 'other transitions' group had the lowest proportion of females (37%). Modified Charlson Comorbidity Index (Hemmelgarn CCI) was highest among 'dependent dialysis only' group (mean CCI=3.7±3.3) and lowest among 'transplant' group (mean CCI=1.4±2.2). The 'dependent dialysis only' group also had the highest proportion of deaths (16%) within the fiscal year. The proportion of deaths was lowest among the 'transplant' group (2%). Average annual number of hospitalizations ranged between 0.8 ('transplant') and 2.9 ('other transitions'). The 'dependent dialysis only' group had the highest (54%) and the 'independent dialysis only' group had the lowest (41%) proportion of patients with lower (neighbourhood income based) socio-economic status. Results from the logistic regression showed that older age (OR=1.06; 95%CI 1.05-1.07), female sex (OR=2.13; 95%CI 1.83-2.49), higher Hemmelgarn CCI (OR=1.10; 95%CI 1.07-1.12), higher hospitalization rate (OR=1.21; 95%CI 1.16-1.26) and dying within the fiscal year (OR=1.75; 95%CI 1.43-2.15) were associated with higher HS use. Higher socio-economic status (OR=0.72; 95%CI 0.62-0.84) was associated with lower HS use. After these adjustments, regional and CKD group variations in HS use remained. When compared to the 'transplant' group, HS use was significantly higher for all other CKD groups ('dependent dialysis only' (OR=3.68; 95%CI 2.08-6.51), 'other transitions' (OR=2.64; 95%CI 1.42-4.90), 'non-ESRD CKD' (OR=2.33; 95%CI 1.34-4.05) and 'independent dialysis only' (OR=2.12; 95%CI 1.05-4.26)).

Conclusions: After adjustments for demographic factors, socio-economic status, comorbidity, hospitalizations and death within the fiscal year, there were remaining regional and CKD group variations in publicly subsidized HS use in CKD. Additional studies that explore other factors, including functional status and the availability of informal family support, that may be associated with HS use among CKD patients are needed. These studies will provide evidence base for decision makers in health authorities and clinicians who are reorganizing their HS programs.

AGING RELATION OF INDICES, RESPONSIBLE FOR BRAIN FUNCTIONING

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Introduction. Recently have been shown, that brain metabolic balance provide by functional integration of its vascular system, system of circulation of cerebrospinal fluid and biomechanical skull properties as united structural-functional system. Each of these systems takes the place in this integration. However, every system independently changes with age. This is means that age may influent to functional integration, responsible for brain metabolic balance, which could reflect to brain functioning. Aim of this study is to elucidate age related changes of functional integrations, responsible for brain metabolic balance, connected with brain functioning.

Methods. The study of aging peculiarities in functional integration, responsible for brain functioning was based on simultaneous recordings of changes of brain blood volume, recorded by rheoencephalography (REG) and brain blood flow, recorded by transcranial dopplerography (TCDG). Analysis of REG and TCDG during pulse cycle permits to calculate intracranial "pressure – volume" relations, which permits to evaluate in standardized units CSF – mobility (CSFm) skull placibility (CCe) and cerebral blood flow (CBF). Received by this way data are comparable with data, received from the same persons at different physiological conditions, as well as comparable with data, measured from any other persons, independently of its age. This gives the possibility to investigate aging correlations of CSFm, CCe and CBF values. Recordings and analysis of REG and TCDG recording during pulse cycle were provided by PC "Windows-8" via analog-digital transformer "PowerLab - 8", running by modified software "Chart 5" and "Canvas 11. The principle of analysis was based on transforming of the initially recorded data in coordinates of " REG/TCDG –TIME" to coordinates "REG – TCDG". Investigated were provided at 156 healthy volunteers 18 – 85 aging.

Results. It was have found, that CBF in MCA and V.A. gradually changed with age from from 66 ± 12 cm/s (age 18-20, n=22) to 28 ± 9 cm/s (age 80-85, n=19). Decline of aging change of CBF increase after age 50 – 55. Changes of CSFm has more complicate character. From level 0.44 ± 0.16 (age 18-20, n=19) it practically not change up to age 40-50, n=24) and, then, increase up to value 0.64 ± 0.22 (age 80 – 85, n=18). CCe gradually decrease from 0.9 ± 0.12 (age 18-20, n=20) up to 0.20 ± 0.11 (age 80-85). These date indicate, that functional integration, responsible for brain metabolic balance is changed with age and two critical aging periods have taken place. One of them include 40-55 age, where significant decrease of CBF and CCe. Result of this is decrease brain metabolic balance changed to the direction of inctease collecting in brain tissue products of its metabolism, which couldn't fully evacuate by CBF and brain circulatory insufficiently is appeared. This may accompany by some neurological symptoms, for example, hearache and decrease of working capability. The second critical period is after 80-ty age, when significantly decrease value of of CCe and increase CSFm, accompany low level of CBF. This situation could be a reason for ageing circulatory demecia, manifestsation of which depends from ratio of CCe and CSFm. The first of them responsible for decrease brain metabolic supply, but the second – compensate the bdecrease of CBF. It was confirmed by of correlation of level of demencia, determined by psycho-physiological tests, with levels of CCe and CSFm. Momeone, analysing of received data show, that SCFm play some compensatory role for metabolic brain balance during aging decrease CBF., and

Conclusion. Data received, demonstrate that process of aging decrease of brain blood supply is accompany with decrease of CCe and inctease of CSFm. Integration of these functions are determined sufficient brain functioning during wide aging ranges, newertheless significant aging decrease of CBF. However, in situations, which observed at middle ages persons and alderly ones, when aging CBF decrease accompany significant decrease of CCe, but not enaugh CSFm increase for compensation of CBF and CCe changes, symtoms brain circulatory insufficiently may appear.

Poster Presentation Abstracts

ALTERATION OF HIPPOCAMPAL MICROGLIA DURING THE ASYMPTOMATIC STAGE OF ALZHEIMER'S DISEASE

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Our main goal was to assess glia activation during the asymptomatic stage of Alzheimer's disease. The hippocampal expression of TNFalpha and mitochondrial translocator (TSPO) protein were used as out-read of glia activation. To determine whether both microglia and astrocytes contribute to putative glia activation, the expression of their respective (Iba1 and GFAP) phenotypic markers was correlated with the level of TSPO and TNFalpha.

Transgenic APPswePS1dE9 and the littermate non-transgenic female mice aged 3 months (n=6-11 per genotype) were used. Amyloid precursor protein (APP), TNFalpha, TSPO, GFAP and Iba1 expressions were quantified in the hippocampus by western blot. TNFalpha and TSPO were additionally assessed by ELISA and [3H]-PK11195 autoradiography, respectively.

Considered globally, the inter-individual variability was important independently of the genotype and no statistically significant difference was found between mean values for any of the studied parameters. However, linear regression analysis indicated that the increase in APP correlates positively with both TNFalpha ($r = 0.878$, $p = 0.0002$) and GFAP ($r = 0.913$, $p = 0.0001$) which are also mutually correlated ($r = 0.907$, $p = 0.0001$ for GFAP versus TNFalpha). By contrast, APP is not correlated with Iba1 ($r = 0.372$, $p = 0.2338$). Moreover, TSPO induction is not correlated with APP ($r = 0.362$, $p = 0.2469$), but is correlated positively with Iba1 ($r = 0.768$, $p = 0.0035$) which is in turn correlated with TNFalpha ($r = 0.586$, $p = 0.0452$).

Taken together, these data indicate that both astrocytes and microglia contribute to the increase in TNF α during the early stages of Alzheimer's-like pathogenesis. However, TSPO appears selectively up-regulated only in microglia.

REVERSAL OF REPLICATIVE SENESCENCE IN PRIMARY HUMAN ADULT FIBROBLASTS

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Senescence is defined in the literature as an irreversible arrest of cell proliferation. Senescent cell accumulation *in vivo* has been linked to age-related pathologies such as liver cirrhosis, osteoarthritis and atherosclerosis. The tumour suppressor protein (p16) is a biomarker of senescence and ageing encoded by the INK/ARF locus. Genome-wide association studies repeatedly link this locus to prevalent age-related diseases such as coronary heart disease and type 2 diabetes. Recently, a landmark paper demonstrated that removal of p16 positive senescent cells in mice prolonged healthy lifespan, suggesting a direct link between senescence and age-related dysfunction (Baker *et al.*, 2011). Therefore, the removal of senescent cells in humans could present a unique therapy to prolong healthy lifespan and treat age-related disorders.

There are multiple routes to senescence. Epithelial cells undergo cellular senescence, a solely p16-mediated stress-associated barrier which occurs in the presence of intact telomeres. By contrast, fibroblasts undergo replicative senescence in response to telomere erosion which is regulated by p16, p53 and p21. Previous work in our group investigated whether siRNA transfection can reverse deep senescence in p16 positive primary adult human epithelial cells (DS-HMECs). p16 siRNA knockdown in DS-HMECs was found to reverse senescence, as defined by the loss of a panel of senescence markers.

We then asked if siRNA transfection can reverse deep replicative senescence in fibroblasts. We discovered that p16 and p21 siRNA knockdown reverses deep senescence in primary human adult fibroblasts. The successful reversal of deep senescence in fibroblasts provided the opportunity to screen for novel siRNAs that induce reversal in both DS-HMECs and fibroblasts. Using gene expression arrays, we identified 200 genes with increased expression in DS-HMECs compared to early proliferating and reversed HMECs. siRNA screening in DS-HMECs identified 28 siRNAs that strongly induced the reversal phenotype. An siRNA screen was then performed in fibroblasts examining these 28 hits as well as known interactors of these proteins. The results of this will be presented. The hits that emerge from these screens may represent novel drivers of senescence.

Baker, D. J., Wijshake, T., Tchkonja, T., LeBrasseur, N. K., Childs, B. G., van de Sluis, B., Kirkland, J.L & van Deursen, J. M. (2011). Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. *Nature*, 479, 232-236.

ALTERED EXPRESSION OF PATTERN RECOGNITION RECEPTORS AFTER CARDIAC SURGERY NECESSITATING CARDIOPULMONARY BYPASS: IMPLICATIONS FOR POST-OPERATIVE INFLAMMATION AND DIFFERENCES WITH AGE

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Introduction: Cardiac surgery necessitating cardiopulmonary bypass (snCPB) is often associated with the systemic inflammatory response syndrome (SIRS); for a minority, SIRS becomes severe and is associated with acute lung injury and other organ failure. Recovery from snCPB is more complex in the elderly; the likelihood for development of severe SIRS is much greater in this population and consequently, has an increased risk of mortality and morbidity. Pattern recognition receptors (PRRs) such as the receptor for advanced glycation end products (RAGE) and toll-like receptors (TLR) are important regulators of innate immunity, recognising pathogen-associated molecular patterns (PAMPs) and damage-associated molecular pattern molecules (DAMPs), released after tissue injury and inflammation. Changes in expression of these receptors on inflammatory cells may have important implications for post-operative inflammation and recovery from snCPB and they might contribute to 'inflamm-aging'.

Aims & Objectives: To examine the effects of snCPB on the expression of TLRs, RAGE and other surface markers of neutrophils in two age groups, age $\leq$ 69 years and age $\geq$ 70 years.

Methods: Blood was obtained pre- and post-operatively from patients undergoing snCPB (n=25). Surface and intracellular expression levels of RAGE and TLRs (2, 4 and 9) in neutrophils were assessed by multi-colour flow cytometry.

Results: The percentage of RAGE expressing cells was somewhat higher and interestingly increased post operatively (from 8.5% to 11.5%) in the older group (age $\geq$ 70 years), whilst the opposite was observed

(from 7.7% to 5.2%) in the younger population (age ≤ 69 years), possibly suggesting that pro-inflammatory RAGE signalling is augmented due to the operative procedure in older patients. Additionally, TLR4 expressing neutrophils were significantly fewer in the older group (1.6% compared to 4.9%) pre-snCPB and remained unchanged post-operatively whereas TLR2 expressing cells were reduced with snCPB in both age groups. TLR9 (an intracellular TLR that recognises bacterial DNA) was expressed with higher levels in the older group and was slightly increased after surgery in both groups (MFI from 1065 to 1154 in the older group and from 877 to 934 in the younger group).

Conclusion: Changes in expression of PRRs resulting from snCPB give an indication of a potential compromised innate immune response, especially for higher age groups and perhaps these preliminary findings allow us to assign, a previously unrecognised, importance to modulation of the RAGE axis of inflammation in the more elderly undergoing snCPB.

GENDER- AND REGION-DEPENDENT CHANGES OF REDOX BIOMARKERS IN THE BRAIN OF SUCCESSFULLY AGING LOU/C RATS

Emmanuel Moyses^{a,b,*}, Madeleine Arseneault^{c*}, Pierrette Gaudreau^{a,d}, Guylaine Ferland^{e,f}, Charles Ramassamy^c

The LOU/C (LOU) rat is an obesity resistant strain with higher longevity and health span than common laboratory rat strains. Since the management of oxidative stress (OS) is important to successful aging, we characterized it in this animal model. Male and female LOU rats were sacrificed at 4, 20, and 29 months. Macrodissected hippocampus, striatum, parietal cortex, and cerebellum were assayed for tissue concentrations of reduced glutathione (GSH), γ -glutamyl-cysteine-synthetase (γ -GCS), total thiols, protein carbonyls, and mRNA of four protein involved in OS (thioredoxine-1 (TRX1), glutaredoxine-1 (GLRX-1), superoxydismutase-1 (SOD-1), clusterin/apolipoprotein-J). In male rats, levels of GSH remained constant in all regions during aging while γ -GCS concentrations increased with age in the striatum, hippocampus and cerebellum. Clusterin mRNA levels increased in the hippocampus with age. Levels of the protective enzymes GLRX-1 and SOD-1 were lower in the hippocampus and higher in the cortex of aged rats than young ones. Age-dependency of the markers often differed between sexes. Since it was previously reported to decrease with age in the brain of Wistar rats, maintenance of GSH in specific structures of the LOU rat brain, together with an increase of clusterin mRNA levels and preservation of GLRX-1 and SOD-1 mRNA levels, could contribute preserving their cognitive functions in old age. Altogether, the *successful aging* of LOU rats may, at least in part, involve the conservation of functional antioxidant mechanisms in the brain.

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Day 1, Session 2: Slowing down progression, Rejuvenation and Self Repair

Invited Speakers Abstracts

Can we currently slow down the progression of Alzheimer's disease?

[Dr Naji Tabet](#) BS, MSc (Immunol), MSc (Psych), PGCert (Med Ed), MD (Lon), MRCPsych, Senior Lecturer & Consultant, Old Age Psychiatry, Course Leader, MSc Dementia Studies Clinical Lead, Cognitive Treatment & Research Unit, Medical Lead for Research, R&D Sussex Partnership NHS Foundation Trust, Postgraduate Medicine, DME & Centre for Dementia Studies, Brighton & Sussex Medical School, UK

The natural progression and unrelenting cognitive decline in Alzheimer's disease will be first reviewed. The benefit to patients from current licensed memory enhancers is at best modest with little proven disease modifying property. Increasing interest is being directed at anti-amyloid and anti-tau medication which are currently in phase III trials, but results so far have been disappointing. Other pharmacological (vitamins, herbal extracts, antihypertensive medications) and non-pharmacological approaches (exercise/physical activities, diet, social networks, and brain exercise/education) have also been assessed. Findings will be reviewed for any evidence of efficacy that may currently help in management of Alzheimer's patients.

Mild cognitive impairment

[Professor Emeritus Amos D Korczyn](#), Tel Aviv University, Department of Neurology, Ramat Aviv, Israel

Mild cognitive impairment (MCI) is defined as a condition characterized by newly acquired cognitive decline to an extent that is beyond that expected for age or educational background, yet not causing significant functional impairment. The concept of MCI has received considerable attention over the past few years, and aspects related to its definition, prevalence, and evolution have been extensively studied and reviewed.

The current status of this entity, focusing on the conceptual, methodological, and, in particular, the social and ethical aspects of MCI which have attracted less attention will be discussed, including the weaknesses of the concept, which is heterogeneous in etiology, manifestations, and outcomes. The formal diagnosis of MCI, with its implications that the person may develop dementia, may have a grave impact on the psychological state of the individual, at a stage when prediction of outcome is tenuous and possibilities of useful interventions are meager with significant social and legal implications.

Nutritional Interventions in Ageing: Lessons from Rhesus Monkeys

[Dr. Joseph W. Kemnitz](#), University of Wisconsin - Madison, USA

Reduced caloric intake reliably extends healthspan and lifespan in a wide range of non-primate species. Two continuing studies begun nearly 30 years ago have been evaluating the effect of moderate calorie restriction (CR) in rhesus macaques, an established nonhuman primate model of human aging. Both studies have demonstrated beneficial effects of CR on healthspan, but only one resulted in increased lifespan. Differences between studies in composition of the diet and implementation of CR may account for these discrepant findings. It seems likely that CR has similar effects in primates as in species that are more divergent from humans.

Extrinsic versus Intrinsic mechanisms of stem cell aging and rejuvenation

[Dr Irina M. Conboy](#), Associate Professor at UC Berkeley, Dept. of Bioengineering, University of California, Berkeley, USA

Oral Presentation Abstracts

TELOMERE LOOPING: A NEW PARADIGM FOR THE REGULATION OF GENE EXPRESSION WITH PROGRESSIVE TELOMERE SHORTENING

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Studies of human telomeres have focused on their role as a tumor-suppressor dependent on DNA damage signals from too-short telomeres. We here describe a new paradigm for how telomere shortening can progressively affect gene expression during the human lifespan, long before telomeres become short enough to generate damage signals. ISG15 (Interferon Stimulated Gene 15 kda) is 1 Mb from the telomere and its expression is regulated by telomere length. Many genes between it and the telomere are not affected by telomere shortening. We here demonstrate that the distance between the telomere and ISG15 is small when telomeres are long but the loci separate when telomeres are short. We call this phenomenon TPE-OLD (Telomere Position Effects-Over Long Distances). We next developed high-resolution Hi-C to directly map TPE-OLD interactions in a disease whose locus is adjacent to the telomere of 4q and which exhibits an age-associated phenotype (**F**acio**S**capulo**H**umeral muscular **D**ystrophy: FSHD) and show multiple interactions, which can extend at least 10 Mb into the subtelomeric region. Global analysis of expression then established that 100s of changes can be regulated by telomere length. Our results suggest new mechanisms for how telomere shortening could influence human aging and disease initiation/progression long before shortening produced DNA damage signals. These changes could be local, affecting stem cell behavior, inflammation and repair. They could also be global, for example where secretory signals from glial cells dividing on a regular basis every seven years could influence hormonal signals governing energy distributions throughout the body. We have found TPE-OLD effects in both myoblasts and fibroblasts, and are investigating its manifestations in epithelial cells. Length-regulated long-range (Mb) telomere chromatin conformation changes may alter gene expression to optimize fitness in species such as humans that live for many decades, and where the optimization of energy utilization may differ significantly between newly mature and aged individuals. These changes may profoundly affect human physiology, aging and disease.

DIETARY RESTRICTION IMPROVES VASODILATOR DYSFUNCTION CAUSED BY ACCELERATED VASCULAR AGING DUE TO GENOMIC INSTABILITY

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Objective Recently we discovered that genomic instability is associated with accelerated vascular aging in humans and mouse models, and that DNA repair-defective mice (*Ercc1^{d/-}*) display accelerated age-dependent deterioration of endothelium-dependent and vascular smooth muscle dilator function (Durik M. et al. Circulation 2012). Dietary restriction (DR) is known to slow aging. We explored whether DR would inhibit accelerated vascular aging caused by genomic instability by measuring vasodilator function in both male and female *Ercc1^{d/-}* mice vs. wild-type (WT) littermates.

Methods WT and *Ercc1^{d/-}* were fed with DR (increasing 10 to 30% nutrient restriction) or ad libitum (AL) diets for 9 weeks, whereafter thoracic aortas were isolated and used for *ex vivo* organ bath experiments. To investigate endothelial and vascular smooth muscle dilator function, aorta precontracted with U44619 (thromboxane analogue) was exposed to acetylcholine (ACh: 10^{-9} - 10^{-5} M) and sodium nitroprusside (SNP: 10^{-9} - 10^{-4} M), respectively. Maximal dilator responses (mean $\pm$ SEM) are shown between brackets, and were calculated as % decrease of precontraction. Vasoconstrictive responses to the pressor hormone angiotensin (Ang) II were tested. Significance values are those of dose-related responses tested by general linear model for repeated measures.

Results In *Ercc1^{d/-}* mice fed AL both ACh and SNP responses were significantly smaller than in WT (ACh: 67 $\pm$ 9% (n=8) vs. 41 $\pm$ 5% (n=11); SNP: 80 $\pm$ 5% (n=5) vs. 59 $\pm$ 3% (n=5), $p<0.0001$, WT vs. *Ercc1^{d/-}*). Whilst without effect in WT, DR normalized the SNP responses of *Ercc1^{d/-}* (79 $\pm$ 7% (n=6)) to that of WT. ACh responses were also improved (from 41 $\pm$ 4% AL (n=11) to 56 $\pm$ 4% DR (n=11), $P<0.05$). Maximal vasoconstrictions to Ang II tended to increase in AL-fed *Ercc1^{d/-}* vs. WT (95 $\pm$ 10 vs. 127 $\pm$ 12, $p=NS$), and were lowered in *Ercc1^{d/-}* by DR feeding (82 $\pm$ 6, $p<0.05$ vs AL-fed *Ercc1^{d/-}*).

Conclusion In *Ercc1^{d/-}* mice, DR improved vasodilator responses. Also, a tendency towards hyperresponsiveness to Ang II was observed, which was prevented by DR. Therefore, DR is beneficial for vasomotor function during vascular ageing caused by genomic instability.

Poster Presentation Abstracts

Poster abstracts will be finalised weeks before the event

MODIFIED PROGRESSION OF ARTERIAL STIFFNESS WITH AGING BY ATHEROSCLEROSIS RISK FACTORS

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Aim: We tested an association among atherosclerotic lesions, aging and risk factors, using a new clinical indicator of arterial stiffness, cardio-ankle vascular index (CAVI). CAVI, which calculated from values of cardio-ankle PWV (pulse wave velocity) and blood pressure (BP), was developed in order to eliminate an influence of BP fluctuation by measurement moments.

Subjects and Method: We conducted 1,878 voluntary subjects who had the general health check-up, including anthropometric measurement, BP, CAVI, blood examination relating to risk factors of atherosclerosis, function of vital organs and inflammatory reaction. Among them, 577 subjects took an examination of carotid ultrasound.

Results: CAVI correlated with age the most ($R=0.68$), compared to other risk factors including systolic BP ($R=0.31$) and low HDL-C ($R=0.09$). Limiting to the subjects who underwent carotid ultrasound ($N=577$), a correlation of age with CAVI ($R=0.689$) was stronger than that with maximum carotid intima-media thickness (maxIMT) ($R=0.415$). Although a multiple regression analysis revealed that CAVI correlated with most of traditional and recent risk factors, serum LDL-C, a well-known potent risk factor for atherosclerosis, indicated a negative association with CAVI. On the analyses divided by the status of risk factors and degree of maxIMT, CAVI correlated inversely with serum LDL-C concentration only in non-risk groups including non-diabetes, non-hypertensive subjects, non-elderly ones or subjects with maxIMT <1.0 mm, in those who with expected low extent of advanced atherosclerotic lesions. In contrast, the comparable risk-positive groups did not show any correlations between CAVI and LDL-C.

Discussion and Conclusion: The correlation of the arterial stiffness evaluated by CAVI and serum LDL-C level changed depending on characteristically with the stage of atherosclerosis progression in each individual. This association should be explained by the pathological findings of our previous study that a histological aortic fatty streak lesion, containing abundant foamy cells without a little proliferation of collagen tissue, was prevalent and stayed for a long period in the subjects with hypercholesterolemia,

which should make vessel wall soften. CAVI is thought to correspond well with a histological change with aging, which includes intimal thickening mainly composed of collagen tissue, whose histological change can possibly make vessel wall harder. Although CAVI should correspond with arterial stiffness by aging, its property can be modified variously by the effects of risk factors.

AGING MODULATES VITAMIN C TRANSPORTER EXPRESSION PATTERNS IN THE KIDNEY

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Introduction: Increasing age induces deleterious effects in several organs and systems, including the kidney. Aging theory postulates that this process might be due to damage caused by oxidative stress and inflammation. Vitamin C is a major antioxidant and plays an essential role in defending against free radical-induced cellular damage. Vitamin C transport is mediated by distinct classes of membrane proteins, such as facilitative glucose transporters (GLUTs) that transport the oxidized form of vitamin C, dehydroascorbic acid and sodium vitamin C cotransporters (SVCTs) that, in turn, mediate transport of the reduced form of vitamin C, ascorbate. The aim of this study was to develop a morphological study in the kidney and to investigate the expression patterns of SVCT1 and GLUTs transporters in renal tissue obtained from a senescence-accelerated mice model (SAM mice).

Material and Methods: SAMP8 mice, aged 2 (young), 6 (middle age) and 9 (aged) months were used (n=30). The morphological study was performed using Hematoxylin-eosin and Azan-Mallory staining. The transporters investigated were SVCT1, GLUT1, GLUT2 and MCT1 as a proximal tubule segment S1 marker. Expression levels of vitamin C transporters were analyzed in the kidney medulla and cortex by QRT-PCR and western blot, using specific primers, Brilliant SYBR-Green QPCR master mix and specific anti-SVCT1, GLUT1 and GLUT2 antibodies from Alpha Diagnostic and Santa Cruz; conventional immunohistochemical using peroxidase-conjugated secondary antibodies; and multi-labeling immunofluorescence analysis employing secondary antibodies conjugated to Cy2, Cy3 and Cy5 and confocal laser microscopy. The confocal analysis was performed in the Center for Advanced Microscopy CMA BIO-BIO, University of Concepción with a confocal microscope LMS 780 NLO, Zeiss. All animals received humane care according to the guidelines for ethical care.

Results: Aging induces morphological alterations in the kidney of SAMP8 mice. The main findings observed were tubular degeneration and cytoplasmic vacuolization in the proximal tubules located in the cortex. Also, an induction of SVCT1 expression was observed in aged mice. SVCT1 distributes as a gradient of expression in the apical domain of proximal tubules with increasing levels in medullary region (segment S3), together with an induction of SVCT1 staining in renal cortex (segments S1 and S2). Only mild changes were observed in the GLUTs expression during aging by studies of molecular biology and microscopy.

Conclusions: Aging modulates the expression of Vitamin C transporters. Aging increases the expression of SVCT1, probably due to an increased need for uptake and reabsorption of Vitamin C as an antioxidant agent. Therefore, the expression of SVCT1 can be modulated by circulating levels of Vitamin C and for the status of the renal function. Thus, our results indicate a role of the transport of the different chemical forms of the Vitamin C during aging.

Acknowledgement: FONDECYT 3120159, FONDECYT 1140477, CMA BIO-BIO PIA-ECM-12

EFFECTS OF SELECTED MEDICINAL HERBS ON DEMENTIA AND OSTEOPOROSIS

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Introduction

Health burdens arising from aging is becoming apparent in the last few decades. Currently, aging-related degenerative diseases such as dementia (Alzheimer's disease "AD" and vascular dementia "VD") and osteoporosis are big threats and cannot be totally prevented [1]. The currently used drugs on dementia and osteoporosis aim to regulate neurotransmitters and prevent the loss of bone mass, respectively. However, the genuine underlying causes of the degenerative problems are not tackled by these medications. [2] [3] [4]. The chemical components and organic extraction from some Chinese Medicinal plants such as Tianma (天麻"TM"), Nuzhenzi (女貞子"NZZ") and Danshen (丹參"DS") have been reported to have neuroprotective and osteoprotective effects. The bioactivities of these water extracts are not well-investigated yet. In this present study, *in vitro* studies were performed to examine the efficacy of individual selected Chinese herbal water extracts on AD, VD and osteoporosis. Subsequently, this study will provide evidence and justification for the establishment of a combined formula to be used as a multi-targeting preventive agent.

Materials and Methods

In vitro assays

1. Anti-oxidation study on PC12 cells
2. Anti-oxidation study on UMR 106-01 cells
3. Anti- β -amyloid-induced toxicity
4. Establishment of combined formula

Results and Conclusions

1. DS, NZZ, TM individual water extracts showed dose-dependent protections against H₂O₂-induced oxidative stress on both PC12 cells and UMR 106-01 cells.
2. Dose-dependent neuroprotection against anti- β -amyloid toxicity was observed from DS, NZZ, TM individual water extracts.
3. Dose-dependent amelioration on β -amyloid-induced toxicity from various combinations of DTN formula was demonstrated.
4. Further investigation will be conducted to study the additive effects of these extracts on neuroprotection and osteoprotection, in order to establish an innovative combined herbal supplement for the elderly to prevent both dementia and osteoporosis.

Reference

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AGING GRACEFULLY ACROSS ENVIRONMENTS USING TECHNOLOGY TO SUPPORT WELLNESS, ENGAGEMENT, AND LONG LIFE (AGE-WELL)

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Abstract:

Rapid advances in technology are occurring at the same time as many world populations are aging. This presentation will describe *Aging Gracefully across Environments using technology to support Wellness, Engagement, and Long Life (AGE-WELL)*, a newly funded pan-Canadian Network of Centres of Excellence (NCE). The mission of AGE-WELL is to stimulate technological, social, and policy innovations that support 'aging well' by harnessing the potential of emerging and advanced technologies in areas such as information and communication technologies, artificial intelligence, mobile technologies, sensor networks, and e-health. The AGE-WELL program will produce practical applications in the next five years and drive the development of novel technologies in the longer term to open up new avenues for innovation. AGE-WELL offers an example of transdisciplinary work, which transcends perceived boundaries between disciplines and integrates diverse perspectives from scientific and non-scientific sources to create new ideas and solutions to difficult problems. Among the strengths of AGE-WELL is its heterogeneous network of researchers, industry partners, service providers, and older Canadians and their caregivers all working together. The AGE-WELL team spans social and health sciences, engineering, and computer science, with expertise in all facets of technology development, knowledge translation, and technology exploitation in the support of older adults. Attendees of this presentation will learn how AGE-WELL will help provide viable solutions to support older adults in their own homes and communities through new technologies that will: 1) address the effects of physical impairments and restricted mobility; 2) bring people together for interaction, learning, and support; 3) understand an individual's behaviour and physiological state to proactively mitigate the risk of injury from accidents or disease and disability; and 4) enhance cognitive and mental health through new screening and enhancement tools. These outcomes will be achieved through a set of integrated research themes [called workpackages (WPs)] comprising individual projects in areas, such as user needs analysis, technology development, and policy and ethical issues. There is a set of crosscutting activities that work across all WPs and projects to ensure cohesiveness across the NCE in key areas of knowledge mobilization, commercialization, team working, and training. WPs and activities will be described in this presentation. AGE-WELL will allow Canada to be at the forefront of innovation in the field of technology and aging by collectively supporting the growing population of older adults and their caregivers. AGE-WELL aims is to help older Canadians optimize their later years through accessible technologies that increase their safety and security, support their independent living, and enhance their social participation. Significant societal and fiscal benefits result when older citizens are assisted in maintaining their independence and health. At the same time, invention and commercialization of

technologies to provide this assistance enhances a nation's capacity for innovation, advancing a major economic goal.

Day 2, Session 1: Genetic and Epigenetic regulation

Invited Speakers Abstracts

The role of the telomerase protein TERT in brain ageing and neurodegeneration

[Dr. Gabriele Saretzki](#), Lecturer in Ageing Research, Institute for Ageing and Health, Newcastle upon Tyne, UK

Although telomerase is best known for its telomeric function, its protein component TERT (telomerase reverse transcriptase) has additional non-telomeric functions like the protection of mitochondria.

We found increased mitochondrial TERT in neurons of Alzheimer's disease brains and demonstrate a mutual exclusion of neurons with tau pathology and those expressing TERT protein.

As a model of tau pathology we expressed tau in cultivated neurons with and without telomerase and found that neurons lacking TERT protein displayed higher levels of mitochondrial ROS and more peroxidised lipids than wild type neurons.

We conclude that mitochondrial TERT might have a protective function in neurons.

Expression of phosphorylated H2AX histone in the aging mouse brain and its relation with slowly cycling neurons

[Professor Adalberto Merighi](#), Dipartimento di Scienze Veterinarie, GRUGLIASCO (Torino), Italy

Phosphorylation of the histone H2AX is an early response to DNA damage and a marker of aging. γ H2AX appears in foci within interkinetic/apoptotic nuclei and mitotic chromosomes from development to senescence. Immunoreactivity is mainly detected in neurogenetic areas, but also in the adult and senescent cerebral cortex. γ H2AX in neurogenetic areas is temporally and functionally related to proliferation and apoptosis of neuronal precursors (type C transit amplifying cells in SVZ and granule cell precursors in cerebellum). In senescent SVZ cells, displaying an extremely long cell cycle and slow proliferation rate, H2AX phosphorylation is primarily related to DNA repair

Genetics of Healthy Ageing: What do genes tell us about Ageing Better?

[Dr Irene Maeve Rea](#), Queens University Belfast and Belfast City Hospital, Belfast, Ireland

This session will explore how genetic and life-style profiles from nonagenarians may help our understanding about malleable factors which can contribute to longer lifespan accompanied by healthspan. Genetic, immunological, cardiovascular and nutritional factors contributing to good quality ageing will be presented with evidence from the nonagenarian BELFAST cohort together with early results from the GeHA study of European nonagenarian siblings and insights from the nonagenarian siblings themselves about factors involved in their good quality longevity.

Oral Presentation Abstracts

THE SUPPLY AND DEMAND OF PROGENITOR CELLS GOVERNS ORGAN MASS LOSS IN AGEING HUMANS AND THEIR AGE-SPECIFIC CANCER INCIDENCE RATES

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The mean values of cell turnover times for 31 different organs and tissues in adult humans and animals (when data in humans were lacking) were estimated as well as functional mass loss for 5 organs, accounting for actual mass loss and tissue conversion to fat, in humans over the adult period, age 25 to 70. We found that greater actual and functional mass loss was significantly associated ($P = 0.001$ and $P < 0.0001$, respectively) with the log of shorter cell turnover times. This year, in *Experimental Gerontology*, we proposed that this mass loss is linked to replicative senescence of stem cells, an evolutionary adaptation that effectively limits cancer in young adults, and accelerates in the more elderly as biological conditions deviate away from those prevailing in youth, when the selective pressure on pleiotropic genes is greatest. Furthermore, it was hypothesized in *Mechanisms of Ageing and Development* (also in 2014) that neoplasms preferentially arise when stem cell exhaustion creates a short supply of progenitor cells at ages of high proliferative demand. To test this hypothesis, published datasets were employed to model the age distribution of osteochondroma, a benign lesion, and osteosarcoma, a malignant one. Results show that progenitor cell demand-to-supply ratios are a good risk indicator, exhibiting similar trends to the unimodal

and bimodal age distributions of osteochondroma and osteosarcoma, respectively. The hypothesis was tested by its ability to convincingly explain and demonstrate, for the first time, a tumour's bimodal age-incidence curve. The supply-and-demand hypothesis also helps explain Peto's paradox, as to why whales, humans and mice have similar cancer rates, and provides explanations for males and taller individuals being more prone to cancers and having shorter lifespans.

CONDUCTING FOCUS GROUPS WITH COMMUNITY DWELING OLDER ADULTS: A PROCESS PAPER

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This paper will explore and elaborate on some of the considerations taken into account when conducting qualitative focus group research with older men. We will describe some of the benefits and challenges that our research team experienced when recruiting older men and conducting focus groups with them. In the first year, our team conducted 17 focus groups with older men in order to develop a toolkit aimed at starting a National Men's Shed across Canada; we will conduct three pilots using that template in year 2 in order to assist us in developing a final toolkit in year 3. This paper discusses the process we engaged in as a research team during the first year: it will include a discussion of the recruitment of our focus group participants, the process of conducting focus groups with older men, selected outcomes of our focus group research, as well as some reflection on our work as a research team.

This topic is highly relevant because we know that depression and suicide are at an elevated risk for older men in Canada (Mackenzie et. al, 2006; Mackenzie et al, 2012). Research has shown that higher rates of depression and suicide among older men may result from the masculine ideal that associates being a 'real' man with traits such as autonomy, independence, emotional detachment, and toughness – traits that may inhibit men from seeking mental health services (Tannenbaum, & Frank, 2011). This is coupled with the fact that there is a striking lack of male-focused community services, which are crucial for meeting the unmet psychological and social needs of older adults (Cohen-Mansfield & Frank, 2008). Men's sheds may be one option to address this gap.

AGING SHIFTS BDNF PATHWAY TO DYSFUNCTION FOR REGENERATION OF MYOCARDIAL INFARCTION

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Myocardial infarction (MI) is leading cause for morbidity and mortality in the world. Until now, regeneration of infarcted myocardium structurally and functionally is still a big challenge in clinic. This is mainly due to the detail molecular mechanism regarding to poor healing and regeneration existed in aged heart is still unclear. Recent studies revealed that aging changes in microenvironment of cardiac consisted cells play a crucial role in dysfunction of regenerative potential in aged heart. Using proteomics and functional genomics platforms, we have identified that cardiac microvascular endothelial cells (CMECs) express three types of brain-derived neurotrophic factor (BDNF) receptors, full length form-TrkB-FL, and truncated forms-TrkB-T1 & TrkB-T2, while the expression of TrkB-T1 was increased in aged CMECs. This age-related change involves in the BDNF-TrkB pathway which triggers the super-inflammation in aged infarcted heart is disadvantage regeneration of infarcted myocardium. In addition, we also found that BDNF can promote young CMECs to migrate via the activation of the BDNF-TrkB-FL-PI3K/Akt pathway, which may benefit angiogenesis after MI. However, the ageing of CMECs led to changes in the expression of receptor Trk isoforms in that among the three isoforms (TrkB-FL, TrkB-T1 and TrkB-T2), only one of its truncated isoforms, TrkB-T1, continued to be expressed, which leads to the dysfunction of its ligand, a decrease in the migration of CMECs and increased injury in ageing hearts. This shift in receptor isoforms in aged CMECs, together with changes in the ageing microenvironment, might predispose ageing hearts to decreased angiogenic potential and increased cardiac pathology. Our results suggest that BDNF-TrkB pathway is critical for physiological and pathological situation of CMECs. The aging change of BDNF-TrkB pathway in CMECs, which is from BDNF-TrkB-FL shifted to BDNF-TrkB-T1, is the important reasons for the poor healing and regeneration seen in aged heart. The interventional strategy for the aging changes in this pathway will shed light for us to tailor novel therapy for regeneration of aged MI.

ACKNOWLEDGEMENTS This work was supported by the Collaborated grant for HK-Macao-TW of Ministry of Science and Technology (2012DFH30060); Research grant of Department of Education of Guangdong (2012gjhz0003); the National Natural Science Foundation of China (30770886, 30570369, 30340038, 30973158, 81170324, 81470433); 863 grant (2007AA02Z105); Guangdong Key grant for Natural Science Foundation (04105826; S2012020010895); Guangdong grant for Science and Technology Development (2004B30601007); International collaborated grant of Guangdong (2009B050900007; 2013B051000062).

ALZHEIMER'S RISK VARIANT PICALM AND ALTERATIONS IN BRAIN FUNCTION DURING AGING

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Cognitive decline is a main predictor of disability among older adults, and Alzheimer's disease (AD) is the most common cause of dementia in the elderly. AD has a strong genetic basis, and considerable progress in revealing putative AD associated genes has been made using genome wide association study (GWAS). Recent GWAS studies identified a polymorphism in phosphatidylinositol binding clathrin assembly protein (PICALM) gene (rs3851179) as a risk factor for AD (Harold et al., 2009; Lambert et al., 2009). PICALM is implicated in clathrin-mediated endocytosis (Thomas et al., 2011). It has been proposed that PICALM causes synaptic perturbations and alterations in APP processing through endocytic pathways (Parikh et al., 2014). PICALM also regulates autophagy and clearance of tau, an autophagy substrate (Moreau et al., 2014). However, the mechanism by which PICALM genotype influences brain function in non-demented subjects remains largely unknown.

This study was aimed at determining whether PICALM genotype influences EEG characteristics in non-demented adults, as well as estimating whether this possible effect is modified over the course of aging.

We examined quantitative EEG in resting state in 116 healthy volunteers (age range 20-80 years), stratified by PICALM (rs3851179) genotypes and divided into cohorts of those younger and older than 50 years of age. Informed written consent was obtained from all participants. Participants underwent a neurological examination and cognitive screening. The significance of the differences between the log-transformed EEG parameters in different groups was estimated using ANOVA in the general linear model (GLM). The effects of ApoE genotype and gender were controlled.

The homozygous presence of the AD risk variant PICALM GG in non-demented subjects was associated with an increase of beta1 and beta2 relative powers. In the older cohorts, an increase of beta relative power was observed, which is consistent with the results of previous studies (Holschneider and Leuchter, 1995); moreover, the observed increase was significantly higher in the older PICALM GG carriers. The level of state anxiety was higher in the carriers of PICALM GG genotype as compared with the PICALM AG&AA carriers. The rise in beta activity was associated with the increase of state anxiety.

Beta power elevation in resting EEG is a marker of disinhibition and hyperexcitability in the brain (Rangaswami et al., 2002). The increase of beta relative power is consistently reported in the elderly. The development of AD increases the excitability in excess of the rise of excitability connected with normal aging (Born et al., 2014), resulting in significantly increased incidence of seizures (Amantniek et al., 2006). The results of the present study imply that AD risk PICALM GG genotype may underlie the increase of excitability in the subjects predisposed to AD.

Research was supported by Grants from the Government of the Russian Federation (No 14.B25.31.0033), RFBR No 11-04-01896-a, and in part by the Ministry of Education and Science of the Russian Federation (Contract No 8053), RFBR (11-04-02106-a), Rosbiolab and NIH/NIA AG029360.

MEN BORN IN 1913 FOLLOWED TO AGE 100 YEARS

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Objectives To follow men from age 50 to 100 years with special emphasis on factors related to survival.

Design A representative 1/3 of all men born in 1913 and living in Gothenburg, Sweden were first examined in 1963 at age 50 and were re-examined at age 54, 60, 67, 75, 80 and 100 years. Conventional statistical methods including multivariable regression were used.

Subjects Of 973 selected men, 855 (88%) were examined in hospital at age 50-80 years and 10 of the men (1.0%) were alive at age 100 and 7 of these men were examined in their homes.

Results Twentyseven 27% lived until 80 years of age and 13% to age 90. Cardiovascular disease was the most common cause of death. Dementia was recorded in 23% and further 2 men (20%) had dementia at age 100. Non-smoking and a mother, but not a father, who survived to high age were associated with survival to 100 years in these men. These findings are supported by another prospective study in Honolulu. A high performance of a bicycle exercise test at age 54 also predicted good survival as well as low serum cholesterol and high housing costs at age 50. At age 100 these men had low/normal blood pressure. Serum troponin T, N-terminal PRO brain natriuretic peptides and C-reactive protein were elevated, which might indicate ongoing myocardial infarction and heart failure, respectively, in these apparently healthy men with normal echocardiographic findings.

Conclusions Ten men (1% of the original sample) experienced their 100th birthday. Low levels of cardiovascular risk factors as well as mother's high age at death were positive for survival, as well as indices of good economy at age 50 and high physical working capacity at age 54. Reference values for laboratory tests have to be adjusted for age.

PORTUGUESE RETIREES' PERCEPTIONS ABOUT THEIR TRANSITION TO RETIREMENT

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Introduction: Retirement is one of the major transitions in a person life. The work identity is, many times, the only identity the person has and so a loss of identity can be felt after retirement. It can also lead to different vulnerabilities, including health vulnerabilities. Increasing longevity leads to more years after retirement with all the social and economic costs around this situation. People need to be prepared to deal with retirement and prepare themselves for more active and functional years.

Objective: Our main objective is to know the perceptions of Portuguese retirees about their transition to retirement. We intend to understand how Portuguese retirees experience their transition to retirement, if this transition affects their health, which are the networks in which they rely and the strategies they use to deal with this transition.

Methodology: We conducted a descriptive study of a qualitative nature. The target population was retirees (retired for less than five years) registered in health care providers in Primary Health Care of the Regional Health Administration Center. The selected participants were subjected to an approach by focus group, after signing informed consent, and the information was gathered by digital audio recording and subjected to thematic analysis using the NVivo10® program.

Results: The following themes emerged: before retirement, after retirement, the retirement moment, the future perspective and recommendations for future retirees. Before retirement included the themes about their perception of their job and why they decided to get retired. The theme after retirement included the themes about how they use their time now, namely hobbies and new family members, like grandchildren. In the retirement moment, the themes that emerged were related what they felt at that moment. In future perspective, themes like death and fear emerged. Retirees also gave recommendations for future retirees.

Conclusion: Individuals perceive retirement depending on their personal characteristics, especially their experience of the past and how they became retirees. Their job was a very important part of their lives and they need to explain what they used to do. It was also perceived that retirement interfered with their usual routines and that these were strongly marked by the socio-economic and political context in which they experienced this phenomenon. The economic crisis that Portugal is facing appears as a common marker in their speeches, noting disrespect for their condition as retirees because of the cuts in pensions. It was noticed that the individual and also his/her family health was subject to change, being highlighted in this scope the interference that retirement had on the marital relationship.

Poster Presentation Abstracts

RESTORATION OF PULMONARY FUNCTIONS IN AGED ANIMAL BY ELIMINATING SENESCENT CELLS

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Senescent cells accumulate in many tissues as animals age, but little is known about their functions in age-associated pathologies. To clarify the role of cellular senescence in tissue aging, we generated a mouse model in which senescent cells can be ablated using toxin receptor cell-knockout system. The mice express luciferase and toxin receptor under the control of *CDKN2A* promoter/enhancer, thereby enabling the detection of senescent cells by *in vivo* imaging as well as the elimination of senescent cells by administering diphtheria toxin (DT). In these mice, luciferase activity was detected in lung and adipose tissues within 12 month of age, which well-correlates with the endogenous *CDKN2A* expression.

Senile lung is characterized by an increased lung compliance, which is attributed to progressive loss of the elastic fibers during aging. DT treatment successfully eliminated senescent cells from lung tissue of old animals. In DT-treated animals, elastic fibers were recovered and the alveolar size was reduced to near those of young mice. Consistent with these results, we observed a significant decrease in the lung compliance in DT-treated mice. Together, these results suggest that age-associated decline in pulmonary function is, at least in part, attributed to the senescent cell accumulation, which can be reversibly restored by eliminating senescent cells from the tissue.

VASCULAR REACTIVITY INDUCED BY COGNITIVE TASKS IN PATIENTS WITH VASCULAR ENCEPHALOPATHY

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The role of autonomic nervous system (ANS) in the regulation of cognitive function may be significant in normal subjects and especially in persons with cerebral vascular disease. Vascular reactivity induced by cognitive task was investigated in 51 women with vascular encephalopathy (VE), mean age 69.6 ± 1.2 years. Performance of the word fluency test (WFT) in woman with VE was associated with the changes of ANS reactions: blood pressure and heart rate (HR). More successful performance of cognitive tasks was accompanied by a greater reactivity of the indices of blood pressure and HR during WFT performance as well as by a more rapid return of these indices to the resting level.

Performance of WFT was also accompanied by statistically significant increase of direct current (DC) potentials in different areas of head and the changes of interhemispheric difference of DC potentials in temporal areas. A more successful performance of the WFT was associated with a large rise of averaged DC potentials and higher values of DC potentials in the left temporal area compared with the right one. The lower scores in WFT were observed at low generalized reactivity of DC potentials and higher values of DC potentials in the right temporal area compared with to the left one. Thus, vascular and heart rate reactivity together with the activation of left temporal area are factors of the successful performance of WFT in patients with VE.

OMEGA-3 FATTY ACID STATUS INFLUENCES THE PROTECTIVE EFFECT OF B VITAMIN TREATMENT ON COGNITIVE DECLINE

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Background: Approximately 50% of older people with mild cognitive impairment eventually convert to Alzheimer's disease. Elevated concentrations of plasma homocysteine (tHcy) are associated with development of cognitive impairment and dementia while omega-3 fatty acids (FA) may be protective. We investigated whether plasma omega-3 FA concentrations (docosahexaenoic acid, DHA) modify the treatment effect of tHcy-lowering B vitamins on cognitive performance in a placebo-controlled trial.

Design: This study, from the VITACOG trial included 266 older persons (≥ 70 y) with mild cognitive impairment, randomly assigned either to placebo ($n=133$) or to daily high-dose B-vitamin supplementation (folic acid, 0.8 mg; vitamin B₆, 20 mg; vitamin B₁₂, 0.5 mg) ($n=133$) for 2 y. The participants underwent cognitive testing at baseline and 2 y later although some tests including the HVLT with delayed recall (DR) and the TICS-M were repeated more regularly. The effect of the intervention on cognitive performance was analyzed according to baseline DHA concentrations. The analysis was adjusted for age, gender, *APOE4*, education and plasma homocysteine (tHcy) at baseline.

Results: The linear mixed effect model showed that the effect of B-vitamin treatment on HVLT-DR depends on the initial plasma concentration of DHA ($F = 3.82$, $df = (2,1184)$, $P = 0.02$), both for continuous and categorized levels of DHA. When DHA concentrations were divided into tertiles the treatment effect was only significant for high baseline DHA ($>339 \mu\text{mol/L}$); (time by treatment interaction = the slope in treated minus the slope in placebo = 0.66; $SD = 0.25$, $P = 0.012$). This effect, apparent after 6 months treatment, was further modulated by baseline tHcy levels. Those with high baseline tHcy on B vitamin treatment, and with high DHA levels, had improved HVLT-DR scores while the placebo group scores showed a marked decline by 24 months. The results were similar for the TICS-M, which tests memory and other cognitive domains.

Conclusion: The beneficial effect of B vitamin treatment on cognitive performance may be optimal for subjects with good omega-3 FA status. These results highlight the importance of multimodal effects of different nutrients on cognition in older persons with MCI.

MEASURING HEALTH INEQUALITIES IN THE CONTEXT OF MULTIPLE CHRONIC DISEASES

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Introduction: Multiple chronic diseases (MCD), defined as co-occurrence of 2 or more diseases, are common clinical feature, particularly among older people. Nevertheless, most of previous studies have ignored presence of other diseases in measuring health inequalities for a disease. We explored 1) the extent of changes in health inequalities with and without consideration of MCD and 2) socioeconomic difference in the course of MCD development in Korea.

Methods: 23853 observations from 7951 individuals aged over 40 were driven from 3 waves of Korean Health Panel between 2010 and 2012. Comprehensive disease list were developed to include 61 chronic diseases in concordant with chronic condition classification. Among these, 12 most frequent diseases such as cancer, diabetes and hypertension were selected to compare differences in health inequalities with and without consideration of MCD. Changes in health inequalities over t-1 and t year were analyzed against three socioeconomic variables (i.e., employment status, poverty, and educational attainment) by fitting random intercept multinomial logistic regression model.

Results: MCD were prevalent among the elderly people (62.0% for those with age more than 60 vs 19.2% for those with age between 40 and 59). Socioeconomic difference of a disease was larger when measured against free of any disease group as a reference group rather than free of a target disease; for example, Odds Ratio(OR)s of educational differences in diabetes was 2.54 (95% CI: 1.95-3.13) for the former measure vs 1.74 (95% CI: 1.35-2.23) for the latter. Further, the impact was more pronounced in a stage of comorbidity than a single disease only, except for diabetes. Effects of education were generally larger than the other socioeconomic measures across diseases, among which the associations with diabetes were the largest.

Conclusion: Health inequalities vary depending on the stages of MCD development (ie, comorbidity status) as well as types of disease and socioeconomic measures. The current practices used in measuring health inequalities in late life may be misled when based only on information with a single disease.

Day 2, Session 2: Biomarkers

Declining Stress Responses as a Contributing Factor to Ageing

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Young, mammalian cells, *C. elegans* worms, and *D. melanogaster* fruit flies adapt to oxidative stress such that they become (temporarily) much more resistant to oxidative damage. Such adaptive responses include synthesis of stress-protective Proteasome, Immunoproteasome, (PA28) proteasome regulator, and mitochondrial Lon protease, all of which are stress-protective. In older cells, flies, and worms, proteolytic activities decline, and adaptational responses mediated by Nrf2 become ineffectual. The antagonistic effects of Bach1, c-Myc and/or Nrf1 may blunt adaptive responses to stress in older cells and organisms. Declining responsiveness to stress in general, may contribute to the ageing process, and to various age-associated diseases.

Biocomplexity, chaos, and fractality in the search of biomarkers of aging and pathology

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The diffusion of paradigms such as complexity, chaos, and fractals in gerontologic field has opened up new perspectives and suggests innovative approaches to understand and study aging in a global vision of the phenomenon. Aging can be considered as a temporal evolution of a complex system governed by the laws of deterministic chaos and generating fractals. Fractal analysis represents a promising tool to give insight into the search of good biomarkers useful to discriminate between physiologic and pathologic aging as well as between age-related and age-associated diseases, two of the main tasks dealing with aging well.

Oral Presentation Abstracts

IMMUNOSENESCENCE-RELATED GENE ZIZIMIN2 IS ASSOCIATED WITH SPLENIC MARGINAL ZONE B CELL LOCALIZATION

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We have identified murine Zizimin2 (Ziz2; Dock11) that is highly expressed in germinal center B cells after T cell-dependent antigen stimulation. It has been demonstrated that Ziz2 is a guanine nucleotide exchange factor for Cdc42, one of the major Rho GTPases, and promotes filopodia formation. Since its expression levels in immune tissues are reduced in aged mice, Ziz2 may be associated with immunosenescence. However, the function of Ziz2 had not been fully examined *in vivo*. In this study, we tried to elucidate the function of Ziz2 *in vivo* by using Ziz2 knock out (KO) or structurally-related Zizimin3 (Ziz3; Dock10) KO mice.

At first, we assessed lymphocyte development in bone marrow (BM), spleen, thymus, or peritoneum cavity by flowcytometry (FACS). We examined also splenic lymphocytes from aged wild type (WT) mice by FACS and qPCR for Ziz2 and Ziz3. Concerning marginal zone (MZ) B cell localization, we performed immunostaining with anti-CD169 and anti-B220 antibodies for marginal metallophilic macrophages and B cell distribution, respectively. For immune responses, we assessed antigen-specific antibody titer by performing ELISA for TNP-LPS or TNP-Ficoll. Proliferation assay was performed for FACS-sorted MZ B cells with LPS. Migration activity towards SDF1 or CXCL13 was analyzed by using transwell and follicular/MZ B cells were detected by FACS.

As a result, no significant difference was detected in B/T cell development in BM, spleen, thymus, or peritoneum cavity of the KO mice. We also detected no significant difference between WT and KO mice in the immune responses or proliferation/migration assay. However, all B cell subsets in aged WT mice were reduced as compared to young WT mice. In addition, Ziz2 expression levels were reduced in only aged WT splenic B cells, but not T/NK/dendritic cells. Interestingly, histological examination revealed that splenic MZ B cell region (B220⁺ region outside CD169⁺ cells) became obviously thinning in the KO mice.

Taken together, our results suggested that both Ziz2 and Ziz3 regulate splenic MZ B cell localization. This study also indicated that ageing may induce delocalization of splenic MZ B cells.

INTERNET USE AND PHYSICAL ACTIVITY CAN IMPROVE QUALITY OF LIFE AMONG OLDER ADULTS: RESULTS FROM THE ENGLISH LONGITUDINAL STUDY OF AGEING.

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Aims and hypothesis: To elucidate whether internet use might be associated with quality of life (QoL) in older adults. Although QoL is strongly related to age and many health conditions, there are modifiable factors that can influence it.

Methods: Data from the English Longitudinal Study of Ageing (ELSA), a biennial prospective observational cohort study of individuals aged 50 years or over living in England. Sample of 11,391 core members followed up for 8 years. The outcome was low QoL defined as the first quartile of the self-enumerated Control, Autonomy, Self-realization and Pleasure 19-items scale (CASP-19). Our main predictors were internet use assessed according to responses to the statement "I use the Internet or e-mail" (yes/no) and weekly level of physical activity (no, mild to moderate, and vigorous). The covariates were sex, age, quartile of total net household wealth, paid work, education measured as the highest qualification obtained and categorized as university degree or equivalent, intermediate qualification, and no educational qualification, self-reported functional impairment categorized as difficulty in at least one of seven instrumental activities of daily living (IADL) (yes/no), smoking, depressive symptoms measured by a score of ≥ 4 points on the eight-item scale of the Center for Epidemiologic Studies Depression Scale (CES-D), self-reported doctor-diagnosed arthritis and cardiovascular diseases. Unadjusted and adjusted incidence rate ratios (IRR) and 95% confidence intervals (CI) were estimated through 2-year lagged Poisson regression models with Generalized Estimating Equations, adjusted for sociodemographic, lifestyle, and health variables.

Results: Higher age (IRR=1.06 CI95% 1.02-1.11), depressive symptoms (IRR=1.42 CI95% 1.33-1.51), smoking (IRR=1.09 CI95% 1.04-1.15), cardiovascular diseases (IRR=1.08 CI95% 1.05-1.12), arthritis (IRR=1.24 CI95% 1.15-1.33) and IADL impairments (IRR=1.30 CI95% 1.22-1.39) were associated with lower QoL. Physical activity (IRR=0.90 CI95% 0.87-0.93), higher socioeconomic position (IRR=0.82 CI95% 0.79-0.85), paid work (IRR=0.87 CI95% 0.80-0.95), use of internet (IRR=0.88 CI95% 0.81-0.94) were protective factors against low QoL.

Conclusion: Physical activity and use of internet are modifiable factors that can help maintain quality of life of older adults.

HOW DO COUPLES ADJUST THEMSELVES TO RETIREMENT?

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Introduction Ageing population is a great challenge for modern societies which have to adapt themselves to this new reality. Increasing longevity and low birth rates also contribute to an aged population, with implications both socially and economically. With increased longevity, people live more years after retirement and should be more prepared to deal with the difficulties that can arise from this transition. Retirement is one of the major transitions in adult life and it can originate different kind of vulnerabilities. If it difficult to retire alone, it can be even more difficult when it happens as a couple.

Objective The project REATIVA is a Portuguese project funded by the European Union and the Portuguese government which has as goal to promote health during the transition to retirement. We aimed to know the perceptions of couples who experience adaptation to the retirement process and the strategies adopted to address them.

Methodology The research team conducted a descriptive study of a qualitative nature. The target population was couples in which at least one of their spouses was retired for less than five years, registered in health care providers in Primary Health Care of the Regional Health Administration Center. The selected participants were subjected to an approach for semi-structured interview, after signing informed consent, and the information was gathered by digital audio recording and subjected to thematic analysis using the NVivo10® program.

Results The following themes were revealed: Before retirement, Moment of retirement, Today's experience, Expectations for the future and Recommendations for future intervention with couples. The theme before retirement presented two subthemes: expectations and idealizations and marital dynamics. Regarding the moment of retirement, the three sub-themes that emerged were: perceived changes, resources used and vulnerabilities. The theme of today's experience consisted of portraits of conjugality, resources and vulnerabilities of this moment of couples. The theme expectations for the future unveiled idealized resources and difficulties that couples expect to have. Recommendations for future intervention with couples were located at the level of individuals, couples and formal and informal networks.

Conclusions We concluded that retirement planning and organizing is beneficial for a successful transition and it happens at an individual but also at a marital level. The individual is central in the process but the conjugality seems to be a key resource in this phase. A functional couple, and with a good history of marital dynamics, is more prepared for retirement. Networks provide a bridge to social and family activities that allow individuals to escape from the isolation that can happen after retirement. Retired couples are an important aid to plan and carry out intervention with couples in the pre-retirement period, to prepare them to this new phase.

LONG TELOMERES PROTECT VESSELS FROM DIABETES MELLITUS.

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It is known that glucose disturbances contribute to micro- and macro vascular complications and vascular aging. The length of telomere (TL) is considered as a biomarker for cellular aging. It is crucial to determine the role of the telomere length in structural and functional vessels changes in patients with DM.

The aim of our study was to determine the role of the telomere length in vascular aging in patients with T2DM.

Methods The study group included 50 patients with T2DM in mean age 58.4 ± 7.83 years. The duration of diabetes was 3.3 ± 0.34 years. Mean blood pressure: SBP 131.76 ± 1.4 mm Hg, DBP 83.02 ± 11.3 mm Hg. Carbohydrate metabolism was assessed by fasting plasma glucose and Glycated hemoglobin (HbA1c) measuring.

TL and telomerase activity (TA) was assessed by quantitative polymerase chain reaction (PCR).

Intima-media thickness (IMT) and plaque presence (PP) were determined by ultrasonography in both left and right carotid arteries. Arterial stiffness (AS) was appreciated by aortic pulse wave velocity (PWV) measuring by SphygmoCor (AtCor Medical).

Endothelial dysfunction was assessed by flow-mediated endothelium-dependent dilation (FMV) in response to reactive hyperemia and endothelium-independent vasodilation in response to nitroglycerine (NDV); by homocysteine, von Willebrand factor measuring.

Oxidative stress was assessed by malondialdehyde measuring, inflammation was estimated by interleukin-6 (IL-6), C-reactive protein (CRP), fibrinogen measuring.

Results All patients were divided into 2 groups by the median of TL (9.75): «short» telomeres (mean TL 9.19 ± 0.32) and «long» telomeres (mean TL 9.97 ± 0.43). Patients were similar in blood pressure and HbA1c.

Vessels changes were more pronounced in patients with «short» TL than patients with «long» TL: PWV 14.11 ± 3.22 m/s vs 11.78 ± 3.26 m/s ($p=0.016$), IMT 1.00 ± 0.15 mm vs 0.84 ± 0.16 mm ($p=0.0010$), PP 2.63 ± 0.31 vs 1.36 ± 0.26 ($p=0.0032$), FMV 7.93 ± 3.40 vs 10.95 ± 3.10 ($p=0.0022$), NDV 12.63 ± 4.25 vs 15.68 ± 4.51 ($p=0.0186$), homocysteine 14.39 ± 2.68 mkmol/l vs 12.32 ± 2.52 mkmol/l ($p=0.0077$), von Willebrand factor 120.0 ± 36.7 % vs 87.91 ± 31.76 % ($p=0.0020$). There were now no significant differences in TA between two groups. We found significant increasing of oxidative stress and chronic inflammation in diabetic patients with «short» TL: malondialdehyde 3.43 ± 1.06 mkmol/l vs 2.94 ± 0.87 mkmol/l ($p=0.058$); CRP 9.43 ± 2.01 mg/l vs 3.30 ± 0.37 mg/l ($p=0.0062$).

Correlation analysis showed in diabetic patients significant association between telomere length and next parameters: PWV ($r=-0.50$, $p=0.0003$), IMT ($r=-0.39$, $p=0.0059$), FMV ($r=0.49$, $p=0.0003$), NDV ($r=0.41$, $p=0.0035$), fasting plasma glucose ($r=-0.42$, $p=0.0027$), CRP ($r=-0.40$, $p=0.0039$), reduced TA ($r=-0.32$, $p=0.0353$), homocysteine ($r=-0.39$, $p=0.0063$), von Willebrand factor ($r=-0.42$, $p=0.0026$).

Conclusion In patients with T2DM and "short" telomeres signs of vascular aging, chronic inflammation and oxidative stress were more pronounced. Perhaps long telomeres protect patients with short duration of diabetes from the damaging effect of oxidative stress and chronic inflammation, leading to the development of subclinical atherosclerosis and increased vascular stiffness.

AGE-RELATED DECREASE IN BROWN ADIPOSE TISSUE AND ITS POTENTIAL METABOLIC COMPLICATIONS

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Brown adipose tissue (BAT), a recently rediscovered tissue in human adults, has been proposed as a potential target-tissue against obesity and its metabolic consequences. Current evidence supports that BAT depots may decrease with age. However, the majority of the published studies are retrospective studies conducted under non-standardized conditions, while the existing experimental studies performed a relatively short cold exposure protocol, which might have been insufficient to activate BAT in older individuals. Considering the increased prevalence of obesity and its metabolic complications with aging, purpose of this study was to investigate the role of BAT in metabolic regulation in young and older human adults.

Methods To address this question, we studied sixteen healthy men (19 to 75 years old) under prolonged (5h) non-shivering cold exposure (CE) and thermoneutral (TN) conditions using positron emission tomography-computed tomography, stable isotope infusions, indirect calorimetry and PCR analysis of supraclavicular adipose tissue biopsies.

Results Age was correlated with decreased BAT mass ($r=-0.61$, $p=0.01$), mean ($r=-0.63$, $p=0.02$) and maximum metabolic activity ($r=0.72$, $p=0.009$). Conversely, participants' age was also correlated with the amount of subcutaneous ($r=0.52$, $p=0.06$) and visceral abdominal tissue ($r=0.71$, $p=0.005$), but not with the BMI. Moreover, BAT activity was positively correlated with higher increase in resting energy expenditure ($r=0.52$, $p=0.05$), whole-body glucose uptake ($r=0.55$, $p=0.03$), adipose tissue lipolysis ($r=0.61$, $p=0.01$), and free fatty acid oxidation ($r=0.64$, $p=0.04$). Expression of uncoupling protein 1 (UCP1), deiodinase type 2 (DIO2), beta 3 adrenergic receptor ($\beta 3AR$), PR domain containing 16 (PDRM16), glucose transporter 4 (GLUT4), and peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1 α) were not significantly correlated with age.

Conclusions Our results suggest that the age-related decrease in BAT maybe related to increased rates of abdominal fat accumulation, diabetes and hyperlipidemias noted among older adults. Further research is needed to establish the role of BAT in metabolic regulation in older adults.

NATURAL ANTIOXIDANTS; A KEY TOWARDS HEALTHY AGEING

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The medicinal properties of plants have been investigated in the light of recent scientific developments throughout the world, due to their potent pharmacological activities, low toxicity and economic viability. The study is mainly focused on establishing the antioxidant property of flower extracts of two Indian medicinal plants, *Ervatamia coronaria* and *Leucas aspera*. The water extracts of the flowers were taken and its activity was determined by ferric thiocynate method and ascorbic acid, a commercial antioxidant, was taken as the control. Two concentrations of the sample were taken for the analysis; *L. aspera* (0.1mg/ml and 0.2mg/ml), *E. coronaria* (1mg/ml and 2mg/ml). The result obtained in the present study indicates that the flower extracts are capable of inhibiting lipid peroxidation and exhibited higher activity than ascorbic acid, a commercial antioxidant.

Antioxidant compounds can scavenge those free radicals which can damage cellular macromolecules and also unsaturated lipids in organised assemblies such as cell membranes and lipoproteins. It is especially important to boost up cellular antioxidant defence mechanisms in aged individuals otherwise which may ultimately lead to several neurodegenerative diseases along with other common problems of ageing. So the antioxidants are especially important in maintaining normal life processes, which may get weaker as the ageing occurs. Another aspect regarding the importance of natural antioxidants lies in its protective effect, as a nontoxic component, derived from plants. Synthetic antioxidants are widely used to increase shelf life by retarding the process of lipid peroxidation, which may cause deterioration of food and pharmaceutical products during processing and storage. The safety of these antioxidants has recently been questioned due to toxicity (carcinogen). Thus the result that obtained in the present study reveals the possibility of utilizing active components in medicinal plants as a key for a better and healthier ageing as well as a substitute for synthetic antioxidants.

Poster Presentation Abstracts

LYMPHOCYTE SUBSETS IN AGEING - DATA FROM TWO LARGE ITALIAN COHORTS

[Roberto Paganelli](#), Marika D'Urbano, Angelo Di Iorio

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We conducted a survey of two separate cohort studies, in which we participated, dated from 2004 and 2006 and one still ongoing. In these studies, subjects above 65 yrs of age were enrolled after screening for several chronic diseases, including arthritis, cancer and heart failure, and selected for being free of mobility disability. Both studies were conducted in Central Italy, and some or most of the clinical and laboratory findings have already been reported, including papers from the authors of the abstract.

However we focused our attention on the less investigated immunological findings, namely the lymphocytic subpopulations as determined by monoclonal antibodies and cytofluorimetric analysis. Here we report the first results which have not been yet sketched against all clinical and sociodemographic data, as well as with the follow up findings.

In the SACS study, 148 out of 321 subjects aged 65 to 89 met the criteria for successful aging, only 11 over 85, and disability was discovered in 3-4% for IADL and mobility. In this selected group no relationship of lymphocyte number to age was found, despite significant decrease compared to younger healthy subjects. Of those evaluated for subsets, 45 males and 57 females, age 72.8 ± 5.3 , there were no differences for total T, and CD4, CD8 or CD19 cells. However CD45RA+ cells were decreased within CD4+ in both genders. A trend to increased numbers of CD4+ cells lacking both the CD45RA and the CD28 molecule was also seen throughout the age groups ($p=0.043$ Kruskal-Wallis test), and dividing the subjects into age groups we found a conserved M:F ratio, with males representing 15/33 in 65-69 y.o.; 15/36 in 70-74 y.o. and 15/32 in >75 y.o. A significant inverse relationship between age and memory CD27+ B cells was observed. This was present in both sexes although more evident in females. The percentage and total number of B cells declined sharply after the age of 74 with a decrease also of naive CD27- B (40 vs 68 cells/ μ l). We stratified cases for number of CD45RA- CD4 T cells (<150, 151-300 and 301+) and observed more females in the first (lower) group, with lower CD3+, CD4+ and CD8+ cells, lower CD4/CD8 ratio, but higher % and number of B cells, both CD27+ and CD27-, and a slight increase of %Treg CD4+CD25hi. Tregs were overall decreased compared to normal.

The second more robust study and with a 6 yrs follow-up carried information on 505 subjects. Lymphoid cells decreased with age in both males and females, despite females tend to have higher CD4+ (both total and %, $p<0.04$) and B lymphocytes ($p<0.001$ for %) whereas males have higher numbers of CD8+ and NK cells (both <0.01), with resulting significant differences for CD4/CD8 ratio ($p=0.008$). There were significant trends to decrease of total lymphocytes, CD4+, and B cells and increase of T DR+ (activated) and of NK cells with age. Predictors of survival at 6 yrs were represented by total number of CD4+ and %lymphocytes, but not CD4/CD8 ratio or other parameters obtained by immunophenotyping.

Our data represent a very large reference set for comparison of these immune parameters in elderly subjects affected by age-related diseases to validate their pathogenetic relevance.

The authors wish to thank Prof. L. Ferrucci and A. Mezzetti† for permission to report these data.

LOW-INTENSITY INTERMITTENT WALKING EXERCISE REDUCES POSTPRANDIAL HYPOTENSION IN OLDER PEOPLE

Z.A. Kopsaftis, R. Visvanathan, S. Nair, H. Arunasalam, [D. Piscitelli](#)^{1,2}

Background Postprandial hypotension, which occurs frequently in older people, is associated with an increased falls risk and represents a major cause of morbidity and mortality. Our recent study has established that 120 minutes of low-intensity intermittent walking exercise is effective in attenuating the hypotensive response to oral glucose (1). It is not known, however, whether a shorter period of walking exercise is sufficient to induce the same effect and if the blood pressure response to the walking exercise is sustained after the exercise has ceased; this information is relevant to management strategies for the prevention of postprandial hypotension. We have, therefore, evaluated the effects of 60 and 120 minutes of low-intensity intermittent walking exercise on systolic blood pressure in older people with postprandial hypotension.

Methods Nine older participants with postprandial hypotension (8F, 1M; age 72 - 90 years) were studied on three separate, randomised days. Systolic blood pressure (automated device) was measured between t = 0 - 180 minutes following ingestion (t = 0 minutes) of a 200 ml drink containing 50 g glucose. On the study days, participants either: (i) walked at a self-selected speed for 30 metres at t = -5 minutes and then every 30 minutes until t = 60 minutes (study day A), (ii) walked at a self-selected speed for 30 metres at t = -5 minutes and then every 30 minutes until t = 120 minutes (study day B) or (iii) did not walk after ingestion of the drink (study day C).

Results There were comparable mean maximum falls in systolic blood pressure during all study days (A vs B vs C: 20.89 ± 3.04 mmHg vs 21.89 ± 3.80 mmHg vs 22.78 ± 3.55 mmHg; $P < 0.67$) with no significant difference ($P = 0.73$) in the timing of the falls between the days (A vs B vs C: 40.33 ± 6 minutes vs 35.33 ± 5 minutes vs 41.0 ± 5 minutes). There were no significant treatment effects for the area under the curve (AUC) for the change in systolic blood pressure from baseline between the study days for t = 0 - 60 minutes ($P = 0.12$), t = 120 - 180 minutes ($P = 0.61$) and t = 0 - 180 minutes ($P = 0.16$).

However, between t = 60 - 120 minutes there was a significant treatment effect ($P = 0.008$) such that during this time period, systolic blood pressure was significantly less during study day C than during study day B (95% CI = -978.57 - -33.10, $P = 0.036$) but not during study day A ($P = 0.15$). When systolic blood pressure at t = 60 minutes and t = 120 minutes (i.e. time of last exercise) on study days A and B were compared to all time-points until t = 180 minutes, there were no differences in systolic blood pressure during both days.

Conclusion A minimum of 120 minutes of low-intensity intermittent walking exercise is required to attenuate the hypotensive response to oral glucose in older people with postprandial hypotension; an effect that is sustained for up to 180 minutes post drink ingestion. This finding may represent a simple approach to the management of postprandial hypotension.

(1) Nair S, Visvanathan R, Gentilcore D. J Am Med Dir Assoc. 2014 Oct 8. doi: 10.1016/j.jamda.2014.08.013.

THE CALPAIN-CALPASTATIN SYSTEM IN HUMAN LYMPHOCYTE AGEING

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The calpain-calpastatin system (CCS) in the lymphocytes contains two neutral, cytoplasmic, cysteine proteases (mu- and m-calpain) and their endogenous, very specific inhibitor – calpastatin. Their property of cleaving only relatively few specific sites in the proteins and peptides, as well as their list of substrates, makes them potentially important regulators of the immune response. Thus it is feasible that the system may take part in the process of immune system ageing; consequently, a hypothesis of different activity of the CCS in the immune cells of centenarians (as compared to younger healthy elderly) is explored in this project. Centenarians form a selected group of long living humans; their longevity is conceivably associated with fitter immune systems.

Thus, the detailed aim of the Polish-Italian CALPACENT project is to establish the role of CCS system function for the effective immune response and of its malfunction as a potential participant in the mechanisms of the immune cells' ageing.

We assess the numbers and activation of lymphocyte populations and the amount and the activities of CCS proteins in the various subpopulations of peripheral blood cells from healthy Polish and Italian: centenarians, elderly and young people. We demonstrate the influence of calpain on the cell proliferation as well as the consequence of inhibition of calpains in the in vitro lymphocyte culture. Our results suggest

the differences in the expression and activities of CCS members between the different lymphocyte populations (including the CD4+, CD8+, CD19+), age groups different, bearing on the cells' functions.

Day 3: Expression and Pathology

Invited Speakers Abstracts

The 'hidden' Epidemic of Adult Alzheimer & Neurological deaths in the USA and 20 Western countries 1989-2010: A Controlled Study

[Professor Colin Pritchard](#), Professor in Psychiatric Social Work, School of Health & Social Care, Bournemouth, UK

Neurological disease deaths, including Alzheimer's, of people <74 years in 10 major developed countries are increasing and dementias starting ten years earlier. Does the Gompertzian hypothesis, of increased longevity, explain these changes?

Using as the classic disease of the elderly (75+) cancer, as a control, we contrasted Alzheimer and Nervous Disease Deaths with Cancer mortality between 1989-2010.

Cancer deaths were slightly lower than previously but average combined neurological male deaths increased 5% pa, females by 9% p.a. Average Odds ratios of cancer to combined neurological deaths were 1:2.39 men and 1:2.84 women. Results very indicative of likely environmental aetiology?

The Long and Winding Road of Arterial Aging: A Journey from Evolution to Dysfunction

[Dr Majd AlGhatrif](#), MD, IPA appointee, Human Cardiovascular Studies Laboratory of Cardiovascular Science, National Institute on Aging, Assistant Professor, Medicine, Johns Hopkins Bayview Medical Center, Johns Hopkins School of Medicine, USA

Unicellular organisms evolved in physically stable, chemically renewable micro-environments. The evolution of complex multicellular organisms required a system that maintains the same micro-environments to the individual cells via a continuous steady flow. While the left ventricle generates a pulsatile flow, it is the elastic aorta that dampens this pulsation into an almost continuous flow in the periphery. While, this system works elegantly in youth, major alterations ensue with aging leading to a vicious cycle of dramatic changes in arterial mechanics and hemodynamics. Earlier manifestations of these alterations are observed in young adulthood with a sharp decline in aortic strain and distensibility accompanied by an increase in diastolic blood pressure. Subsequently aortic mechanical reserve is exhausted, and aortic remodeling with wall stiffening and dilatation ensue. These two phenomena affect pulse pressure in opposite directions and different magnitudes. With early remodeling there is an increase in pulse pressure (PP), due to the dominance of arterial wall stiffness, which in turn accelerates aortic wall stiffness and dilation. With advanced remodeling, which appears to be greater in men, the effect of diameter becomes more pronounced and partially offsets the effect of wall stiffness leading to plateauing in PP in men, and slower increase in PP than that of wall stiffness in women. The complex nature of these hemodynamic changes with aging makes the ³one-size-fits-all² approach suboptimal, and urges for therapies that addresses the vascular profile that underlies a given blood pressure, rather than the blood pressure values themselves.

Targeting age-related hearing loss

Professor. Isabel Varela Nieto, Neurobiology of Hearing Group, Hearing Evaluation Service, Instituto de Investigaciones Biomédicas "Alberto Sols". CSIC-UAM, Madrid, Spain

Age-related hearing loss affects 50% of the population over 65-year old, making it the second most common cause of disability in older people. Human insulin-like growth 1 (IGF-1) serum levels decrease with ageing and this reduction is associated with cochlear degeneration and hearing loss. Neuronal and vascular alterations contribute to the cellular phenotype that leads to an accelerated hearing impairment. IGF-1 promotes cell survival by activating RAF and AKT protein kinases that in turn target AP1, MEF2 and FoxM1-mediated gene transcription. IGF-1 deficit impairs metabolic homeostasis and increases neuroinflammation by means of pP38 MAPK and FoxP3. IGF-1-based treatments offer novel opportunities for the protection of hearing loss. Work supported by FP7-AFHELO and FP7-TARGEAR.

The Ageing Eye: A delicate metabolic balancing act

[Dr Jeremy M Sivak](#), PhD, Assistant Professor, University of Toronto School of Medicine, Glaucoma Research Chair, Toronto Western Research Institute, University Health, Toronto, Ontario, Canada

The vertebrate eye is highly evolved, combining sensitive optical, neuromuscular, and neurosensory components into an integrated function. However this specialization leaves ocular tissues vulnerable to damage and stresses with age. In particular, the retina maintains a fine balance between high metabolic

activity and damage due to oxidative stress, UV light, toxins, and strain. This balance tips irrevocably with age, leading to the most common forms of vision loss and blindness. My laboratory has been investigating the molecular and cellular mechanisms that maintain this balance. In a broader context, the eye is a sensitive early indicator for many related aging processes.

Healthy Ageing through technoculture

[Dr Marios Kyriazis](#), ELPis Foundation for Indefinite Lifespans, Italy

Interacting with our environment is a neglected area of ageing research. And yet, the nature of this interaction may hold essential keys about healthy longevity. Research shows that every time we change something about our daily routine, this has an impact on our biology. I am going to discuss how to maximise healthy longevity by positively interacting with the world around us, and by making best use of positive stress or hormesis. This covers areas such as immunity, sexuality, social interaction and engagement with technology.

Towards a greater cortical control of balance with advancing age

[Dr Stéphane Baudry](#), Faculty for Motor Sciences, Universite Libre De Bruxelles, Belgium

Biological ageing causes changes in the neuromuscular system that impact motor control. In this context, postural stability has been reported to decline with ageing, such decline being accompanied by changes in neural adjustments and muscle activation inherent to upright standing. The emerging picture points toward an age-related reorganization in the control of upright standing, characterized by differential modulation of spinal pathways, greater cortical activation and cortical disinhibition during postural tasks. Accordingly, the aim of this talk is to present recent evidences and hypotheses on the influence of age on postural control.

Role of tele-technology in 21st Century NHS

[Dr. Amit Arora](#), Consultant Physician/Geriatician and Honorary Clinical Lecturer Chairman, England Council, British Geriatrics Society West Buildings University Hospital of North Staffordshire Stoke On Trent, UK

Human Ageing at the Individual Level is a Unique Experience and Chronic Degenerative Diseases are Variants of that Ageing Process.

[Dr Michael Singer](#), Queen's University Kingston, Ontario, Canada.

Although much has been written about ageing at the level of the species, ageing at the level of the individual human has not received the same focus. The observation that there is extensive genomic and epigenomic variation across individuals and that environmental cues can reprogram epigenetic marks indicate that each individual human will have a unique ageing phenotype in terms of longevity and ageing trajectory. The uniqueness of each individual's ageing pattern is the primary theme of this talk. Several important secondary themes are also developed. First, it is impossible to dissect the ageing process from the living state itself. There are no specific "ageing" or "longevity" genes. Secondly, the pattern of the ageing process is strongly determined by environmental cues (experiences) and how a specific individual responds to those cues. Third the ageing process is molded by the social and cultural context in which that individual lives. The uniqueness of an individual's ageing phenotype as determined by that person's unique genome and epigenome has important implications for our understanding of what constitutes a disease and whether in fact current molecular biology renders the disease construct outmoded.

RCSI developing healthcare leaders who make a difference worldwide

[Dr Claire Donnellan](#), PhD, MA, Reg. Psychol., RGN, PG Dip Stats Senior Lecturer in Psychology RCSI Bahrain, Adliya, Trinity College Dublin and RCSI-Bahrain, Kingdom of Bahrain

The definitions and indicators used to explain ageing assume that people become old at age 65 although generally, 65-year-olds today live longer than 65-year-olds have in previous centuries. The dramatic rise in life expectancy has resulted in increasing interest in promoting healthier ageing and the study of how people actually age successfully. Although the concept of successful ageing dates back to the 1960s, the goal of successful ageing is now more realistic in today's ageing society as a result of more effective interventions to control and reduce disability and health risks. It has recently been proposed as a field of interest in gerontological research and as a challenge for the design of social policy. This talk will address how realistic are our ageing indicators, the challenges associated with ageing and how the promotion of successful ageing supports the demands of the ageing revolution.

Oral Presentation Abstracts

There is considerable debate over which adiposity measure(s) best discriminate cardiometabolic health risk. Body mass index (BMI) is a ratio of weight to height, which is routinely used by researchers and clinicians to categorize individuals as underweight, normal weight, overweight, or obese. A primary drawback is that it fails to differentiate lean and fat mass. Waist circumference (WC: measured at the narrowest area or umbilicus), waist-to-height ratio (WHtR), and sagittal abdominal diameter (SAD) are measures used to assess central adiposity and predict onset of obesity-related diseases, such as hypertension and diabetes. Bioelectrical impedance analysis assesses percent body fat (% BF by BIA) on a portable, electronic device by measuring the strength and speed of an electrical current through body tissues. The purpose of this pilot investigation was to determine the relationship between simple methods for assessing adiposity in older adults. Subjects were 31 females and 14 males (aged 58.3 ± 6.8 years; 93.0% Caucasian). At a single study visit, adiposity was assessed using BMI (27.3 ± 6.0 kg/m² M, 26.8 ± 6.6 kg/m² F, 26.7% obese); % BF by multi-frequency BIA ($22.7 \pm 7.8\%$ M, $34.2 \pm 9.4\%$ F, 20.0% obese); WC at the narrowest area (94.3 ± 10.4 cm M, 84.1 ± 13.6 cm F, 33.3% obese); WC at the umbilicus (98.1 ± 12.1 cm M, 91.6 ± 14.5 cm F, 46.7% obese); WHtR at the narrowest area (0.54 ± 0.07 M, 0.51 ± 0.08 F, 57.8% obese); WHtR at the umbilicus (0.56 ± 0.08 M, 0.56 ± 0.09 F, 73.3% obese); and SAD (22.9 ± 3.4 cm M, 21.0 ± 3.5 cm F, 68.9%). In males, all adiposity measures were positively correlated with % BF. Correlations ($p \leq 0.001$ for all) were strongest between BMI ($r = 0.907$), SAD ($r = 0.878$), WC-narrowest ($r = 0.804$), and WC-umbilicus ($r = 0.787$). Correlations ($p < 0.05$ for both) with WHtR-umbilicus ($r = 0.714$) and WHtR-narrowest ($r = 0.638$) were less strong. In females, correlations ($p < 0.001$ for all) between BMI ($r = 0.801$), SAD ($r = 0.809$), WC-narrowest ($r = 0.782$), and WC-umbilicus ($r = 0.806$) and % BF were very strong. WHtR-umbilicus and WHtR-narrowest were not correlated with % BF. These results indicate that % BF, BMI, WC, and SAD provide similar assessments of adiposity. WHtR demonstrated a weaker relationship with % BF, particularly among women, and may over-detect adiposity-related health risks. Using all adiposity measures, 15.6% of all subjects were classified as obese and 22.2% were classified as healthy.

Variable results (i.e., obese using some measures, healthy using others) were noted in 62.2%. Accurate health risk classification of older adults has long-term effects related to cost and intervention. Further studies are required to determine if results are consistent across older adults of different nationalities and racial/ethnic groups.

WHOLE BLOOD GENE EXPRESSION ASSOCIATIONS WITH MUSCLE STRENGTH IN HUMANS

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Introduction: Muscle strength in midlife is predictive of disability and mortality in later life; loss of muscle strength is a key feature of aging. Blood factors influence muscle function and repair, and inflammation may play a role. We aimed to identify the whole blood-derived transcripts most closely associated with muscle strength in adults.

Methods: Meta-analysis of whole blood gene expression and hand-grip strength in four independent CHARGE study cohorts (N=7781, ages: 20:104), adjusted for confounders including age, sex, height, weight, and leukocyte subtypes. Three cohorts used Illumina HumanHT-12 microarrays, one used Affymetrix Exon-array data (gene level). Separate analyses were also performed in subsets (old/young, male/female).

Results: In the meta-analyses, expression of 222 unique genes was significantly associated with muscle strength. Analyzing the Affymetrix and Illumina cohorts separately, 21 of the top 30 significant genes (70%) showed independent replication. Gene Ontology pathway analysis found enrichment for "hemoglobin biosynthesis" and "innate immune activation". Significant genes include *ALAS2* (rate limiting enzyme in heme synthesis), *PRF1* (perforin, a cytotoxic protein previously associated with age-related chronic inflammation), and *IGF2BP2* (previously linked to muscle strength). The results differed between men and women.

Conclusions Blood transcripts associated with muscle strength in adults may reflect genes involved in innate immune pathways plus heme synthesis, but also include novel markers needing characterization. To examine aging in more detail, future studies should explore longitudinal trajectories of transcripts in persons who experience accelerated decline of muscle strength, compared to those with relatively preserved muscle strength with aging.

AGEING, FRAILTY AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

[Lies Lahousse](#)^{1,2}, [VJA Verlinden](#)², [G Ziere](#)², [MC Zillikens](#)², [AG Uitterlinden](#)², [F Rivadeneira](#)², [H Tiemeier](#)², [GF Joos](#)¹, [A Hofman](#)², [MA Ikram](#)², [OH Franco](#)², [BH Stricker](#)², [GG Brusselle](#)^{1,2}

Background With the aging of our population, there is an increasing prevalence of chronic illnesses such as Chronic Obstructive Pulmonary Disease (COPD). The most problematic expression of aging is frailty. Although COPD has been described to be common in frail elderly, little is known on the relationship between such chronic illnesses and frailty.

Methods This study was part of the Rotterdam Study, a prospective population-based cohort study performed in subjects aged ≥ 55 years. Diagnosis of COPD was confirmed by spirometry. Frailty was defined as meeting three or more of five established criteria for frailty, including nutritional status, physical activity, mobility, strength, and energy.

Results Of the 2142 subjects with assessments of both frailty and lung function, 100 subjects were frail, i.e. 41 of the 402 (10.2%) subjects with COPD and 59 of the 1740 (3.4%) subjects without COPD. The prevalence of frailty was significantly increased in subjects with COPD, especially in those with severe airflow limitation, dyspnea and frequent exacerbations. A stepwise regression analysis resulted in following most important risk factors of frailty: COPD (OR 2.2, 95% CI 1.34-3.54, $p=0.002$), age, sex, smoking pack years, cholesterol and hematocrit levels, stroke, osteoporosis, current beta-blocker and calcium channel blocker use, and cumulative use of corticosteroids. COPD elderly who were frail had significant worse survival.

Conclusions This population-based cohort study in elderly demonstrates that COPD is associated with frailty, independently of common risk factors and comorbidities. Our findings suggest that frailty might identify those COPD subjects at high risk of mortality.

THE ROLE OF AGE-RELATED CHANGES IN BODY COMPOSITION ON BODY MASS INDEX: A PILOT INVESTIGATION

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In the United States over 82 million individuals, or approximately 26% of the population, are aged 50 and older. The National Health and Nutrition Examination Survey estimates the prevalence of obesity in this group to be 32.6%. However, most healthcare providers rely upon Body Mass Index (BMI) as the primary indicator of obesity-related health risks. The purpose of this pilot study was to investigate the relationship between BMI and body fat percentage in people undergoing age-related changes in body composition. Participants were 45 healthy individuals (14 M, 31 F) aged 50 and older (58.3 ± 6.8). Height and weight measurements were assessed via stadiometer and calibrated electronic scale; BMI was calculated as kg/m^2 . Each participant completed body composition analysis via air-displacement plethysmography (ADP). All participants met pretesting requirements (e.g., no food, water, or exercise for 2 hours) to ensure accuracy. BMI calculations and body fat percentage measurements were $27.0 \pm 6.3 \text{ kg/m}^2$ and $32.8 \pm 9.2\%$, respectively. Sex-specific BMI results were 27.3 ± 6.0 for males and 26.8 ± 6.6 for females. Body fat percentages were $26.9 \pm 6.0\%$ in males and $35.5 \pm 9.1\%$ in females. Based on WHO-accepted BMI categories, 22 (6M, 16F) participants were classified as normal weight (18.5-24.9), 11 (5M, 6F) as overweight (25.0-29.9) and 12 (3M, 9F) as obese (≥ 30.0). However using body fat percentage, 24 participants were classified as normal weight, 7 as overweight, and 14 obese using sex-specific cut-points to indicate excess fat (Gallagher et al. 2000). Sensitivity and specificity were calculated comparing BMI to body fat percentages using the above criteria. Overall, the sensitivity of BMI in properly identifying overweight and obese participants was 0.90 and 0.71, respectively. The sensitivity of BMI for overweight and obese participants was 0.83 and 0.94, respectively. Based on this initial investigation, there is a slight discrepancy in the classification of obesity-related health risk between BMI and body fat percentage. Therefore, BMI does not always correctly identify excess fat. These findings demonstrate the need for the further investigation of age-related changes in body composition and assessment techniques in an older population.

A CONSERVED TRANSCRIPTIONAL SIGNATURE OF DELAYED AGEING AND REDUCED DISEASE VULNERABILITY IS PARTIALLY MEDIATED BY SIRT3

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Ageing is the most significant risk factor for a range of diseases, including many cancers, neurodegeneration, cardiovascular disease, and diabetes. Caloric restriction (CR) without malnutrition delays ageing in diverse species, and therefore offers unique insights into age-related disease vulnerability. Previous studies suggest that there are shared mechanisms of disease resistance associated with delayed ageing, however quantitative support is lacking. We therefore sought to identify a common response to CR in diverse tissues and species and determine whether this signature would reflect health status independent of ageing. We analyzed gene expression datasets from eight tissues of mice subjected to CR and identified a common transcriptional signature that includes functional categories of mitochondrial energy metabolism, inflammation and ribosomal structure. This signature is detected in flies, rats, and rhesus monkeys on CR, indicating aspects of CR that are evolutionarily conserved. Detection of the signature in mouse genetic models of slowed ageing indicates that it is not unique to CR but rather a common aspect of extended longevity.

Mice lacking the NAD-dependent deacetylase SIRT3 fail to induce mitochondrial and anti-inflammatory elements of the signature in response to CR, suggesting a potential mechanism involving SIRT3. The inverse of this transcriptional signature is detected with consumption of a high fat diet, obesity and metabolic disease, and is reversed in response to interventions that decrease disease risk. We propose that this evolutionarily conserved, tissue-independent, transcriptional signature of delayed ageing and reduced disease vulnerability is a promising target for developing therapies for age-related diseases.

ABILITY ASSESSMENT OF THE ELDERS TO MANAGE THEIR OWN MEDICATION: A FIRST STEP FOR THE EMPOWERMENT OF THE GERIATRIC POPULATION

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Background: Three key factors are unanimously pointed for a successful aging: health, autonomy and independence, as long as possible. The aging process is characterized by a gradual change of biological, psychological and social structures, lifelong. Progressively, the elderly lose the ability to perform essential tasks for an independent living. Early detection of this functionality loss will allow predicting the need of intervention, for example, through the introduction of devices that facilitate the medication self-administration. Taking medication is a methodical process leading to an everyday habit. The decrease of cognitive skills, visual acuity or manual dexterity has a significant impact on unintentional non-adherence. Although cognitive and functional barriers to administer the medication are not easily modifiable, there are acting strategies already tested. A specific assessment for medication management for the elderly is essential because it makes it possible to detect problems in the medication management and allow an intervention in an important factor of treatment failure. The main objective of the study is to assess cognitive and functional ability of older people to manage their medication, using validated tools for the Portuguese population.

Methods: The working plan will be run into three phases.

Phase 1 – Development of a descriptive literature review (DLR) to search the available tools to assess the medication management ability [keywords: “medication management”, “self-administration”, “functional ability” and “elderly”; bibliographic databases: PubMed, EBSCOhost, ISI Web of Science, Scopus and International Pharmaceutical Abstracts] and a systematic literature review (SLR) to know the assessment of medication management ability outcomes obtained by other authors [search query was performed according to PICO method and it was run into PubMed, CINAHL Plus, Scopus and ISI Web of Science].

Phase 2 – Validation of the selected tools in the analysis of the systematic review previously carried out. This process was initiated by the authorization requirement to the original authors. The first step of the adaptation process was a symmetric translation of the tools from source language (English) to Portuguese and it was followed by a back-translation. It was promoted several expert meetings to assess the cultural, linguistic and operational specific questions. Actually, a pre-test is been performed (test-retest) of the preliminary Portuguese versions of the tools in a sample of Portuguese elders (context: community pharmacies and elderly day centers).

Phase 3 – Implementation of the validated tools for Portugal, through a cross-sectional study with a sample of elderly users of the healthcare centers of the Regional Health Administration of the Alentejo (South of Portugal).

Results: The search of DLR resulted in 15 tools [years: 1986-2011] (11 to assess the ability to manage simulated medication regimens, 3 to assess real medication regimens and 1 to assess the two types of medication regimens. The SLR resulted in a total of 18 papers corresponding to 17 studies. In the majority of the studies, the functional ability of the elders to manage their medication was assessed with specific tools. It was observed that the elders have more difficulty to manage a simulated regimen (new information) than a real regimen (routine information). To adapt and validate to the Portuguese

population two tools were selected, according to their different characteristics: DRUGS [USA] (real medication) and SMAT [Canada] (real and simulated medication).

Final Remarks: The adaptation process is performed and a pre-test is being carried out (test-retest) of preliminary Portuguese versions of the two selected tools. The sample dimension for the pre-test was calculated according to the number of items of each tool, DRUGS (n=50 elders) [elderly day centers] and SMAT (n=150 elders) [community pharmacies].

SAFETY AND EFFECTIVENESS OF NEW SURGICAL TECHNIQUE TO PREVENT CONTRALATERAL HIP FRACTURE

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INTRODUCTION The second fracture of the upper part of the femur is associated to dependency and to a dramatic increase of the mortality rate (from 20 to 50% depending of the studies). Therefore, it is clearly important to prevent this second fracture. The purpose of this study is to evaluate the impact of a new prevention dedicated osteosynthesis implant (PDOI) in its use for osteoporotic fracture prevention in terms of safety and effectiveness.

METHODS This study to prevent osteoporotic fracture (POF) is an on-going prospective series of 15 PDOI. To date, 4 patients female were implanted. The PDOI was implanted into the contralateral hip during the same surgery time of fractured hip gamma nail implantation. Clinical evaluation includes the Oxford Hip Score, the WOMAC scores, plantar pressure measurements and imagery. Three (3) patients have a one year follow-up. Five (5) years follow-up is planned.

RESULTS Mean Age and BMI of patients were 83 ± 3 years and 25 ± 7 kg/m². Mean duration of implantation was 48 (35-65) minutes and 46 (22-90) minutes for POF and contralateral hip fracture fixation respectively. Mean cement quantity was 7cc (6-10) for POF. At 3 weeks and 3, 6 and 12 months, comparison between the two legs' plantar pressures revealed no differences. At 3 months, Womac scores for pain and functionality were 9 and 36 respectively, and 2 and 10 at 12 months. OHS score was 41 at 12 months. No osteolysis or implant loosening was observed at the different follow-ups.

CONCLUSION Preliminary results of this prospective study demonstrated the feasibility and safety of the implantation of this new PDOI to prevent contralateral hip fracture. Further data are required to confirm this preliminary experience.

AGEING AT THE 21 CENTURY LIFE AND SOCIAL SCIENCES RESEARCH

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Life expectancy has almost doubled in developed countries since the beginning of the 20th century. More people than ever survive now to their eighties and nineties; the number of centenarians has also been growing. Certainly, prolonged longevity is the successful outcome of research in the life sciences during the 20th Century: better hygiene, vaccines, antibiotics and sophisticated surgery. Undoubtedly this has been a remarkable triumph of Science.

Paradoxically, however, while prolonged longevity is generally applauded, ageing is not. Ageing is regarded as, and many times is, a frail and debilitating condition; which demands huge allocation of resources. This paper explores prolonged longevity, its value, and its discontents; the paper examines the future of ageing from the perspective of research in the life and social sciences; and observes that active ageing may postpone and/or avoid many of the conditions which ageing is plagued with.

BODY FAT OR LEAN MASS – WHICH IS MORE IMPORTANT FOR AN AGEING POPULATION?

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It is well accepted that body fat increases and muscle mass decreases as a part of the normal ageing process. While increased levels of body fat are a concern for health-related diseases (e.g., diabetes, coronary artery disease), losses in lean mass have implications for an individual's ability to function independently – both subsequently impact morbidity and mortality.

The purpose of this investigation was to examine the relationship between body fat (% fat) and lean tissue in adults aged 50 and older. Participants were 31 females (57.3 ± 6.3 yr) and 14 males (60.5 ± 7.6 yr) who reported to the laboratory after refraining from food, water, and exercise for at least 2 hours. During a single visit, % fat and appendicular lean mass (ALM) were assessed via bioelectrical impedance analysis (BIA) (InBody230; Biospace, Seoul, Korea). Body mass index (BMI) was calculated from measured height (stadiometer) and weight (via InBody 230). Based on different operational definitions for sarcopenia, lean mass is reported as 1) ALM alone, 2) ALM adjusted for stature (ht in m²) (ALM/Ht), and 3) ALM adjusted for BMI (ALM/BMI). Our results showed a significant relationship between BMI and % fat ($r=0.686$, $p<0.001$) as well as between % fat and ALM/BMI ($r = -0.854$, $p<0.001$). Of our 45 participants, 23 (15F,

8M) were categorized as overweight according to BMI (≥ 25 kg/m²) and 21 (12F, 9M) when utilizing % fat (sex specific cut-points according to Gallagher et al., 2000; i.e., $\geq 36.5\%$ F, $\geq 24\%$ M). In terms of lean mass, 2 females were identified as having low lean mass when using the criteria associated with ALM or ALM/Ht; neither participant was overweight. In contrast, the ALM/BMI criteria identified 2 females and 1 male with low lean mass; all three were also categorized as overweight or obese by both BMI and % fat. In our population, a much higher proportion of individuals were categorized as having issues with body fat ($\sim 47\%$) than low lean mass (sarcopenia $\sim 7\%$). Our results suggest that the ALM/BMI method suggested by Dam et al. (2014) more accurately identifies those with sarcopenia. In conjunction with this value, % fat can be used to identify those who are sarcopenically obese – a population that is at risk for both long-term health and short-term functional issues.

Poster Presentation Abstracts

THE SUPERIORITY OF GERIATRICIAN DOCTORS TO ESTIMATE AGE OF OLDER ADULTS: A STUDY ON THE EFFECT OF THE PROFESSIONAL EXPOSURE ON THE PERCEPTION OF AGE

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Estimation of a person's age is more accurate if the observer has regular contact with other people of the same age. Although estimation of the age of young people (children or young adults) has been extensively investigated, very few studies have focused on estimation of the age of older adults. The objective of the present study was to test whether expertise (through practice as a geriatrician) is associated with the ability to accurately estimate the age of older people. On the basis of photographs, 18 geriatricians, 12 physicians from other medical specialties and 12 controls from other professions evaluated the age of 66 people in three age groups (young, middle-aged, and older adults). We observed an effect of both medical specialty and gender of the perceivers, since women geriatricians estimated the age of older adults more accurately than the other groups did. The results are interpreted with respect to the literature data on contact-based enhancement and stereotypes of aging. Key-Words: Elderly, Age perception, Geriatrician

PREDICTIVE UTILITY OF BODY COMPOSITION ASSESSMENTS ACROSS AGE GROUPS

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Introduction Body mass index (BMI) is frequently utilized to classify obesity and predict cardiometabolic disease risk. Although BMI is independent of age, its predictive ability across age groups has been questioned.

Objective This pilot study sought to identify age-dependent variations in simple anthropometric indices and body composition (% fat) in sex-, height-, and BMI-matched adults of varying ages.

Methods 'Older' participants were middle-aged and older adults and 'younger' participants were college freshmen. Older (n=28, 7M, 21F; age: 57.3 ± 5.4 years, range: 50-74 years) and younger participants (n=28, 7M, 21F; age: 18.0 ± 0.2 years, range: 18-19 years) were matched for sex, height (± 1 cm), and BMI (± 1 kg/m²). Waist circumference (WC) and height were measured to the nearest 0.1 cm and waist-to-height ratio (WHtR) was subsequently calculated as WC/height. Body composition was assessed by air-displacement plethysmography (ADP via BODPOD).

Results Older (height: 167.4 ± 7.8 cm, BMI: 23.9 ± 3.4 kg/m²) and younger adults (height: 167.2 ± 7.8 , BMI: 23.9 ± 3.2 kg/m²) had similar WC (86.7 ± 11.0 cm vs. 82.2 ± 9.7 cm, $p=0.113$) and WHtR (0.52 ± 0.06 vs 0.49 ± 0.05 , $p=0.108$). However, body fat was higher in older adults ($29.9 \pm 7.9\%$) compared to younger adults ($24.9 \pm 9.5\%$, $p=0.037$).

Discussion Older individuals demonstrate higher body fat percentage than younger individuals despite similar height, BMI, WC, and WHtR. Thus, body composition assessment may be a better indicator of obesity and cardiometabolic disease risk in these individuals.

LONELINESS IN MIDDLE-LATE AND OLD AGE

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Loneliness is an experience often associated with being old, and with increasing age. However, little is known about the empirical basis of this association, or the underlying determinants of feelings of loneliness. The main purposes of the present study were to know how much loneliness is self-reported in the Portuguese population over 50 years of age, and whether loneliness can be predicted by any socio-demographic, health related, or social characteristic of the population. 1174 middle- and old-age adults were interviewed, and loneliness was assessed by asking: *How often do you feel lonely?* The results showed that loneliness was not highly prevalent among the older-adults' Portuguese population, with 12% of the respondents reporting feeling lonely often or always, against 40% reporting never feeling lonely. Additionally, predictors of feelings of loneliness include individual variables such as age, marital status, type of housing, residence settings, health conditions, social satisfaction, social isolation, lack of interest, and transportation.

FAMILIES' EXPECTATIONS ON ICT AND AAL ROLE IN CAREGIVING OF OLD ADULTS

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An important part of care provided to individuals in their old age is guaranteed by their family members. These often called "Informal caregivers" perform a diverse range of tasks in an unpaid and systematic way. However, caring for older and dependent individuals is a challenging and complex task, in which the balance between own needs and others' needs is not easily accomplished. Effects of caring have been found in caregivers, such as poorer health, higher levels of economic, financial, professional or psychological stress, among others (Pinquart & Sorensen, 2003, 2006, 2007). Moreover, with estimates of an increase in the old aged population worldwide, it is expected that these problems will be aggravated as more strain will be put in the governments but also, and especially, in the families. Therefore, it is important to develop solutions that lessen some of the negative effects of caring and turn easier the caregiver role and tasks. Some of these solutions will be necessarily technological, and therefore it is important to know whether the potential users have already considered some of these solutions and what they expect from them. A total of 187 family caregivers completed a survey on their expectations regarding the role of information and communication technologies (ICT) and ambient assisted living (AAL) in assisting them as caregivers (Rashidi & Mihailidis, 2013). Results showed that caregivers considered more relevant and beneficial the technological solutions within the domains of monitoring health indicators and life-care of the care-receivers (e.g., tele-monitoring), and technological solutions that facilitate the independence/autonomy of the care-receiver in the activities of daily living. Beyond having already considered the technologies in those domains, caregivers also showed a median/high expectations about their usefulness in their daily life.

THE DECREASE OF THE "TOOL EFFECT" WITH AGE: EVIDENCE OF AN INSUFFICIENT UPDATING OF THE BODY-SCHEMA IN THE ELDERLY

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Holding a phone or grasping an object are daily activities that involve the activation of complex processes. In particular such activities require an internal representation of action based on accurate spatial representation of each part of the body: The body schema. The body schema is often considered as an unconscious representation involved in both the simulation of action and the actual action. Even if it has certain permanence in a given individual, it is sensed to be updated to a certain extent such as for instance, during the growth phase.

In young adults, previous researches have revealed a modulation of the body schema when using a tool (known as "Tool-effect"). The tool-effect is usually interpreted as the result of an embodiment of the tool reflecting the high plasticity of the body schema. By contrast, its decline or its disappearance can reveal a defect of the body schema updating process. In 2013, Lafargue, Noël & Luyat made the assumption that the overestimation of postural abilities observed in the elderly could be the consequence of a mismatch of the body schema. The goal of our research is to test the possible decline of the flexibility of the body schema in older adults, especially in participants suffering from neurocognitive disorders.

Forty-six young control participants, 10 non-demented older participants and 37 older participants with cognitive impairment took part in the experiment. The task consisted to judge visually the possibility to reach several targets positioned at different locations on a flat surface (on a table) before and after having use a rake. The results showed a strong tool-effect in the young participants group. They overestimate their competence once they no longer use the tool. This result, in accordance with previous research suggests a tool-embodiment in young adults: the body schema has been modified to incorporate the tool. By contrast,

we observed a decrease of the tool effect in the older participants group and even a quasi-complete loss in the participants suffering from neurocognitive disorders. These results showed that the classic “tool effect” observed in young people, decreases with age and even could disappear if the person suffers from neurocognitive disabilities. This is in line with the assumption of an updating process deficit of the body schema with advanced age and could explain over- and under- estimation of motor capabilities often found in researches on the elderly.

Key-Words: Elderly, Tool effect, over-estimation, Body schema

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ASSESSMENT OF VERBAL EPISODIC MEMORY: Standardization OF A NEW memory TEST WITH SELF-INITIATED ITEM (MAI TEST)

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The assessment of episodic memory is a critical aspect of psychometric assessment conducted among the elderly, in particular for the diagnosis of demential pathologies. However, the evaluation of episodic memory in the elderly is not always feasible because most of the existing tests are not entirely suitable. Several factors such as a non-native language, a different culture, a solid visual disturbance, a non-enrollment or fatigability make the assessment of episodic memory very difficult. To overcome these difficulties, our team has developed a rapid assessment of episodic memory, the Auto-Initiated Memory Test (MAI test). The goal of our research is to validate and standardize this test. To achieve the standards, we have included 84 non-demented older participants (74.24 ± 6.9 years). Moreover, we included 171 older participants with cognitive impairment and 33 older participants with a Mild Cognitive Impairment. The results showed that the MAI test has good psychometric properties in phase 2 of the pathology (sensitivity = 75.75%, specificity = 100%). It appears to be an useful screening tool for pre-dementia stages.

Key-Words: Elderly, Episodic Memory, Mild Cognitive Impairment

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NEURAL CORRELATES OF WORKING MEMORY IN ADVANCED AGING: AN FMRI STUDY

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Working memory declines with age. Previous studies have reported that, relative to young adults, older adults demonstrate greater and more widespread working memory related brain activity. The present functional magnetic resonance imaging (fMRI) study investigated whether this pattern of ‘over-recruitment’ continues into advanced age. During fMRI scanning, two groups of older adults (‘young-old’; n=13; 61-70 years and ‘old-old’; n=13; 77-82 years) performed an n-back task, a working memory paradigm that manipulates number of items to be stored in memory. Participants were shown with a face or a dot on a screen. In the 0-back task, participants were asked to judge whether the face is female or male for face condition, or whether the dot is located in the center of the screen for location condition. In the 1-back task, participants were asked to judge whether the current stimulus is the same as the one presented one trial back. Working memory related brain activity (1-back > 0-back) common to two groups were identified in several regions, including the right dorsolateral prefrontal (DLPFC), lateral temporal cortex, the bilateral medial frontal, inferior parietal cortex, and insula. Compared with young-old group, old-old group showed greater activity in the bilateral DLPFC, middle cingulate, and the left medial frontal cortex. Moreover, the magnitude of activity in the left DLPFC positively correlated with working memory performance only in old-old group. There were no regions where working memory related brain activity was greater in young-old group. These findings suggest that age-related over-recruitment continues into advanced age, and that increased activity in the left DLPFC may serve a compensatory role in mediating working memory performance in old-old adults.