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Research Interest Areas: Aging and Gait

Research Support Sources: National Institutes on Aging and American Federation of Aging Research Paul Beeson Career Development Award

Research Title: Challenging the motor control of gait: gait variability during slower and faster pace walking conditions in younger and older adults

Project Authors: Maha Almarwani, MS, PT, Jessie M. VanSwearingen, PhD, PT, FAPTA, Subashan Perera, PhD, Patrick J. Sparto, PhD, PT, Jennifer S. Brach, PhD, PT

Abstract:  
Study. Gait variability is a measure of motor control of gait. Little is known about age-related changes in the motor control of gait (gait variability) during challenging walking conditions, such as slower and faster pace walking. The purpose of this study was to examine the impact of challenging walking conditions (slower and faster speeds) on gait variability in younger and older adults.

Methods. Forty younger (mean age = 26.6 ± 6.0 years) and 111 community-dwelling older adults (mean age = 77.3 ± 6.0 years), independent in ambulation, were studied. Gait characteristics were collected using a computerized walkway (GaitMat II™). Step length, step width, step time, swing time, stance time and double support time variability were derived as the standard deviation of all steps across the 4 passes.

Results. Compared to younger, older adults had a significant change in their gait variability from usual to slower in step width (-0.006 ± 0.003), step time (0.028 ± 0.006), swing time (0.023 ± 0.004), stance time (0.042 ± 0.008), and double support time (0.024 ± 0.005). Changes in gait variability from usual to faster were not significantly different between younger and older adults.

Conclusions. Walking slowly places a greater demand on the motor control of gait and may be more sensitive to age-related declines in gait than usual and faster speed walks.

Significance. The assessment of gait variability during challenging walking conditions such as walking slower may uncover motor control deficits among older adults that are not identified during usual walking testing. Many gait interventions focus on increasing gait speed alone. Clinicians may want to consider interventions that not only focus on gait speed but also on the motor control of gait.
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**Research Interest Areas:** Parkinson's Disease

**Research Support Sources:** NINDS T32 NS086749 Training Grant, “Training in the Neurobiology of Neurological Disease”

**Research Title:** Forging a Link Between Aging and Parkinson's Disease: The Lon Protease Degrades Dopamine-Modified GPx4

**Project Authors:** Barrett, CW., Mortimer, AD., Chu, CT., and Hastings, TG.

**Abstract:**
Parkinson’s disease (PD) is the second most common neurodegenerative disease and the leading neurodegenerative movement disorder. Increasing evidence suggests that aging greatly influences the progression of PD: advanced age is associated with increased motor progression rate, more severe postural and cognitive impairment, and the development of dementia. This suggests that the molecular determinants of PD are impacted by pathways that undergo normal decline during aging and that modification of such pathways may decrease PD severity and/or progression. The phospholipid hydroperoxide glutathione peroxidase (GPx4) is the only GPx capable of reducing phospholipid hydroperoxides in the membrane. GPx4 knockout in adult mice results in neurodegeneration driven by lipid peroxidation. We have seen that, in PD models and human PD, GPx4 levels are reduced in the affected dopaminergic neurons of the substantia nigra. In vitro treatment of isolated mitochondria with dopamine quinone (DAQ) indicates that this reduction in protein may be due to DAQ modification of the selenocysteine in GPx4 and subsequent targeting for proteolytic breakdown. Co-IP studies indicate that GPx4 interacts with the lon protease (LonP1). LonP1 specifically degrades oxidatively modified proteins and its activity is decreased with age. Treatment of testes lysate exposed to DAQ with the LonP1 inhibitor CDDO results in increased monomeric and high molecular weight aggregates of GPx4. These data suggest that LonP1 interacts with damaged GPx4, clearing it under conditions of oxidative stress. Importantly, as LonP1 declines with age, in the setting of PD, damaged GPx4 and other oxidized proteins may not be as efficiently cleared, causing build-up of potentially toxic proteins and mitochondrial dysfunction.
Abstract:
Aging is associated with increased susceptibility to Idiopathic pulmonary fibrosis (IPF). Alveolar type II cells (AECII) in IPF lung have marked accumulation of dysmorphic and dysfunctional mitochondria, associated with low expression of the PTEN-induced putative kinase 1 (PINK1). These mitochondrial abnormalities can be recapitulated in mice combining advancing age and ER (endoplasmic reticulum) stress stimulation and in PINK1 deficient mice. However, the molecular mechanism linking ER stress and PINK1 expression are still unknown.

PINK1 transcription is significantly reduced in A549 cells exposed to increased doses of tunicamycin (TM), a well-known ER stressor. This reduction is reversed in the presence of actinomycin D suggesting transcriptional repression of PINK1 by ER stress. In sharp contrast, TM induces expression of genes involved in the unfolded protein response (UPR) including the activating transcription factor 3 (ATF3), a member of the ATF/CREB family that can act as a transcriptional repressor. Analyses of the human PINK1 promoter reveals the presence of two ATF3 consensus sites upstream of the transcriptional starting site of the PINK1 gene. Depletion of ATF3 in cells showed reduced ATF3 expression and increased PINK1 transcript levels at baseline and after TM treatment. Immunohistochemistry studies found that ATF3 is highly expressed in aging human lungs and AECII lining honeycomb areas of IPF lungs.

These data are the first to link ATF3 to PINK1 expression in any system and suggest that ER stress, via ATF3, can regulate mitochondrial homeostasis by repression of PINK1 gene transcription. Also, strategies designed to modulate PINK1 or ATF3 expression might lessen severity of pulmonary fibrosis, especially in the context of the aging lung.
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**Current Position:** Professor

**Research Interest Areas:** Neuroplasticity

**Research Support Sources:** Aging Institute

**Research Title:** Effect of Intermittent Physical Activity on Working Memory in Older Adults: The Healthy Brain Aging Workgroup Pilot Study

**Project Authors:** Kirk Erickson, John M. Jakicic, Howard Aizenstein, Caterina Rosano, Meryl Butters, Abbe de Vallejo, Charles F. Reynolds, Judy L. Cameron

**Abstract:**
BACKGROUND: Working memory is susceptible to age-related impairment, and participation in a traditional regular exercise regimen (increasing heart rate for at least half hour periods several times a week) has been shown to improve working memory in older subjects. This project was undertaken to determine whether an exercise regimen that involves multiple shorter periods of moderate intensity activity (3 10-minute sessions per day) for a 6-month period may improve working memory compared to light-intensity activity.

METHODS: Older adults (N=30) were recruited to participate in a 24-week intervention with randomization to one of two intervention conditions: 1) intermittent moderate-intensity physical activity (INT-PA), 2) contact control that includes intermittent light-intensity physical activity (CONTROL). Eligibility criteria for this pilot study included 65 to 74 years of age (N=20) or 75 to 85 years of age (N=10) with less than 12 years of education, and participation in <60 minutes per week of structured physical activity. Working memory function was tested using an n-back task with two conditions (1-back and 2-back).

RESULTS: To date 11 subjects have completed testing (9 females, 2 males, mean age: 69.68 years, mean education: 16.7 years), and there is a large range of individual differences in the change between 1-back and 2-back over the 6-month study both in terms of accuracy and speed of performance. In the 11 subjects reaction time on the 1-back showed a 15% improvement, and a 9% improvement on the 2-back at 6 months compared to baseline.

SIGNIFICANCE: At the time of the presentation we will be able to determine if those engaged in moderate-intensity physical activity will show improved working memory compared to light-intensity physical activity group.
Study: Pharmacists are embedded in our geriatric healthcare team providing continuous medication management across all levels of care. The objective of this study, part of the Pharmacists-led InterVentions on Transitions of Seniors (PIVOTS) group, is to quantify the impact of pharmacists on the care of older adults by describing 1) most common drug therapy problems (DTPs) identified by pharmacists, 2) medications most frequently involved in DTPs, and 3) actions taken to resolve DTPs, while comparing and contrasting these findings across the care continuum.

Methods: This prospective chart review analyzed data from 1,275 patient-pharmacist encounters in a geriatric care practice from August 2014 to February 2015. Pharmacists utilized The Assurance System™ to document each DTP, medications involved, patient’s current care setting (e.g., home, personal care, skilled nursing), and actions taken to resolve the DTP. At the end of the 6 months, reports were generated for analysis.

Results: Over the 6-month timeframe, 1,275 encounters were identified for 236 patients—53% resided at home. Mean age was 82 years, 72% were female. A mean of 1.53 DTPs were identified by a pharmacist per encounter. The most common DTP was ‘dose too low,’ followed by ‘dose too high’ and ‘needs additional therapy.’ The medication most frequently associated with DTPs was warfarin, followed by enoxaparin and insulin. Pharmacists made 3,325 interventions on 189 different medications, with ‘lab monitoring initiation’ and ‘dose change’ as the most common interventions. Home-dwelling patients had a greater prevalence of compliance-related DTPs.

Conclusion/Significance: With a growing emphasis on healthcare quality, pharmacists can be valuable members of the geriatric care team as they address unresolved DTPs.
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**Medical School:**  
**PhD:**  

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**Research Interest Areas:** Parkinson's Disease and Aging  

**Research Support Sources:** NS070825, AG024827, AG039477, AG034464, and the Aging Institute of University of Pittsburgh and University of Pittsburgh Medical Center  

**Research Title:** An enriched environment modulates factors associated with healthy brain aging in rats  

**Project Authors:** Sandra L. Castro, Juliann D. Jaumotte, Donna L. Korol, Lori A. Newman, Laurie H. Sanders, Richard J. Smeyne, and Michael J. Zigmond  

**Abstract:**  
The sedentary and environmentally impoverished lifestyle that characterizes many older individuals within modern society may play a critical role in the motor, cognitive, and emotional decline that often occurs during advanced years. Clinical and animal studies suggest that an enriched environment (EE) can increase socialization, mobility, and promote changes in the brain that appear to facilitate healthier aging. F344/BN male rats 18 month old at the outset of our studies were housed individually in a standard shoebox cage (SE) or in groups of 6 in an EE (1 m³) containing running wheels, tunnels, platforms, and toys. Although the physical activity would not be considered aerobic exercise, we observed a considerable amount of daily exploration, climbing, playing, and social interactions. Body weight increased significantly in the EE rats, but not in the SE rats. After 4 months, rats were euthanized and peripheral tissues, blood samples, as well as numerous brain regions were collected. We found that EE rats had a 3.8-fold increase in BDNF in the hippocampus and a 60% increase in the ratio of dopamine (DA) metabolites to DA in the striatum, consistent with an increase in striatal DA turnover. In addition, significant changes in mRNA expression were measured in Azin1, Tssc4, Ddit4, Nfkb1a, Pdk4, and Sgk1 (upregulated) and Cxcl13 and slc47a1 (downregulated) in substantia nigra tissue. Our results suggest that housing in an EE produces significant changes consistent with increased neuroplasticity even in the absence of increased aerobic activity, emphasizing the likely importance of other behavioral components of environmental enrichment. We hypothesize that these changes are associated with an increase in brain health and improved behavioral capacity during aging.
Abstract:
Aging populations exhibit increased pain prevalence and sensitivity. The central nervous system mechanisms responsible for these age-related sensory changes however are relatively unknown. In these studies, we assessed pain-like behaviors and supraspinal pain signaling in young, middle, and old male mice prior to and following peripheral injury. Prior to injury, there is an age-related decrease in metabotropic glutamate receptor 5 (mGluR5) expression in the central nucleus of the amygdala (CeA). Previous studies in this limbic brain region have linked decreased expression of mGluR5 signaling to decreased sensitivity during inflammatory pain in young animals. Here, we extend that finding by demonstrating age-dependent increases in mechanical hypersensitivity following intraplantar formalin injection. Explaining this apparent paradox, mGluR5 expression in all age groups increases to the same level following peripheral injury, despite the age-dependent differences that existed in naïve mice. Thus it appears that the dynamic range of mGluR5 may be heightened with age leading to increased pain-like behavior. We also assessed formalin-induced activation of extracellular signal-regulated kinases 1 and 2 (ERK1/2), two proteins downstream of mGluR5 involved in CeA pain modulation. Following injury, there are age-dependent increases in ERK1 phosphorylation that echo formalin-induced changes in mGluR5 expression. Taken together, these data establish the CeA as a brain region that is critical for age-dependent changes in pain sensitivity, and more specifically highlight mGluR5 as a therapeutic target for peripheral pain conditions.
Abstract:
Background: Urgency urinary incontinence (UUI) is a major problem in older adults. Bladder-centric explanations alone are inadequate; deficiency in cerebral control is increasingly identified as a cause. Functional MRI of repeated infusion and withdrawal of fluid within the bladder is a reliable method of stimulating urgency and assessing the brain’s role in continence, however, test-retest repeatability of the brain’s response to this has not yet been evaluated.

Methods: Women had fMRI with concurrent bladder filling. Into a full bladder, 22ml of fluid was infused over 12 seconds, then 20ml was withdrawn over 12s, repeated four times in a ‘block’. Two consecutive ‘blocks’ were used. The fMRI ‘contrast’ is the difference in brain activity between infusion and withdrawal of fluid. Areas of the brain assessed included the dACC/SMA – motor control, the mPFC – executive control, and the right insula - visceral sensation. Intraclass correlation of mean brain activity in each region of interest was calculated between the two ‘blocks’.

Results: 59 women >60, mean(SD) age 70(7.5), reporting >5 UUI episodes/week were eligible. In t-tests, there was no significant difference of activity in any of the 3 regions between measurement blocks. Intraclass correlation was 0.19 for the right insula, 0.32 for the dACC/SMA and 0.44 for the mPFC.

Conclusions: No difference between blocks suggests no habituation to stimulus. Measurement block agreement is poor to fair, suggesting need for greater stimulation and highlighting inherent difficulty in measuring such physiological signals. The protocol requires improvement, but this gives a framework to compare new protocols. While this protocol is valuable in assessing brain-bladder control in group analysis, it cannot be applied to individuals.
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**Current Position:** Research Instructor

**Research Interest Areas:** Incontinence

**Research Support Sources:** NIH

**Research Title:** White and gray matter damage are related to urge incontinence

**Project Authors:** Becky D Clarkson, PhD, Stasa D Tadic, MD, Neil M Resnick, MD, Derek J Griffiths, PhD

**Abstract:**  
**Study:** The cause of urgency urinary incontinence (UUI) is increasingly thought to be central in origin. The aim of this study was to locate structural brain abnormalities in white and gray matter related to UUI, by comparing diffusion tensor imaging (DTI) and voxel-based morphometry (VBM) from MRI scans of older incontinent women with those from continent controls.

**Method:** We recruited 62 women with urge-predominant incontinence (=5x/week), aged ≥60 with detrusor overactivity (DO) on urodynamics. 11 continent controls were recruited with no DO/UUI. From structural MRI we assessed: White matter hyperintensities - global white-matter damage; DTI with tract-based spatial statistics (TBSS) - local white-matter integrity; and VBM - local gray-matter atrophy.

**Results:**  
- Global white-matter damage was greater in UUI than controls (p = 0.02).
- TBSS showed white-matter integrity was poorer in UUI than controls in the fornix (p < 0.05 uncorrected cluster level). There was significant loss of integrity in the body and crura of the fornix (connects the hippocampus to the hypothalamus)
- VBM showed that local gray-matter volume in the parahippocampal complex was smaller in UUI than in controls, confirming hippocampal atrophy.

**Conclusion:** In older women with UUI, there are subcortical abnormalities that may cause or contribute to incontinence: they include atrophy of the hippocampus and loss of white-matter integrity specifically in the fornix – a sub-cortical tract connecting hippocampus with hypothalamus.

**Significance:** Finding causes and contributors to a costly and morbid condition which affects a significant proportion of the aging population is imperative to targeting and improving treatments (e.g. exercise to increase hippocampal size) and relieving burden on sufferers.
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**Research Interest Areas:** Productive Aging

**Research Support Sources:** UPMC Rehabilitation Institute

**Research Title:** The Prevalence of Frailty in Patients Receiving Occupational Therapy Services in Skilled Nursing Facilities

**Project Authors:** Pamela Toto, PhD, OTR/L, BCG, FAOTA

**Abstract:**
Study: It is a common misconception that frailty is a natural consequence of aging and that all older adults in skilled nursing facilities (SNF) are frail. Frailty is a complex compilation of age and disease-related factors that lead to poor health outcomes in older adults. The old-old and females are frequently considered the highest risk populations for experiencing frailty. The aim of this study was to determine the prevalence of frailty in SNFs using the Survey of Health, Ageing, and Retirement in Europe Frailty Instrument (SHARE-FI).

Method: This cross-sectional prevalence study was conducted in an urban SNF from April 2014 to June 2015. Participants (N=170) were short-term patients admitted to the SNF for skilled rehabilitation. The SHARE-FI is a quick, valid, and reliable assessment for determining frailty in older adults. The SHARE-FI includes 5 measures related to frailty conditions: weakness (assessed through grip strength using a dynamometer), exhaustion, weight loss, slowness, and physical activity (evaluated through self-report). Occupational therapists administered the SHARE-FI to patients as part of their initial evaluation. Each measure was scored as “0” with the condition’s absence or “1” with the condition’s presence. The total score ranged from 0 to 5. Scores of 3 or greater were coded as “frail” while scores under 3 were “not frail”. We examined frequency of frailty in the total sample, the relationship between age and frailty using the point biserial correlation, and the association between gender and frailty using the phi coefficient.

Results The average age of patients = 77 years (range 45-96 years), with 72.9% (N=124) considered frail (score of 3 or higher) using the SHARE-FI. There was no correlation between age and frailty (rpb=.043, p=.576) a
Abstract:
In the USA, when retirement approaches many try to decide where to stay after retirement. Among the various options available, the majority prefer to remain in their own place of residence. No matter where they decide to live one of the major concerns they have is how to get Long Term Care (LTC) when they need it and pay for such services in a cost effective manner. LTC is a complex type of care that involves providing assistance to individuals who cannot effectively undertake basic activities of daily living (ADLs) such as eating, bathing, dressing, toileting, transferring from one place to another (walking), and continence. Since employee health insurance and medicare do not cover the costs of LTC various other mechanisms including Long Term Care Insurance (LTCI) have been used to pay for LTC. In recent years private insurance carriers providing either individual or group coverage for LTC have either withdrawn from the market or they have increased their premiums in a dramatic manner thus making it difficult or the subscribers to depend on them to provide the needed LTC. Are there any alternatives to cover the cost of LTC and get better and reliable service? This presentation addresses these issues and presents Continuing Care at Home programs as one effective way of securing LTC when one needs it in a cost effective manner.
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Research Interest Areas: medication adherence

Research Support Sources: None

Research Title: Assessing Psychometric Properties of the "Medication Deficiency Checklist"

Project Authors: Judith A. Erlen; Jennifer Lingler; Lisa Tamres; Susan Sereika, Robert Kaufman; Martin Houze; Fengyan Tang

Abstract:
The "Medication Deficiency Checklist" (MDC), an investigator-developed tool, was designed to detect issues caregivers of patients with memory loss associate with medication management in the home setting. The MDC allows the identification of the total number of deficiencies and specific issues like patient refusal.

The purpose of this study was to examine the reliability and validity of the MDC. The sample included 91 dyads of caregivers and patients with memory loss living in the community. The caregivers were 70% women (n=64) and 85% white (n=77). Their average age was 67 years; they had completed an average of 15 years of education. The patients were 60% women (n= 54) and 85% white (n=77). Their average age was 80 years; they had completed an average of 13 years of education. The average MMSE score of the patients was 17 (SD=7.9). On average patients were taking 10 medications and had nearly 9 co-morbidities. To be enrolled in the study the patients had to need help with medications and there had to be at least one identified error with medication management.

Assessment of reliability demonstrated a Cronbach's alpha of .38 and test-retest at 8 weeks r=.661, p=.000 (n= 49 control subjects). Concurrent validity was assessed using the 4-item Morisky self-reported adherence measure; findings showed a correlation of r=-.296, p=.007. Convergent validity was assessed by examining relationships between the MDC and depressive symptoms, social support, self-efficacy, and MMSE scores. There were no significant relationships demonstrated with either depressive symptoms, social support, or self-efficacy; however, there was a trend in the association between MDC total and average MMSE scores (r=.204, p=.068). An exploratory factor analysis revealed three factors that explain
Abstract:
Senior citizens move to reside in senior communities to maintain or increase their social engagement, receive care by qualified staff and enhance their quality of life. The majority of residents have significant hearing loss which leaves them with complex listening needs due to low incidence of hearing aid use, group communication situations that are common for social activities, interactive dining environments, and the need for telephone use to connect with loved ones. These challenges are often overlooked or misunderstood by busy staff and family members who may not be sensitive to the impact of decreased hearing on quality of life and caregiver burden. With hearing loss being associated with increased depression, increased falls and cognitive decline, residents with untreated hearing loss may be more prone to health status decline.

HearCARE is a quality improvement project developed by the Audiology department at UPMC (University of Pittsburgh Medical Center) that aims to evaluate the efficacy of a new model of delivering audiology services and communication assistance to residents at assisted living facilities, employing Communication Facilitators who are trained and supervised by an audiologist. The project proposes that delivering hearing healthcare and implementing communication solutions tailored to the resident and the environment will enhance communication abilities of residents, which in turn increases their social engagement, improves their quality of life, and reduces burden on staff and family members. We have collected data on three similar assisted living facilities: one with a daily Communication Facilitator, one with a monthly Consultative Audiologist visit, and one as a control (no change to current procedures). Baseline measures and 6-months post-
Abstract:
Study/Methods: The CDC estimates that 70% of nursing home (NH) residents receive antibiotics per year, most of which are inappropriate or unnecessary. Antimicrobial stewardship (AMS) programs aim to optimize patient outcomes by balancing antimicrobial benefits and safety. Clinical surveillance systems (CSS) are tools that can be used to support AMS efforts. The objective of this project was to evaluate baseline rates and performance of antimicrobial-related alerts in a UPMC-licensed CSS, and identify barriers to CSS use and to implementation of a NH-focused AMS program. Seven months of retrospective alert data from four UPMC NHs were collected. Alert performance within CSS categories was analyzed based on alert design using microbiology and medication data available in CSS. Questionnaires focusing on AMS and CSS were provided to NH practitioners, including an attending physician, infection control preventionist (ICP), and consultant pharmacist.

Results: 18,147 alerts fired in 7 CSS antimicrobial alert categories; the Therapeutic Antibiotic Monitoring (TAM) category was further analyzed. A sample of 648 of 4,049 TAM alerts was analyzed; 8 of 11 alert types relating to microbiology and antimicrobial therapy mismatches or redundant therapies were potentially actionable. Barriers to NH-focused AMS were identified from surveys. Despite barriers, all 3 practitioners were optimistic about the future of NH-focused AMS teams.

Conclusions/Significance: The CDC has identified NH-focused AMS as a need. After analysis for accuracy and completeness, CSS antimicrobial alerts may be a useful centralized tool for members of a NH-focused AMS team. Antimicrobial start/stop date inaccuracies and inappropriate dosage form inclusion in alerts are barriers to immediate CSS implementation.
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Research Interest Areas: Nursing  

Research Support Sources: URMP  

Research Title: The relationship between diabetes duration and glycemic control among patients with multiple chronic diseases.  

Project Authors: Taylor R. Giambrone, Jeffrey M. Rohay, Ph. D, Jacqueline Dunbar-Jacob, Ph. D, RN, F.A.A.N  

Abstract:  
Study: Attaining healthy glycemic control is a difficult task for many diabetes patients. A factor to consider in diabetes management is the relationship between age, disease duration, and glycemic control. We hypothesized glycemic control would worsen with increased age and disease duration.  

Methods: A secondary analysis of baseline data from a randomized controlled clinical trial of patients with chronic diseases was conducted (NIDDK RO1 DK59048). Participants were treated for Type II diabetes and hypertension using oral medications. The effect of age and duration of diabetes on glycemic control was analyzed using logistic regression models. Poor glycemic control was defined as an HbA1c level = 6.5%.  

Results: The sample consisted of 319 participants and was predominantly female (56%). The average age was 64 (± 10.4) and the average duration of diabetes was 9.5 (± 7.6). Average HbA1c levels were 7.4% (± 1.3 %) with 76% (n=242) exhibiting poor glycemic control. The analysis found that increased duration of diabetes was significantly related to sustained poor glycemic control (OR=1.34 per 5 year increments; 95% CI=[1.09, 1.65]; p= 0.006). Age did not significantly predict poor glycemic control nor did it moderate the effect of diabetes duration (p ~ 0.11 for the interaction between age and duration).  

Conclusions: Results indicate that longer duration of diabetes is associated with higher rates of sustained poor glycemic control. Patients could benefit from continual education about their diabetes and targeted interventions to improve glycemic control.  

Significance: These data suggest that duration of diabetes not age is associated with poorer control. Interventions to improve glycemic control should focus on addressing changing needs as duration of diabetes increase
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**Research Interest Areas:** Integration of multidisciplinary mental health care in Primary Care

**Research Support Sources:** None

**Research Title:** Effectiveness of Multimodal Strategies to Improve Uptake of a Late Life Collaborative Depression Care Protocol in Primary Care

**Project Authors:** Aparna Gupta, CRNP, MSN, PGDBA, Adrian Visoiu, MD, Nancy Jones, MSOL, BSN, Carol Leach, LCSW, Ellen M Whyte, MD

**Abstract:**

Introduction. Collaborative care models are a means to provide adequate screening, identification and treatment for late-life depression. At UPMC Benedum Geriatric Center (BGC), a Level 3 National Center for Quality Assurance accredited Patient Centered Medical Home, we developed a Depression Care Protocol based on the PROSPECT trials that utilize the internal medicine nurse practitioner as the depression care manager. The protocol was initiated on 04/01/2014. We previously reported on barriers to effective utilization of the protocol. We report here our experience in addressing the barriers and the impact on protocol uptake.

Methods. Barriers to protocol utilization were identified via a survey. Interventions to promote protocol utilization were developed and were implemented in a stepped manner. This was initiated on 04/01/2015. The impact was explored by examining pre- and post-intervention rates of (1) patients who screened positive for depression (2) patients referred to the protocol. Pre and post intervention survey responses from providers will be compared, thereby providing insights into the effectiveness of the interventions.

Results. During the first 10 months after implementation, there was a positive change in the percentage of patients that were identified as suffering with depression through systematic screening. The total number of referrals increased from 14 pre-intervention to 43 post-intervention.

Conclusions. At UPMC Benedum Geriatric Center, we have found that interventions targeting both Provider Level and Patient Level barriers to protocol utilization have resulted in increased uptake of this protocol. Next steps in the assessment of this program will include examining outcome measures for patients who have completed the protocol.
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**Research Interest Areas**: Spine  

**Research Support Sources**: Rehabilitation Institute, PM&R  

**Research Title**: The Bioenergetics of Intervertebral Disc Aging  

**Project Authors**: Robert Hartman1, Robert Tisherman1, Shouei Cho1, Qing Dong1, Kevin Ngo1, Prashanti Patil1, Yingchao Han1, Adam Olsen1, Gwendolyn Sowa1, Bennett Van H  

**Abstract**:
INTRODUCTION: Intervertebral disc degeneration is an inflammatory, cell-mediated process marked by a degenerative shift in cellular activity and fate. Aging may subject cells to greater nutritional stress with concomitant elevation of inflammation. It is unknown how energy metabolism changes with aging and inflammatory stimulation. This study examined the bioenergetics of young and old disc cells subjected to IL-1β stimulation to test the hypothesis that aging and inflammation compromise cellular energetic capacity.

METHODS: Annulus fibrosus (AF) and nucleus pulposus (NP) cells were isolated from discs of young (6-9mo) and old (36-48mo) New Zealand White rabbits (n=7 per group). Cells were cultured at 5% O2 and treated ±IL-1β (1 ng/mL) for 24h. Bioenergetics profiles were measured by a Seahorse XFe 96 extracellular flux analyzer (Seahorse Bioscience). Oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) were measured to characterize mitochondrial ATP production, proton leak, reserve capacity, maximum aerobic capacity, non-glucose-dependent respiration, and glycolytic capacity.

RESULTS: Aging significantly reduced mitochondrial reserve capacity, maximum aerobic capacity, and non-glucose dependent OCR in NP cells (p<0.159) (Figure 1). IL-1β reduced basal OCR and maximum aerobic capacity in both cell types (p=.007-0.025). Interestingly, young AF cells responded to IL-1β stimulation with an increased capacity to utilize non-glucose carbon sources, but old AF cells showed a decreased capacity to do so (p=.016).

DISCUSSION: NP cell energy metabolism is susceptible to age-related decline while AF cells do not appear to be so. Both cell types reduce their basal respiration and lose a modest amount of their maximum aerobic capacity with inflammatory
Abstract:
A review of care at the Skilled Nursing Facilities showed that 1 out of 3 residents on Sliding Scale Insulin (SSI) suffered a hypoglycemic event in a month. The Office of the Inspector General notes that 59 % of adverse events and temporary harm was preventable and the most common cause was associated with hypoglycemia. It is also associated with an unnecessary financial burden and resident discomfort.

The plan was to reduce/eliminate unnecessary SSI insulin, reduce the frequency of finger sticks and convert insulin to Regular from Ultra Fast. CRNPs developed strategies for this change, Staff Development Personnel reviewed Protocol for staff, frequent review and monitoring occurred wit RX Partners and the PSI CRNP’s.

Results showed at 15 weeks a 35% reduction in residents on sliding scale insulin, 34% reduction in finger sticks, at 17 weeks a 10% increase in Regular Insulin Conversion, resulting in a $33,979 total savings.

Conclusion is that conversion of insulin in nursing homes can help decrease unnecessary glucose monitoring and SSI can be reduced or eliminated. Significance is that this sheds more light on a concerning and adverse health concern for elderly populations in the Nursing Homes.
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**Research Interest Areas:** Risk Factors for Cognitive Impairment

**Research Support Sources:** 2 R02 AG023651-11A1

**Research Title:** Predictors of Change in Cognitive Activity among Community-Dwelling Older Adults: The MYHAT Study

**Project Authors:** Tiffany F. Hughes, Zhaowen Sun, Ching-Wen Lee, Chung-Chou H. Chang, Mary Ganguli

**Abstract:**  
This study examined patterns of change in the frequency of engagement in cognitive activity over 3 years, and identified predictors of these patterns of change, in a population-based cohort.

**METHODS:** We included 1,321 participants from the Monongahela-Youghiogheny Healthy Aging Team study who completed the Florida Cognitive Activities Scale annually as a measure of engagement in cognitive activity. Latent class trajectory analyses identified patterns of change in 3 subscales: overall cognitive activity (CA), higher cognition (HC), and frequent activities (FA). Multinomial logistic regression models examined associations of these patterns of change with demographic, health, lifestyle, and cognitive performance.

**RESULTS:** Analyses revealed 4 trajectories for CA and FA: stable (reference), increase, slow decline and accelerated decline. A relatively lower, but stable, pattern replaced the slow decline group for HC. Compared to the stable group, those with better cognitive performance were less likely, and those with poorer health and negative lifestyle factors were more likely, to show declining activity over time for all cognitive activity scales. Being female, White, having a higher education, and current employment were associated with relatively higher stable, compared to lower stable, activity for the HC subscale only.

**CONCLUSIONS:** These findings demonstrate that most community-dwelling older adults maintain engagement in activities, and that poorer cognition, health, health behaviors, and demographic characteristics are likely to predict declining or relatively lower activity levels.

**SIGNIFICANCE:** This knowledge can help target individuals most likely to benefit from cognitive activity interventions.
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**Research Interest Areas:** Technology for Self-Management

**Research Support Sources:** AI/HPI

**Research Title:** Social-Behavioral Determinants and Engagement of Older Adults in Their Health Care

**Project Authors:** Taya Irizarr, Marci Nilsen, Jocelyn Shoemake, Scott Beach, Annette Devito Dabbs

**Abstract:**
Study: Patient engagement (PE), involvement of individuals in their health care, is a central driver of health quality and cost. However, only 30% of older adults report the motivation and skills to engage fully in their care. Evidence also points to the role of social-behavioral determinants (SBD) in health and disease progression, yet how these determinants impact engagement of older adults in their health care is unknown. Understanding these gaps is critical for designing strategies to promote PE of older adults. The aim of this study was to examine the relationships between SBD and levels of PE.

Methods: A descriptive, correlational design was used in a sample of 100 community dwelling older participants (aged 65-97) of the UCSUR Research Registry who agreed to complete a telephone survey. Data were collected to examine the relationships between SBD (e.g., socio-demographics, health characteristics, health literacy) and PE (Patient Activation Measure-13). Potential predictors of higher PE were identified using a bivariate threshold of p < 0.2. Cumulative odds ordinal logistic regression was used to identify significant predictors of higher PE (p< 0.05).

Results: Education (OR 3.6; p =0.019; CI: 1.2-10.7) and health literacy (OR 3.6; p = 0.014; CI: 1.29-10.07) were significant multivariate predictors of PE. Conclusions: While many of the SBD of health were significant predictors of PE at the bivariate level, the odds of lower PE was over three times higher for persons with lower health literacy and for persons with lower education.

Significance: Levels of health literacy and education play a significant role in PE among older adults. However, the relationships and interactions among SBD, health literacy and PE are complex and warrant further investigation.
Abstract:
BACKGROUND: Physical activity is an important health behavior in older adults. This pilot study compared engagement of older adults in prescribed multiple daily intermittent sessions of moderate-intensity vs. light-intensity physical activity.

METHODS: Sedentary, older adults (N=19) 65-85 years of age were recruited to participate in a 24-week intervention with randomization to 1) intermittent moderate-intensity physical activity (INT-PA, N=9) or 2) contact control that includes intermittent light-intensity stretching (CONTROL, N=10). Both INT-PA and CONTROL were prescribed multiple 10-minute sessions per day that progressed to a total of 150 min/wk. Both INT-PA and CONTROL were provided an electronic tablet with custom videos that could be used to facilitate the prescribed home-based physical activity. Both INT-PA and CONTROL had regular contact with intervention staff. Physical activity was measured using weekly diaries and a questionnaire that was administered at 0, 12, and 24 weeks.

RESULTS: To date 13 subjects (age: 69.5±3.0 years) have reached the end of 24 weeks. Moderate-intensity physical activity was reported on 0.3±0.5, 4.1±2.7, and 4.4±2.1 days/wk at 0, 12, and 24 weeks for INT-PA compared to 0.7±1.2, 0.8±1.2, and 1.7±1.2 days/wk for CONTROL. INT-PA reported using the electronic tablet for 68.2±19.4% of their non-supervised sessions compared to 86.7±14.4% in CONTROL.

SIGNIFICANCE: Prescribing physical activity in multiple daily intermittent sessions may be effective for engaging older adults in moderate-intensity physical activity, and use of videos provided on an electronic tablet appears to assist with engagement. These alternative intervention strategies for engaging older adults in physical activity warrant further investigation.
Abstract:
Study: B and T cell production in humans is decreased in elderly individuals, resulting in a diminished immune system and reduced response to exposures of viral or bacterial agents. We examined the response in aged rats that were housed in an enriched environment (EE) after exposure to lipopolysaccharide (LPS), an endotoxin produced by bacteria.

Methods: We examined a dose response curve for LPS on individually housed 28 month old male Fisher344/Brown Norway (F344/BN) hybrid rats to determine the highest tolerable dose of a single IP injection of LPS. We then used that dose on a second set of F344/BN rats that were 19 months old at onset of the experiment and were housed in an EE that included toys, running wheels, and tunnels for 8 months and on control animals that were singly housed for the same time period. Seven days after the injection the animals were sacrificed and various regions of the brains as well as blood, liver, and spleen samples were collected. Biochemical analyses were used to assess trophic factors and dopamine and its metabolites, as well as cytokines and chemokines.

Results: Several cytokines and chemokines were significantly increased in the serum isolated from the EE including G-CSF, IL-1α, IL-4, IL-10, IL-1b, IL-6, IP-10, INFγ. Fewer changes were found in the hippocampus or striatum.

Conclusion: Animals housed in the EE had a more reactive immune response which could indicate a greater ability to fight off infections.
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**Research Interest Areas:** Osteoporosis

**Research Support Sources:** Tobago Bone Loss Grant, PI Joseph M. Zmuda

**Research Title:** Correlates of change in cortical bone strength and geometry with aging in African Ancestry men

**Project Authors:** Pallavi Jonnalagadda, Ryan Cvejkus, Clareann Bunker, Yahtyng Sheu, Alan Patrick, Victor Wheeler and Joseph Zmuda.

**Abstract:**
Little is known about skeletal aging in men of African ancestry. To address this knowledge gap, we examined age-related patterns and correlates of cortical bone strength and geometry at the distal radius and tibia. We measured changes in polar strength strain index (SSIp), cortical thickness, periosteal circumference and endosteal circumference using quantitative computed tomography at the 33% sites in the radius and tibia corresponding to cortical bone in 1566 men of African ancestry aged =40 years during an average follow-up of 6.2 years. Bone strength given by SSIp decreased at 5% per decade in the tibia as compared to 0.8% per decade at the radius. Cortical thickness decreased at a rate of 4% per decade at the radius and 5% per decade at the tibia. Periosteal circumference increased 2% per decade in the radius and tibia, whereas endosteal resorption occurred at a rate of 9 – 10% per decade in both limbs. There was a significant linear trend for increased thinning of the cortices with advancing age across 5-year age groups at both skeletal sites. Correlates of the measures of bone strength and geometry varied by measure, bone site and are influenced by the weight-bearing function of the bone. The greatest change in bone geometry was seen in endosteal resorption, which occurs at a similar magnitude in both the limbs and remains stable in all the age groups. Periosteal apposition fails to compensate for endosteal resorption and also appears to decline at the radius in older age groups. Additional research is required to better understand the clinical and biological factors associated with skeletal aging in black men.
Purpose: Few studies have evaluated the long-term effect of childhood maltreatment (CM) on health-related quality of life (HRQoL) among female survivors. We aim to examine if CM is associated with impaired HRQoL over 10 years in the Study of Women’s Health Across the Nation-Mental Health Study (SWAN-MHS).

Methods: Women aged 42 to 52 years were enrolled at the Pittsburgh SWAN-MHS in 1996. HRQoL was ascertained by the Short Form Health Survey (SF-36) at five visits between 2002 and 2012. Abuse and neglect experiences in childhood and adolescence were retrospecively ascertained by the Childhood Trauma Questionnaire (CTQ) in 2004. A total of 341 black and white women with available CTQ data and at least one completed SF-36 was included. Linear mixed-effects analyses were performed to assess the associations of CM with HRQoL over time. Covariates included race, education, marital status, and time-varying variables: age, menopausal status, medical conditions, BMI, financial strain, upsetting events, and social support.

Results: At least one type of CM was reported by 38% of the women. 21% reported emotional abuse, 18% physical abuse, 16% physical neglect, 15% sexual abuse, and 8% emotional neglect. Women with 2 or more types of CM had impaired Physical Component Scores (PCS, b=-3.1, 95%CI: -5.0 to -1.1) and Mental Component Scores (MCS, b=-3.3, 95%CI: -4.9 to -1.7) compared with women without CM adjusting for covariates. Physical abuse and emotional neglect were significantly associated with lower PCS. All five types of CM were significantly associated with MCS deficits.

Conclusions: Early childhood adversity was related to 10-year impaired HRQoL among midlife women.

Significance: Early-intervention for childhood maltreated female survivors may be beneficial for healthy aging.
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Research Interest Areas: Alzheimer's disease and related disorders; health disparities; dancing and physical activity  

Research Support Sources: Alzheimer's Association (NPSASA-14-321093); NIH (T32AG021885-12)  

Research Title: Rhythm Experience and Africana Culture Trial (REACT!): A Culturally Salient Intervention to Promote Neurocognitive Health in Older African Americans  

Project Authors: Alexis Lukach BA, M Kathryn Jedrziewski PhD, George Grove MS, Dawn Mechanic-Hamilton PhD, Shardae Williams BS, Mariegold Wollam BS, Kirk Erickson PhD  

Abstract:  
The Rhythm Experience and Africana Culture Trial (REACT!) is a multi-site randomized controlled intervention study designed to examine the efficacy of using African Dance as a form of moderate-intensity physical activity to improve cognitive function in older African Americans. African Americans are almost two times more likely than Caucasians to experience cognitive impairment in late adulthood. This increased risk may be attributed to lower level and quality of education, lower socioeconomic status, and higher prevalence of vascular diseases, type 2 diabetes, hypertension, and obesity, all of which are recognized as risk factors for dementia. Fortunately, interventions targeting cardiovascular health (i.e., physical activity) are associated with improved neurocognitive function and a reduced risk for dementia, so African Americans may be particularly suited for interventions targeting cardiovascular health and cognitive function. Here, we describe a randomized intervention protocol for increasing physical activity in older (65-75 years) African Americans. Participants (n = 80) at two study locations are randomized into one of two groups. The treatment group participates in African Dance three times per week for six months and the control group receives educational training on Africana history and culture, as well as information about health behaviors, three times per week for six months. If successful, the REACT! study may transform community interventions and serve as a platform and model for testing other populations, age groups, and health outcomes, potentially identifying novel and creative methods for reducing or eliminating health disparities.
Hearing loss is the third most reported chronic condition in older adults in the United States. (Schiller, Lucas, Ward, & Pereygo, 2010). The impact of hearing loss during hospitalization ranges from risk of misdiagnosis (Dubow, 1986) to obstructing the exchange of important health information and healthcare decision-making. (Leo, 1999). Hospital staff are not always able to recognize when inpatients are experiencing hearing difficulties during the admission interview process. (VanCott, 1993).

Purpose: This quality improvement project examined the association between inpatients confirmed with disabling hearing loss using conventional audiometry and those who:
1. Were identified with hearing loss during routine admission procedures
2. Reported difficulty hearing hospital staff during the stay and prior to hearing tests

Methods: Newly admitted patients = 70 were evaluated to identify those with disabling hearing loss as defined by the World Health Organization (PTA > 40dB HL)
Hearing measures on patients included:
1. Pure tone air conduction audiogram
2. Informal self-report measure: “Are you having difficulty hearing your doctors or nurses?”
3. Chart review was conducted to assess whether those patients with disabling hearing loss had been identified with hearing loss during the admissions interview.

Results: Thirty-seven per cent of the patients who participated demonstrated disabling hearing loss on audiometry. Of those, fifty-eight per cent had been identified with hearing loss during the admission interview and 11% self-reported difficulty hearing.

Conclusion: Correlational analysis revealed routine admissions interviews and single item probe questions are insufficient means to identify patients with hearing loss and concomitant communication risks.
Abstract:
Senior citizens move to reside in senior communities to maintain or increase their social engagement, receive care by qualified staff and enhance their quality of life. The majority of residents have significant hearing loss which leaves them with complex listening needs due to low incidence of hearing aid use, group communication situations that are common for social activities, interactive dining environments, and the need for telephone use to connect with loved ones. These challenges are often overlooked or misunderstood by busy staff and family members who may not be sensitive to the impact of decreased hearing on quality of life and caregiver burden. With hearing loss being associated with increased depression, increased falls and cognitive decline, residents with untreated hearing loss may be more prone to health status decline.

HearCARE is a quality improvement project developed by the Audiology department at UPMC (University of Pittsburgh Medical Center) that aims to develop a new model of delivering audiology services and communication assistance to residents at assisted living facilities, employing Communication Facilitators (CF) who are trained and supervised by an audiologist. This poster will describe the training program created to provide the needed skill set for the CF to function in an Assisted Living Facility under supervision of an Audiologist. The tasks that were identified as appropriate for a CF as well as the iterative process that took place after training and during the first three months of practice to refine the training program will be outlined. The CF’s role as an extension of needed audiology services in order to provide accessible and affordable care in facilities with a population with a high incidence of untreated hearing loss will b
Abstract:
Mobility limitations in the elderly are a public health concern due to the association with morbidities and premature death. Although the effect of age related changes in brain structure on gait are well described, little is known about age related functional changes. Our objective was to compare activity in the prefrontal cortex during performance of a dual task in young and old adults. We hypothesized that older adults utilize greater activation of the prefrontal cortex (PFC) under dual-task conditions.

Healthy young (n=15, 18-50) and older (n=15, 65-80) adults were matched on education and gender. Participants were asked to walk on an instrumented treadmill at a self-selected pace at a zero grade slope while subtracting from a predetermined three digit number by seven (Serial7). Near Infrared Spectroscopy was used to measured cortical blood oxygenation. General linear Models were used to analyze the hemodynamic responses. T-tests were utilized to compare Serial7 scores and PFC activation between groups.

Analyses of our first 20 participants showed that older adults walked slower (p=0.048), but performed just as well on the Serial7 task (p=0.18) as the young adults. There is a trend towards greater activation (for O2Hb t=1.84 p =0.06) of the left dorsal lateral PFC in the old compared to the young adults.

This study demonstrated that older adults show greater activation of the PFC while performing a difficult dual task compared to young adults. These functional changes may lead to mobility limitations in older adults. This line of research could lead to the development of interventions.
Study: Diabetes mellitus (DM), a serious public health problem, is common among older adults. There has been strong effort to prevent DM and improve the quality of DM care. Recent data suggests that a significant improvement in quality of diabetes care have made. Yet, limited information is available to examine the effectiveness of DM prevention effort, especially among older adults.

METHODS: We estimated the prevalence of DM using a nationally representative sample of U.S. older adults (aged =65 years) from the 2005-2012 National Health and Nutrition Examination Survey (n=6,806). DM was identified based on four questions: “Have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?” “Are you currently taking insulin?” “Are you now taking diabetes pills to lower blood sugar?” or “Is there one doctor or other health professional for diabetes?” Respondents who answered positively to any of the questions were identified as having DM. All estimations were weighted as recommended.

RESULTS: The prevalence of DM among older adults has been gradually yet steadily increased from 17.6% (95% CI: 15.4%-20.2%) in 2005-6; 18.9% (95% CI: 16.9%-21.1%) in 2007-8; 20.2% (95% CI: 18.1%-22.5%) in 2009-10; and 20.4% (95% CI: 17.8%-23.2%) in 2011-12.

Significance: Between 2005 and 2012; the rates of DM among the U.S. older adults have been steadily increased. To address this public health problem, a two-pronged approach is necessary: (1) continue to improve the quality of diabetes care and DM self-management, and (2) increase effort to prevent DM in all ages.
Abstract:
Depression and cognitive impairments share pathological mechanisms. Thus, individuals with Mild Cognitive Impairment (MCI) and depressive symptoms experience accelerated decline to dementia and disability. As a result, dementia may be delayed if depressive symptoms are reduced. The purpose of these analyses is to examine the influence of a strategy training intervention on depressive symptoms. Older adults adjudicated with MCI and depressive symptoms (>60 years) are randomized to strategy training or usual care (anticipated n=50). Depressive symptoms are measured with the Patient Health Questionnaire-9 at 6 times over a 12 months period. Group differences in depressive symptoms were examined with a linear mixed model. These analyses include 16 individuals with Mild Cognitive Impairment who were randomized to strategy training or usual care. Participants in the strategy training intervention demonstrated a 3.7 point reduction in depressive symptoms and those in usual care demonstrated a 1.6 point increase in depressive symptoms immediately following completion of the intervention time period. The overall linear mixed-model was significant (F(2,50)=4.78, p=0.01), and a significant main effect for intervention group (p<0.01) was found. The strategy training group reported significantly different depressive symptoms than the usual care group. This is consistent with research that demonstrates that older adults who have greater participation in activities of daily living have lower depressive symptoms. Preliminary findings for strategy training are promising as a non-pharmacological intervention that may slow decline to dementia and disability through enhancing participation in activities of daily living and decreasing depressive symptoms.
Abstract:
Abstract Body: There is a paucity of evidence on community-based interventions that target prevention of co-occurring chronic conditions in older adults. We examined the impact of the Arthritis Foundation Exercise Program (AFEP) enhanced with the "10 Keys" to Healthy Aging) on physical function, pain, stiffness, and preventive health behaviors compared with the AFEP alone. The "10 Keys" is a health promotion behavior change program addressing the major risk factors for disease and disability including regular immunizations; regulating blood glucose and LDLc; being physically active; maintaining healthy bones, joints, muscles, and social contact; and combating depression. The study was a cluster-randomized trial with sites matched on community demographic characteristics. Seventy-seven community health workers were trained to deliver the program in 56 sites. There were 462 participants (mean age 73, 88% female, 80% White, 80% arthritis, 34% regular exercisers). Measures included the Short Physical Performance Battery (SPPB), WOMAC Osteoarthritis Index, and assessment of preventive health behaviors. Overall, differences between groups were not statistically significant. Both groups experienced improvements in the SPPB and WOMAC. Generally, participants had high rates of preventive service use at baseline, which remained high throughout. Those in the AFEP+"10 Keys" group with hypertension had greater improvement in blood pressure control (<140mmHg) from 50.9% at baseline to 73.7% at 6 months vs. the AFEP-only group from 81.8% to 87.3%. This study demonstrated that community-based programming can be delivered by the lay community and may improve physical function, reduce pain and stiffness, and support preventive health behaviors.
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Research Support Sources: CTSI - KL2

Research Title: Cognitive function and risk of fall-related fracture and non-fracture injuries in older adults

Project Authors: Andrea L Rosso, Mary E Winger, Jane A Cauley, Tamara B Harris, Suzanne Satterfield, Ann V Schwartz, Theresa M Waters, Kristine Yaffe, Elsa S Strotmeyer

Abstract:
Lower cognitive function is a risk factor both for falls and fall injuries in older adults. Injury type (fracture or non-fracture) may be an important distinction for determining risk profiles. We assessed associations of general cognitive function (Modified Mini-Mental State Examination: 3MS) and speed of processing (Digit Symbol Substitution Test: DSST) in separate Cox Proportional Hazard models for fall-related non-fracture injuries and fracture over 7 years (n=2375, mean age=77, 58.2% women, 41.3% black). Fall-related injury occurred in 619 (26.1%) individuals (26.0% non-fractures, 74.0% fractures). After adjusting for demographics, lifestyle factors, peripheral nerve function, health conditions, and medications, higher 3MS scores were associated with lower risk for non-fracture injuries (HR/5 point increase in 3MS=0.90, CI: 0.82-0.95), but were not associated with fractures (HR=0.95, 95% CI: 0.86-1.05). DSST was not associated with risk for either injury type. Cognitive function may be an indicator of risk for non-fracture injury in older adults.
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**Research Interest Areas:** Body composition, aging muscle, physical function, mobility and fatigability

**Research Support Sources:** Ruth L. Kirschstein National Research Service Award from the NIA (T32-AG-000181) - PI's Anne B. Newman and Jane Cauley

**Research Title:** Body composition remodeling and mortality: the Health Aging and Body Composition study

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**Abstract:**
Study: To examine the association between body composition changes with mortality. Methods: Five-year changes in weight and body composition were assessed with computed tomography (cm2) and dual x-ray absorptiometry (kg) in 869 men and 934 women initially aged 70-79. All–cause mortality was monitored for up to 12 years (2002-03–September 30, 2014) and risk was assessed using sex-specific Cox models. Results: Both men and women lost weight, visceral fat area, thigh muscle area, lean and fat mass (all P<0.01) but gained intermuscular thigh fat area (P<0.01). There were 995 deaths. After adjustment for demographics and chronic diseases, weight loss was associated with mortality in men (HR: 1.12, 95% CI: 1.02–1.24) and women (1.27, 1.16–1.50) and partly (~10%) explained by loss of thigh muscle area. After adjustment for total weight change, demographics and chronic disease, losing thigh muscle area was associated with higher mortality in both men (1.21, 1.08–1.35) and women (1.18, 1.01–1.37, per 9.0cm2) and was especially strong in normal weight (BMI <25kg/m2) individuals and those losing weight. Losing intermuscular thigh fat was protective against mortality only in normal weight (0.66, 0.51-0.86) and weight stable men (0.79, 0.66-0.95, per 3.2cm2). Changes in visceral fat area were not associated with mortality. Conclusion/Significance: Older adults with greater loss of thigh muscle than expected for overall weight change had a higher mortality risk compared to those with relative thigh muscle preservation, suggesting that conservation of muscle mass is important for survival in old age.
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**Research Interest Areas:** Healthy cognitive and brain aging

**Research Support Sources:** Behavioral Brain T32GM081760

**Research Title:** Relationship of brain-derived neurotrophic factor with hippocampal volume after a physical activity intervention in older adults at risk of disability

**Project Authors:** C. Elizabeth Shaaban, Abbe de Vallejo, Howard J. Aizenstein, Anne B. Newman, Nancy W. Glynn, Kirk I. Erickson, Caterina Rosano

**Abstract:**
Study: Due to its beneficial effects on hippocampal volume, physical activity (PA) may represent a preventive strategy for Alzheimer’s disease. One pathway for this effect may be through PA promotion of increased levels of brain-derived neurotrophic factor (BDNF) a promoter of neurogenesis. We sought to evaluate this pathway in a sample of older, frailer adults (N=24, mean age 76) completing a low to moderate intensity PA intervention or healthy aging (HA) classes in a randomized controlled trial. Methods: Participants at the Pittsburgh site were invited to complete 7T MRI scans at study baseline (before intervention) and 2 year follow-up. Hippocampal volume was normalized by whole brain gray matter volume. Serum BDNF was measured by Luminex Assay. Group differences in minutes of PA and percent change in BDNF were assessed with non-parametric tests. Linear regression models were used to evaluate the relationship of PA, BDNF, and their interaction, with hippocampal volume. Results: The PA intervention increased the total minutes of weekly PA in the PA group vs. the HA group (p=0.02). Percent decline in BDNF from baseline to 2 years was lower in the PA group vs. the HA group (p=0.08). Left hippocampal volume at the 2-year follow-up was greater in the PA group vs. the HA group, independent of baseline hippocampal volume, age, and race (p=0.03). The association of PA with larger hippocampus after 2 years was stronger for those with higher baseline BDNF levels, even after adjustment for baseline hippocampal volume (p for interaction=0.03). Conclusions/Significance: Low to moderate intensity PA can reduce age-related declines in BDNF even among older, frailer adults. BDNF may help to create a beneficial milieu in the brain whereby PA has stronger effects on hippocampal volume.
Objective: Several immunological biomarkers are altered in late-life major depressive disorder (LLD). Immunological alterations could contribute to LLD’s consequences, but little is known about the relations between specific immunological biomarkers and brain health in LLD. We performed an exploratory pilot study to identify, from several candidates, the specific immunological biomarkers related to important aspects of brain health that are altered in LLD (brain structure and executive function).

Methods: Adults (n=31) were at least 60 years old and had major depressive disorder. A multiplex immunoassay assessed 13 immunological biomarkers, and we examined their associations with structural MRI (grey matter volume and white matter hyperintensity volume (WMH)) and executive function (Color-Word Interference and Trail-Making tests) measures.

Results: Vascular endothelial growth factor (VEGF) and the chemokine eotaxin had significant negative associations with grey matter volume (VEGF: n=31, r=-0.42; eotaxin: n=29, r=-0.43). Tumor necrosis factor alpha (TNF-α) had a significant, strong, positive relationship with WMHs (n=30, r=0.62); Interferon-γ (IFN-γ) and macrophage inflammatory protein-1α (MIP-1α) were also significantly associated with WMHs (IFN-γ: n=31, r=0.36; MIP-1α: n=29, r=0.46). Only eotaxin was associated with executive function (set-shifting performance as measured with the Trail-making test: n=33, r=-0.39).

Conclusions: Immunological markers are associated with brain structure in LLD. We found the immunological correlates of grey and white matter differ. Prospective studies are needed to evaluate whether these immunological correlates of brain health increase the risk of LLD’s consequences. Eotaxin, which correlated with both grey matter volume and set-shifting performance, may be particularly relevant to neurodegeneration and dementia in LLD.
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**Research Interest Areas:** Social Gerontology/Geriatric Mental Health

**Research Support Sources:** T32 MH019986

**Research Title:** Grandparent Caregiving, Race, and Cognitive Function: A Prospective Study

**Project Authors:** Rodlescia Sneed, Richard Schulz

**Abstract:**
Many studies have explored the health effects of caregiving among grandparents raising grandchildren; however, there is little data regarding the impact of caregiving on cognitive function. Using data from the 2006 and 2010 Health and Retirement study, we prospectively investigated the effects of grandparent caregiving on cognitive function among White and African-American grandparents aged ≥65 years. Caregiving status and cognitive function were assessed at baseline and again at 4-year follow-up. Analyses controlled for age, race, sex, marital status, baseline cognition, employment status, education, baseline health status, and depressive symptoms. Non-residential grandparents who had provided at least 500 hours of care to their grandchildren over the 2 years prior to baseline demonstrated greater cognitive function at 4 year follow-up when compared to non-caregiving grandparents (β=0.71; Beta=0.04; p=0.001). There was no association between grandparent caregiving and cognitive function for grandparents who lived with their grandchildren or for those who provided low levels of care. Further, the effects of grandparent caregiving on cognition were observed among White grandparent caregivers, but not among African-American grandparent caregivers. This is the first population-based prospective study to evaluate the association between grandparent caregiving and cognitive function. Our findings suggest that providing care to grandchildren may be beneficial for some, but not all, grandparents. Future studies should evaluate the mechanisms linking grandparent caregiving to cognitive function and also explore explanations for racial/ethnic differences.
Abstract:
Study Background: The accumulation of amyloid beta (Aß) in the brain is a putative neuropathogenic molecular pathway for Alzheimer's Disease. Identifying potentially modifiable factors associated with Aß levels is therefore an important public health objective. Using longitudinal data from the Cardiovascular Health Study (CHS), we examined whether physical activity (PA)—a modifiable lifestyle factor linked to brain health—could prospectively predict plasma Aß levels in a sample of community-dwelling older adults. We hypothesized that greater amounts of baseline PA would predict lower Aß levels at subsequent study time points.

Methods: During a baseline assessment, 140 adults (mean age 83 years) completed the modified Minnesota Leisure-Time Activities Questionnaire, a self-report measure of PA. They also completed two blood draws occurring 9 (T1) and 13 (T2) years after baseline to quantify plasma Aß levels. Number of blocks walked per week at baseline was the primary PA index. Levels of Aß1-40 and Aß1-42 were the primary Aß outcome measures. Linear regression analyses controlling for age, gender, body mass index, cardiovascular disease burden, white matter lesions, and cystatin C levels (an index of glomerular function) were performed.

Results: There was an effect of baseline PA on Aß1-42 at T2 (ß=-.16), such that greater amounts of PA were associated with lower Aß1-42. There was no effect of PA on Aß1-42 at T1 (ß=-.10), nor on Aß1-40 at either time point (ßs= -.07 and -.11, respectively).

Conclusions/Significance: These results provide longitudinal evidence that higher PA levels in late life relates to lower plasma Aß 142 levels 13 years later. PA may therefore have a protracted impact on a peripheral biomarker of Alzheimer’s Disease and cognitive impairment.
Diabetes Treatment Decisions in Older Patients with Dementia: Provider and Caregiver Perspectives

Carolyn T. Thorpe, Loren J. Schleiden, Megan Hamm, Kelly Williams, Michelle Rossi, Michael Fine, Susan Zickmund

Abstract:
Objectives: Despite guidelines advising against tight glycemic control (HbA1c<7%) in older diabetes patients with comorbid dementia, recent data suggests the majority of these patients have tight control. We aimed to identify barriers to avoiding tight glycemic control in this population.

Methods: Qualitative study using semi-structured telephone interviews with UPMC family practitioners, general internists, and geriatricians (n=11) and family caregivers (n=12) of patients with diabetes and dementia. Interview transcripts were subject to thematic content analysis.

Results: Providers were generally aware of and agreed with guidelines to avoid tight control, and were most likely to implement them when patients exhibited a history of hypoglycemia, high treatment burden, and preference to avoid intense treatment. Providers saw tight control as appropriate when patients had a history of HbA1c<7% with no hypoglycemia and they perceived the patient/caregiver as able to maintain tight control. Most caregivers expressed frustration with daily diabetes management. Some expressed hesitancy in participating in decisions about diabetes treatment, due to lack of knowledge or belief that decisions should be made by providers and patients. Other barriers included 1) specialist/inpatient vs. primary providers with conflicting goals; 2) lack of communication across providers; 3) patient/caregiver hesitancy to de-intensify treatment; and 4) lack of time to educate caregivers about the rationale for less intense treatment.

Conclusions/Significance: These data provide new insight into reasons underlying previous quantitative evidence of diabetes overtreatment in this population. Future interventions should address these barriers to reduce overly intense treatment in patients with dementia.
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Research Interest Areas: Reducing disability in older adults

Research Support Sources: None current for this study

Research Title: Performance-based impairment measures as predictors of preclinical disability in community-dwelling older adults

Project Authors: Pamela Toto, PhD, OTR/L; Lauren Terhorst, PhD; Joan Rogers PhD, OTR/L; Margo Holm, PhD, OTR/L

Abstract:
Study: This research examined whether motor and cognitive impairment-based measures can predict declines in quality of ADL/IADL performance (i.e. preclinical disability) in a sample of community-dwelling older adults.

Methods: Secondary data analysis of community-dwelling older women with chronic health conditions (N=256). Associations between baseline impairment measures and quality of ADL/IADL performance at 6 months were examined. Predictor variables included Performance-Oriented Assessment of Balance (POAB), grip strength, Keitel Functional Test (KF), functional reach, maximum voluntary ventilation, and the Jebsen-Taylor Hand Function Test (JTHFT). Cognitive measures were the Modified Mini-Mental State (3MS) and the Trailmaking A and B. Outcomes for mobility, ADL, Cognitive IADL, and Physical IADL quality of performance scores were determined using the Performance Assessment of Self-Case Skills (PASS). Logistic regression models explored cognitive and motor predictors of ADL/IADL performance quality while controlling for demographics and diagnoses.

Results: Odds ratios of cognitive predictors (1.76 to 2.32) were stronger than the odds ratios of motor predictors (1.02 to 1.80). Functional reach (p =.049) and 3MS (p=.012) were predictive of mobility quality, while the POAB (p =.007) and the KF (p=.005) were predictive of ADL quality. The JTHFT (p =.030), and 3MS were predictive of CIADLs (p=.017) and Trails (p<.001), 3MS (p=.050), and JTHFT (p=.050) were predictive of PIADL quality.

Conclusion: Motor and cognitive impairment measures were found to predict mobility, ADL, and IADL quality of performance after controlling for baseline covariates in this sample population.

Significance: Our findings imply that performance-based impairment measures have diagnostic v
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Research Interest Areas: neurodegeneration

Research Support Sources: NIH

Research Title: Mitochondrial calcium overload in the pathogenesis of Parkinson’s Disease-associated LRRK2 mutations.

Project Authors: Manish Verma, Jason Callio, Isreal Sekler, Zachary P. Wills and Charleen T chu

Abstract:
Study: Mutations in LRRK2 gene has been linked with Parkinson’s disease (PD). In most of LRRK2 linked PD cases abnormality with mitochondrial function has been reported but the mechanisms are poorly understood. Calcium (Ca2+) ions play an important role in regulating neuronal signaling and neurons have intricate transport system to regulate intracellular Ca2+ homeostasis. Previous results have suggested dysregulation of Ca2+ homeostasis with delayed clearance of cytosolic Ca2+ in LRRK2 models of PD. In the present study we hypothesized that PD associated LRRK2 mutations cause mitochondrial damage by mitochondrial Ca2+ overload which may be exacerbated with aging.

Methods: Mice primary cortical neurons were used for; western blot, immunostaining and live cell imaging to measure Ca2+ dynamics. Cytosolic and mitochondrial Ca2+ levels were measured using genetically encoded calcium indicators RCaMP and mt-GCaMP6m respectively. Results: Overexpression of LRRK2 mutants: 1. induce dendrite retraction 2. increase cytosolic and mitochondrial Ca2+ levels upon stimulation with KCl and NMDA. 3. modulate MCU expression in ERK dependent manner. 4. There is age dependent loss of TFAM and SIRT3 in LRRK2 Tg mice.

Conclusions: Neurons expressing LRRK2 mutants show increased cytosolic and mitochondrial Ca2+ compared to wild type or kinase dead expressing neuron leading to mitochondrial Ca2+ overload. This can be attributed to increase in MCU which can be abrogated by inhibition of ERK pathway.

Significance: Our study elaborates the mechanism by which LRRK2 induces mitochondrial damage and loss of dendritic mitochondria; through mitochondrial Ca2+ overload. Inhibition of MCU can potentially lead to therapeutics in future which can prevent or delay LRRK2 associated neurodegeneration.
Significance: Strategies to improve fatigue, inflammation, and physical activity (PA) may help older adults maintain high physical function, which is important in daily activity and quality of life. Study Purpose: We assessed the combined impact of perceived fatigue, PA, and inflammation on physical function in adults across the lifespan.

Methods: The relationship of perceived fatigue, inflammation, and PA to physical function was examined in two generations of adults (N=4,934) from the Long Life Family Study. Physical function was measured using the Short Physical Performance Battery (SPPB, range 0-12); high function categorized as having SPPB=10. Low perceived fatigue (probands: 65%; offspring: 75%) was categorized as those who answered rarely/none of the time to CES-D item “I felt everything I did was an effort.” PA was measured as walking frequency in the past two weeks, with low PA as =1 time, moderate PA as 2-9 times, and high PA as 10-14 times. Inflammatory biomarkers measured were fasting IL-6 and high sensitivity CRP. Probands and offspring were examined separately due to significant group differences.

Results: Probands were 89.6±6.8 years old, 56% female, and 29% had high SPPB. Offspring were 60.6±8.4 years old, 55% female, and 93% had high SPPB. In multivariate logistic regression, low fatigue, lower levels of IL-6, and higher PA were independently and significantly associated with high SPPB in probands, after adjusting for age, sex, BMI, depression, history of heart disease, cancer, and diabetes; while, low fatigue and lower levels of IL-6 were independently and significantly associated with high SPPB in offspring.

Conclusion: Avenues for improving fatigue and inflammation, such as a PA intervention, should be a focus for reducing physical function decline.
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**Research Interest Areas:** Social support in the community

**Research Support Sources:** n/a

**Research Title:** Implementation of Home-Based Palliative Care with CRNPs

**Project Authors:** UPMC PSI, UPMC VNA, UPMC Health Plan

**Abstract:**
As an Integrated Delivery and Financing System (IDFS), the University of Pittsburgh Medical Center (UPMC) and the UPMC Health Plan identified gaps in services related to care transitions from facility to home. These gaps included breakdown in communication across the health care team, limited scope of traditional home health services, and inconsistent follow up for patients with serious chronic illness. A collaborative effort between the UPMC Palliative and Supportive Institute (PSI), the Health Plan and the system-owned home health agency was developed. Specifically, PSI established an independent practice of specialty-trained Certified Registered Nurse Practitioners to support two new payer/provider models of care in community. With autonomy of practice and customized documentation tools, the CRNP visits patients in the home, collaborates directly with the patient’s Primary Care Physician to minimize the burden of serious chronic illness, establish a value-based plan of care, and prevent unnecessary emergency room visits or re-hospitalization. A “Home Transitions” program leverages resources available within the home health team and enhances services with the CRNP, a pharmacist, and medical directors. The “Advanced Illness Care” program is designed to support patients with life-limiting illness/ poor prognosis and is provided by a CRNP and a team of specialty-trained clinical social workers.
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Research Interest Areas: Relationships between leg strength/power and falls/fall injuries in older adult populations

Research Support Sources: NIA Aging Training Grant (PI: AB Newman) T32-AG-000181

Research Title: Lower Extremity Muscle Power in Older Men and Injurious Fall Risk: the MrOS Study

Project Authors: Mary E. Winger, Paolo Caserotti, Jane A. Cauley, Robert M. Boudreau, Peggy Cawthon, Eric Orwoll, Kristine Ensrud, Elsa S. Strotmeyer

Abstract:
Lower extremity power, which incorporates strength and velocity, may be related to injurious fall risk. The Osteoporotic Fractures in Men (MrOS) Study is an ongoing cohort of ambulatory men (N=5,994) aged =65 years (10% minorities) at six U.S. sites with a 2000-02 enrollment. Injurious falls outcome (yes/no) was prospectively collected as a repeated measure from 2 self-reported questionnaires and 2 telephone interviews occurring over 9 follow-up years. Baseline muscle power was measured using Nottingham single leg press. Maximum power was assessed continuously per body weight (Watts/kg) and as quartiles. Generalized estimating equations with unstructured correlation matrix modeled injurious fall risk. Of men (N=4,636), 51% experienced =1 injurious fall over the follow-up (9 years). Weaker power/kg was significantly associated with a 23% increased fall injury risk in models adjusted for age, race, site, height, and comorbidities (p<0.0001). Lower power/kg quartiles had significantly higher fall injury risk vs. highest quartile (quartile 1 risk=1.5; 95%CI:1.3-1.8; quartile 2 risk=1.3; 95%CI:1.2-1.5; quartile 3 risk=1.2; 95%CI:1.1-1.4) with significant trend across quartiles (p<0.0001). Weaker leg power/kg body weight is associated with increased fall injury risk. Identifying older adults with weaker lower extremity power may identify those at higher future risk of experiencing an injury.
Abstract: Background. Health care providers receive little training about how to work with demented patients who have lost language and processing skills. We quantified the impact of a dementia communication skills curriculum on health professions students’ attitudes and confidence about communicating with people living with moderate-to-advanced dementia.

Methods. We taught nearly 200 health professions students about the neuropathology and skills needed to work with communication loss in dementia using the Positive Approach to Care© method at the end of a week-long geriatrics course. 148 medical, 9 nurse practitioner, 9 speech pathology, 12 pharmacy, and 6 physical therapy students responded to pre-test, post-test questionnaires reporting on change in attitudes (6 point Likert scale, not at all likely to very likely) and confidence about working with this population (5 point Likert scale, not at all confident to extremely confident). We conducted paired t-test analyses.

Results. Students reported significant pre-post (p<0.0001-p<0.007) improvement in each of 5 attitude (ex] How likely are you to feel uncomfortable when you have to work with a patient with severe dementia? mean 0.27, 95% CI (0.074, 0.466), p<0.007) and 6 self-confidence (ex] How confident are you in your ability to counsel families about how brain change in dementia causes the behaviors they find challenging? mean -1.184, 95% CI (-1.330, -1.038), p<0.000) items.

Conclusions. A dementia communication skills curriculum achieved an extremely large effect size with improvement in health professions students’ confidence about their ability to work with patients and families who live with dementia.
Abstract:
Study: Aging-induced tendinopathy affects millions of people. On the other hand, exercise is known to enhance the structure and mechanical strength of tendons [1]. In this study we used in vitro and in vivo rat tendon models to investigate the cellular effects of aging and exercise on tendons.

Methods: In vitro - TSCs from the patellar tendons of young (3 months) and aging (20 months) rats were mechanically stretched to 0% (control) and 4% [2], and analyzed. In vivo - Aging rats ran on a moderate treadmill running (MTR) regimen (30 min/day) for 4 weeks. Control aging rats were in cages without running. After 4 weeks, a wound was created in the patellar tendon of each rat, and wound healing was tested 4 and 8 weeks later. TSCs were also isolated from the rat patellar tendons for histology, RT-PCR and Western blot analyses.

Results: Our in vitro study showed that aging changed TSC shape, decreased TSC proliferation and reduced expression of stem cell markers, nucleostemin (NS) and Nanog. Aging also increased the expression of the senescent markers, SA-β-gal, CCN-1, P16, P53 and HMGB-1, and the non-tenocyte genes, PPAR?, Runx-2 and SOX-9. However, these adverse effects were mitigated by moderate stretching (4%), which increased the expression of NS and Nanog, and the tenocyte-related genes, collagen I and tenomodulin. Our in vivo study showed that tendons in control aging rats were yellowish and highly vascular. But MTR restored their intact nature and low vascularity similar to young rat tendons. MTR also promoted quicker closure of wounds, improved the organization of collagen fibers and tendon matrix in aging tendons.

Conclusions: Aging increases cell senescence, reduces TSC proliferation and induces non-tenocyte differentiation. Moderate exercise decreases cell s