Physiology and healthy ageing

Research spotlights

The Physiological Society

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Why is physiology important to healthy ageing?

Physiology is the study of how the human body works. It is core to understanding all the different components associated with age, health and wellbeing. Physiologists use their knowledge and insight to advise on effective interventions to keep people healthy. Physiological research improves the understanding of the underlying biology of ageing, which is essential to weaken the link between ill health and older age.

Research in physiology underpins scientific understanding of the ageing process. It improves understanding of how the body responds and adapts to the challenges of everyday life. It also helps us to determine what goes wrong in disease, facilitating the development of new treatments and guidelines for maintaining human health.

Physiology has already played a valuable role in demonstrating the impact of interventions such as physical activity, diet and sleep for preventing or slowing down age-related decline in health. For example, physical activity can help people maintain cardiovascular health and higher levels of muscular capacity as they grow older.

This booklet features several research spotlights highlighting the important role physiologists are playing in improving healthy ageing. For more information, visit **physoc.org**.

Exercise physiology and healthy human ageing

As our population demographics are changing and people are living longer, attention is focusing not so much on extending our lifespan but how we can maximise our "healthspan". Being healthy at any age is dependent upon a number of factors, which include not smoking, eating a well-balance diet, moderate alcohol consumption and sleeping well. One factor increasingly being recognised as essential for maintaining health throughout the life course, reducing the risk of numerous diseases and maintaining good physiological function is exercise.

Exercise physiology is the branch of physiology that concerns itself with the body's responses and adaptations to exercise, physical activity or simply the increase in energy expenditure caused by movement. Exercise involves the integration of multiple physiological systems requiring neural pathways originating in the brain to initiate movement, skeletal muscles to contract and produce force through to the cardiovascular and respiratory systems delivering adequate supplies of oxygenated blood to match increasing energy demands. These physiological processes are remarkably integrated and carefully controlled and occur in the context of trying to maintain our body's homeostasis, such that we don't overheat, become too acidic or lose flow to the brain and other essential organs.

As we age our physical capabilities and ability to exercise decline. Our muscles get smaller and weaker, our hearts pump less blood and our ability to perform simple tasks of everyday living are progressively reduced. We know this to be due to an ageing process, because it is evident even the most vigorously active master athletes whose performances decline as they get older. However, the performances of these older athletes are quite remarkable and in general highly active older people show levels of physiological function that are far superior to those that are inactive. Thus, one of the challenges for ageing physiological research is determining how much of the decline is due to the ageing process itself and how much due to factors relating to lifestyle.

Being physically active is important in both optimising healthy ageing and in improving function in the previously inactive older person. In many respects exercise can be considered as a physiological and natural "pill". It activates multiple physiological pathways and benefits health across numerous systems – including muscle, the cardiovascular and immune systems through to mental health. One of the biggest public health challenges we face is getting people to reduce sedentary behaviour and increase levels of physical activity.

Stephen Harridge
King's College London

RESEARCH SPOTLIGHT

The ageing immune system and its impact on achieving 'Healthy Ageing'

The immune system plays a key role in maintaining health, protecting us from infections, cancer and facilitating preventive medicine measures such as vaccinations. However immunity declines with age, immunesenescence, contributing significantly to poor health in old age including: reduced efficacy of vaccinations; increased susceptibility to infections and viruses and reduced immune surveillance leading increased cancer risk with age. Another aspect of ageing that is in part influenced by immunesenescence is the increase in systemic inflammation, so-called 'inflammaging'. Importantly the degree of inflammaging has been related to increased risk of most chronic conditions of old age and is a biomarker of how well or badly an individual is ageing. Identifying the factors influencing immunesenescence will make an important contribution to the government's target of improving healthy life expectancy by 5 years by 2035.

A good example of the impact physiological research has had on understanding immune system ageing and health is the role played by physical activity. In most developed countries regular physical activity declines dramatically with age: in the UK less than 10% of adults aged over 65 years meet the Chief Medical Officer's recommendations for physical activity of 150 minutes of aerobic exercise per week. However, the immune system is significantly influenced by physical activity.

One of the major unanswered questions was just how much of immunesenescence was due to increased physical inactivity with age. To address this we analysed the degree of immunesenescence in older adults, aged 55-79 years, who had maintained high levels of physical activity throughout middle and old age (regular long distance cycling). These older adults showed few signs of an aged immune system and had high levels of immune hormones important for maintaining immunity.

Bearing in mind the low involvement of most older adults in regular exercise, what we now need to know is just how little physical activity is required to achieve this immune sparing effect! Additionally we need to understand how physical activity influences immunesenescence and whether it also leads to improved responses to infections and vaccinations. These are key research gaps that are being met by physiological research.

Janet Lord
University of Birmingham

RESEARCH SPOTLIGHT

Using home-based High Intensity Interval Training (HOME-HIIT) to improve health and fitness

Having previously demonstrated that High Intensity Interval Training (HIIT) programs of 3 x 20 minute sessions per week are equally effective as endurance exercise training in improving exercise capacity, the EMARG team have now developed HOME-HIIT to remove known barriers to exercise, which include the costs of gym membership and the need to attend public gyms. HOME-HITT can be delivered in the privacy of a home setting or with groups of equals in community centres without the need to access exercise equipment.

The studies involves 150 volunteers (with nearly a third recruited in collaboration with Sefton Council) and have shown that HOME-HIIT is as effective as HIIT and endurance training, performed in controlled exercise laboratories, in reducing cardiovascular risk and in improving VO2max (the maximum or optimum rate at which the heart, lungs, and muscles human body can effectively use oxygen during incremental exercise) and recognised measures of metabolic health. In addition, online heart rate monitoring using a mobile app has revealed high adherence and compliance rates, further increased by weekly feedback by telephone.

The next step is to roll out HOME-HIIT into the Liverpool community in collaboration with Sefton Council. On the basis of the size of the improvements seen with HOME-HIIT and epidemiological studies, we expect that HOME-HIIT will add a minimum of 5 years to the healthy lifespan, in individuals managing to sustain long-term increases in habitual physical activity levels, with a particularly significant impact among individuals from a low socio-economic status.

Anton Wagenmakers
Liverpool John Moores University

RESEARCH SPOTLIGHT

Using physiological insights to better monitor healthy ageing and prevent adverse events

Physiological resilience – how the body responds and recovers from a stressor – is integral to health in older age. Resilience is a dynamic property, so it can only be determined through "stress testing", that is, measuring both the stressor and response. Examples include blood pressure response to the stress of standing up from lying down, or blood flow to the brain during the stress of a cognitive task. Acute syndromes common in older people, such as delirium or falls, essentially arise through impairments in resilience.

We have been developing methods to define physiological changes in response to controlled stressors in clinical studies. Age-related changes are likely to reveal themselves optimally under physiological stress conditions. Our overall strategy is to perform these laboratory measures (controlled stressors and responses) in participants being followed in a longitudinal study capturing acute events such as illness and hospitalisation.

We hope that this research will achieve three things: establish measures of physiological resilience as a way of predicting future acute health events; develop mechanistic insights into physiological resilience as a target for clinical trials to improve healthy ageing and impact the assessment and management of older people in clinical practice through a Comprehensive Geriatric Assessment that helps healthcare professionals assess older people and tailor their treatment or care plans accordingly to maximise their intrinsic capacity.

Ultimately, better understanding of physiological resilience is likely to have direct clinical utility through individualised risk for therapeutic decision making; enhancing acute care through rapid detection of adverse risk and more targeted rehabilitation strategies before surgery or after acute illness. Taken together, we envisage that our methods to predict and assess resilience and vulnerability in older persons will thus contribute to preventing disease and disability and reduce health and social care costs.

Dan Davis
University College London

Understanding the relationship between ageing and sleep

Sleep is a highly dynamic process showing systematic changes across the night but also across the lifespan. In humans, sleep is deepest up until adolescence, after which it progressively becomes more fragmented and superficial. The fundamental question remains as to whether sleep disturbances in the elderly are related to a reduced function of the circadian clock, impaired homeostatic sleep regulation, or a diminished capacity to generate and sustain deep consolidated sleep. One possibility is that the age-dependent changes in sleep represent physiological compensatory responses, in which sleep plays an active and increasingly important role in maintaining cellular homeostasis and optimal waking functions. It is also possible that the age-dependent changes in sleep are a reflection of anatomical or physiological changes, such as a loss of synaptic connectivity, or a decline in the function of specific brain circuits.

It is well established that the level of electroencephalogram (EEG) slow-wave activity (SWA, 0.5-4Hz) reflects sleep homeostasis, and that in humans SWA is reduced with ageing. This led to the belief that sleep homeostatic mechanisms may be disrupted with ageing. Studies in laboratory animals have been fundamental in addressing this, with rodent studies often able to recapitulate at least some aspects of human sleep. However, rodent studies have also shown conflicting evidence for the effects of ageing on sleep. For example, mice sleep more when they get older, not less. Since both sleep need and sleep depth are mechanistically and functionally related to the expression of slow wave activity within local cortical networks, in our recent study we performed chronic recordings of cortical neural activity and local field potentials (LFP) from mice. Surprisingly, we found that ageing had little effect on sleep-related neural activity within local cortical networks in mice. We must therefore critically reconsider the notion that core brain mechanisms of sleep regulation are deficient in older humans. These studies also highlight the necessity to combine human and animal studies in order to achieve a better understanding of what happens to our sleep as we get older.

Laura E. McKillop
Novo Nordisk Postdoctoral
Research Fellow

Vladyslav V. Vyazovskiy
University of Oxford

RESEARCH SPOTLIGHT

‘Epigenetic clock’ – the future of measuring ageing?

The field of epigenetics addresses chemical modifications of DNA and associated proteins. Epigenetic marks contextualise the information in a cell’s genome, telling a cell which genes it should and should not use. Although the genome largely stays constant, epigenetic information changes throughout life and is influenced by a combination of developmental cues and environmental effects on cells. It is thought that epigenetic information degrades with age, which would impede function as cells become unable to use genetic information appropriately and this has been observed across a variety of organisms.

A particularly exciting discovery is that the biological age of a human can be calculated based on the epigenetic information from a few hundred locations in the human genome. The existence of this epigenetic ‘clock’ has huge implications for ageing because the clock works uniformly from birth in almost all tissues regardless of how often the cells divide or their metabolism. In other words, irrespective of the location or function of a cell, some underlying ageing process is progressively and consistently acting long before any disease or decline occurs.

Physiological insights into this system are critical, especially in analysing how the clock measures differ in individuals with particularly healthy or unhealthy lifestyles, or with various medical conditions. This means lifestyle factors such as diet and exercise which have primarily physiological responses must be communicated across all cells to the underlying mechanism of the epigenetic clock.

The great challenge lies now in understanding the underlying mechanism that causes the progressive epigenetic changes measured in the clock. It is unlikely that ageing is a result of the epigenetic changes, rather the clock is likely one manifestation of an underlying ageing process that we do not yet understand. Understanding this mechanism will be of great benefit in advancing lifelong health. Since the clock reflects ageing health, understanding what drives the clock will reveal critical mediators of healthy ageing. For example, we understand that diet and exercise are important but not why, nor whether more specific advice and interventions are possible to improve ageing health.

Jon Houseley
The Babraham Institute

RESEARCH SPOTLIGHT

The role of the microbiota on development and ageing throughout the life course

Colonisation of the microbiota, a wide variety of bacteria, viruses, fungi, and other single-celled animals that live in the body, begins at birth. Composition of the gastrointestinal microbiota is influenced by multiple factors including mode of birth (vaginal vs. c-section) and feeding patterns (breast vs. formula feeding) and remains malleable for the first few years of life. The microbiota has historically been understood primarily by its diversity; how many bacterial species are present and how abundant they are. More recently, characterisation of bacterial genes within the microbiome has allowed assessment of function, or 'what do they do' in addition to 'who is there'. Changes to the microbiota can occur due to infection, administration of antibiotics, or changes in diet, but it is thought that in adulthood the microbiota remains fairly stable. In the absence of stability, or following a particular insult, disease can occur, although whether this is causative or correlative remains to be determined.

As we move into later life our microbiota changes, with decreasing diversity occurring due to multiple factors associated with ageing, including changes in diet, multiple prescription drugs, and suppression of the immune system. Maintaining the diversity within the microbiota may serve as a novel way to improve healthy life in older populations, reducing disease and maintaining autonomy in individuals. Studies have found that the microbiota in older populations is associated closely with lifestyle, with individuals having the greatest diversity being those who live in their own home and those with the least diversity being those in assisted care living. Finding new ways to maintain microbial diversity in individuals as they age would be an exciting way to improve quality of life.

A critical knowledge gap remains identifying the causes of decreased diversity in the microbiota as people age and how best to improve or delay loss of diversity. The impact of common medications administered to older patients, including anti-inflammatory, cholesterol lowering, blood pressure lowering, and diabetes drugs on microbial diversity would help identify beneficial species that are lost. Establishing the changes associated with ageing in gut physiology, immune response, and composition of the microbiota are ways through which we could have a significant impact on understanding healthy ageing and provide novel avenues to study this phenomenon. In addition, there are emerging links between the microbiota and neurodegenerative diseases, with the microbiota responsible for modulating deposits of protein in the brain that can lead to conditions such as Alzheimer's disease but more research is needed into the relationship between the two aspects of the body.

Melanie Gareau
UC Davis

RESEARCH SPOTLIGHT

Musculoskeletal ageing research

Sarcopenia is the age-related loss of muscle mass and quality that occurs from the age of 40 onwards in both men and women. At the moment we do not know the mechanisms that drive sarcopenia, but based on published literature it is likely to be multi-faceted, including reduced habitual physical activity and anabolic resistance to nutrition (a reduction in stimulation of muscle protein synthesis to protein/amino acids). Sarcopenia is also exacerbated by acute periods of ill-health during which energy intake and physical activity can be markedly reduced, and infection and inflammation increased, all of which will induce muscle mass loss and muscle metabolic dysregulation. Sarcopenia is associated with loss of independence, reduced quality of life in old age and increased falls related injuries.

Physiology is indispensable to understanding the mechanistic basis of sarcopenia, which is currently missing from insight gained from epidemiological and community-based investigation. Without such insight it will be very difficult to arrive at effective strategies to minimise sarcopenia and stimulate muscle mass and functional gains during rehabilitation in older people. Furthermore, longitudinal physiological centred studies need to be performed in humans, as there are fundamental differences too between human and rodent muscle responses to ageing.

Advances in research techniques and technology mean it is now possible to make measurements in humans that were impossible just a few years ago. So, for example, muscle quality can be determined non-invasively using magnetic resonance spectroscopy and the relationship between brain and muscle response is now achievable using non-invasive Magnetic resonance imaging (MRI) based approaches. This provides integrated system-level insight of the physiological drivers of musculoskeletal decline with age.

Collectively these tools combined with clinical physiology and 'omics' technologies will provide unprecedented insight of human sarcopenia (and beyond), particularly if longitudinal study designs are adopted in people – the best model of ageing! This will allow us to understand the causes of sarcopenia and pinpoint and develop the most effective strategies to diminish it and stimulate rehabilitation.

Paul Greenhaff
University of Nottingham

RESEARCH SPOTLIGHT

Physiology research underpins updated public health guidance for older people

The most disseminated general exercise guidelines, up to very recently, recommended 150 minutes of exercise a week. However, our research at Manchester Metropolitan University (MMU) suggests that older people, especially older women, who regularly move throughout the day, are more likely to have better bone health than those who carry out just one bout of high-intensity exercise a day.

The new UK Chief Medical Officers (CMO), updated advice on Physical Activity for Older Adults Recommendations notes that MMU's research "supports the benefits of being active throughout the day, such as better maintenance of bone health with higher volumes of light intensity activity spread throughout the day".

Gladys Onambele-Pearson
Manchester Metropolitan University

The Physiological Society

As the largest network of physiologists in Europe, with academic journals of global reach, The Physiological Society continues a 145 year tradition of being at the forefront of the life sciences. We support the advancement of physiology by promoting collaboration between physiologists around the world, organising world-class conferences and publishing the latest developments in our scientific journals. Research in physiology helps us to understand how the body works in health, what goes wrong in disease, and how the body responds to the challenges of everyday life.

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