



Conference on Nutrition and Healthy Ageing Plenary Lecture IV

Locomotion, cognition and influences of nutrition in ageing

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Gait and cognitive impairments in older adults can reflect the simultaneous existence of two syndromes that affect certain brain substrates and pathologies. Nutritional deficiencies, which are extremely common among elderly population worldwide, have potential to impact the existence and rehabilitation of both syndromes. Gait and cognition are controlled by brain circuits which are vulnerable to multiple age-related pathologies such as vascular diseases, inflammation and dementias that may be caused or accentuated by poor nutrition or deficiencies that lead to cognitive, gait or combined cognitive and gait impairments. The following review aims to link gait and cognitive classifications and provide an overview of the potential impact of nutritional deficiencies on both neurological and gait dysfunctions. The identification of common modifiable risk factors, such as poor nutrition, may serve as an important preventative strategy to reduce cognitive and mobility impairments and moderate the growing burden of dementia and disability worldwide.

Gait: Cognition: Nutrition: Ageing

The population of adults aged 60 years and older worldwide is projected to grow from 605 million in 2000 to 2 billion in 2050⁽¹⁾. These findings have brought a sense of urgency to understanding ageing processes and the associated risk factors of many morbidities and mortality. Typically, the 'normal ageing' process entails a myriad of alterations in sensory, motor and cognitive functions that have been linked to nutritional deficiencies⁽²⁾, poor quality of life^(3–5), functional decline⁽⁶⁾, increased risks of falls^(7–10) and impaired mobility⁽⁶⁾. Moreover, the causal role of nutritional deficiencies has been described for many of these premature cognitive and motor decline^(11–15).

Disease-related motor impairments, including gait disorders and slowing of movements, are increasingly common with advancing age. A population-based study in the USA showed a 35% prevalence of clinically diagnosed gait disorders among community-dwelling persons over age 70⁽¹⁶⁾. The prevalence of cognitive impairments of varying severity also increases with age with one study reporting that 17% of adults aged 65 years and older in their population-based cohort had cognitive impairments without meeting criteria for dementia and 8% had dementia⁽¹⁷⁾.

Increasingly, the simultaneous existence of both gait and cognitive impairments in ageing has been

recognised. Camicioli *et al.*⁽¹⁸⁾ reported that gait impairments were seen in over 50% more of cognitively impaired participants compared with cognitively normal participants. While the co-occurrence of gait and cognitive impairments in older adults may reflect a simple co-existence of common age-related syndromes⁽¹⁸⁾, others have proposed that the co-occurrence of these two geriatric syndromes may be related to a common underlying pathology^(19,20). Moreover in many cases, poor diet and nutrition among elderly populations may accentuate these syndromes and in some cases may even be the underlying cause of pathologies. Nutritional deficiencies have been cited as risk factors for balance and mobility issues as well as falls in the elderly^(15,21).

Intact gait control requires the efficient integration of many neural systems, including motor, sensory and cognitive processes, and cognitive subsystems such as memory, attention and executive function^(19,22). Gait control is predominately mediated by frontal subcortical circuits. This circuitry is also known to facilitate memory, attention and executive functions^(23,24). Therefore, as this circuitry is particularly susceptible to impairment as part of the normal ageing process, mechanisms such as poor diet and nutrition that are related to common pathologies such as vascular diseases and

Abbreviations: MCI, mild cognitive impairment; MTR, motoric cognitive risk.

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inflammation could trigger cognitive, motor or combined cognitive and motor impairments in older patients^(25–27).

In the following sections, we review several classifications of gait dysfunction, cognitive impairments and nutritional deficits, as well as some common mechanisms of pathological processes that have been linked to cognitive and motor dysfunctions. Furthermore, we will examine the clinical utility of diagnosing combined gait and cognitive impairments, and discuss emerging intervention strategies that build on the interplay of gait and cognitive functions.

Gait dysfunction, cognitive impairments and nutritional deficits

Gait dysfunction

Gait impairments can be classified into neurological or non-neurological subtypes following clinical examination of walking patterns. Neurological gait abnormalities result from focal or diffuse lesions affecting the neural pathways that link cortical motor centres to the peripheral neuromuscular systems⁽²⁸⁾. Neurological gait abnormalities are further classified into: unsteady, ataxic, neuropathic, frontal, Parkinsonian, haemiparetic and spastic subtypes^(28,29). Non-neurological gait abnormalities result from physical limitations to walking, such as arthritis or foot deformities. Combinations of neurological and non-neurological subtypes can also exist in older adults.

An alternate clinical gait classification divides abnormalities into low-, middle- and high-level disorders^(30,31). In low-level gait disorders, only one major afferent sensory system (visual, proprioceptive or vestibular) is affected. Middle-level disorders result from spasticity (due to myelopathy from cervical spondylosis and stroke), Parkinsonism or cerebellar ataxia. High-level gait disorders include cautious gait, frontal gait disorders and psychogenic gait disorders, and may result from disruptions in cortico-cortical and cortico-subcortical connections.

The reliability and validity of most gait classification systems have not been verified and many gait subtypes overlap. This may in part explain why there is a paucity of studies that have employed clinical gait subtypes, an essential part of the neurological evaluation, to predict geriatric outcomes.

Accurate identification of neurological gait subtypes enables anatomical localisation of lesions, guides investigations, and provides hints to the underlying pathology. Identifying gait subtypes is also helpful in risk prognostication for motor and cognitive outcomes in clinical practice. For instance, while neuropathic gaits that present with foot drops were reportedly associated with increased fall risk⁽³²⁾, frontal gait disorders that present with short shuffling steps and difficulty lifting feet have been associated with increased risk of developing dementia, especially vascular dementia⁽²⁸⁾.

Cognitive syndromes

Cognitive disorders, unlike gait disorders, are categorised on a spectrum of cognitive decline, beginning with cognitive normalcy, transitioning to intermediate states such as the mild cognitive impairment (MCI), and often reaching an endpoint of dementia. MCI is defined as an impairment in one or more domains of cognitive function, without interference in daily activities in non-demented individuals⁽³³⁾. It is sub-classified into three categories, amnesic MCI, which predominately involves memory impairments; non-amnesic MCI, which involves impairments in cognitive domains, such as executive function, language or visuo-spatial impairments, and lastly combined MCI, which involves multiple impairments across both memory and other cognitive domains⁽³⁴⁾. Patients who meet MCI criteria in clinical practice are at higher risk of transitioning to dementia⁽³⁴⁾.

Presence of neurological gait subtypes as well as quantitative gait impairments have been linked to MCI^(28,35,36). Recent studies suggest that gait slowing may precede declines in cognitive tests in older adults^(37,38). Hence, gait may complement cognitive assessments in MCI. The role of gait assessment in predicting transitions to dementia in MCI patients requires further investigation.

Nutrition

A high prevalence of malnutrition and nutritional deficiencies has been reported among elderly populations^(15,21). The elderly are particularly vulnerable for malnutrition due to many age-related pathological and physiological risk factors⁽²⁾. Some common age-associated physiological risk factors among the elderly include a reduced sense of smell and taste, impaired absorption of certain micronutrients and minerals, such as vitamin D, and a reduced metabolic rate⁽²⁾. Other risk factors include depression, isolation and use of medications, which may decrease appetites⁽²⁾. Malnutrition and deficiencies are associated with negative physical and cognitive outcomes among the elderly^(2,15,39,40). Specifically, vitamin deficiencies have been associated with poor physical function^(2,41,42) as well as cognitive decline⁽⁴⁰⁾. Conversely, dietary patterns and adherence to specific diets have been shown to prevent risk factors, such as inflammation and vascular diseases that in turn are associated with both cognitive and mobility decline^(43–46). Thus, malnutrition and dietary deficiencies represent a modifiable link between mobility and cognitive decline with potential to slow or prevent the transition to disability and dementia.

Gait dysfunction and cognitive impairments

Mild cognitive impairment

MCI is diagnosed in individuals who have more cognitive deficiencies than expected for their age and education⁽³³⁾, and is considered to be a transitional stage between normal ageing and dementia. Deficits in fine

and complex motor skills equilibrium, and limb coordination have been reported in older adults with MCI^(47,48). In particular, results show participants with MCI to have reduced performance on assessments of balance, gait function and coordination when compared with normal controls^(47,48). Moreover, early motor dysfunction, assessed by presence of gait slowing, co-exists with and may even precede the onset of cognitive decline in older adults⁽⁴⁹⁾. In addition to slow gait, poor performance on individual quantitative gait variables was reported to be more common in those with MCI when compared with individuals with no cognitive impairments⁽³⁵⁾. These findings and others support^(19,20,25,50,51) the notion that higher level cognitive processes such as executive attention and memory are associated with gait and indicate an important link between motoric and cognitive impairments in MCI. Therefore, quantitative gait assessments could provide early diagnostic clues of cognitive deficits in regions of the brain involved in gait very early on in its course.

Motoric cognitive risk syndrome

Despite growing evidence of the link between cognitive impairments and motor performance in ageing, there have been limited attempts to capitalise on these findings in dementia risk prognostications. The recently described motoric cognitive risk (MCR) syndrome offers preliminary support for a motor-based MCR syndrome that identifies older individuals at high risk for transitioning to dementia, especially vascular dementia⁽⁵²⁾. MCR is diagnosed when a patient meets all four of the following criteria: (1) cognitive complaints; (2) slow gait (velocity one SD or more below age and sex appropriate mean values); (3) preserved activities of daily living; (4) absence of dementia. Thus, the MCR criteria are similar to those employed to define MCI, with the exception of the objective cognitive criteria in MCI being substituted by the slow gait requirement in MCR syndrome. MCR has strong predictive validity for dementia: older participants meeting criteria for MCR were over three times likely to develop dementia and more than twelve times likely to develop vascular dementia. Interestingly, MCR syndrome was a better predictor of dementia than cognitive complaints or slow gait alone. While there is overlap between MCR and MCI cases, MCR syndrome still predicted risk of dementia after accounting for MCI subtypes. Furthermore, this research provides a clinical approach to identify high-risk individuals and those who may benefit from preventive interventions.

Nutrition, gait and cognition

Nutritional deficiencies can simultaneously impact gait and cognition, and contribute to the growing prevalence of cognitive disorders and mobility disabilities worldwide. The negative effects of poor nutrition are potentially modifiable, suggesting that a better understanding of the impact of nutrition on gait decline and cognitive

functions could be used as a springboard to develop new interventions to prevent or diminish gait and cognitive impairments in the elderly.

Nutritional deficiencies

Vitamin D deficiency is a prevalent condition among the elderly, affecting approximately 40–100% of those living in Western countries^(40,53), and has been reported to negatively impact physical performance^(41,42). Vitamin D acts as a stimulant for calcium absorption; therefore, deficiencies resulting in reduced bone density and softening can make certain groups of people particularly vulnerable to fractures, osteoporosis and other consequences⁽⁵³⁾. Studies have reported that vitamin D was positively associated with all three components of a physical performance test, including a walking test, chair rise and tandem stand^(41,42). Moreover, the authors reported the strongest predictor of physical decline was the walking test⁽⁴¹⁾, indicating a potential role for vitamin D supplementation as a prevention strategy of future mobility disabilities in the elderly.

Low levels of vitamin D have also been associated with cognitive decline⁽⁴⁰⁾. A 6-year prospective study of the link between vitamin D deficiencies and cognitive decline indicated that those with severe deficiencies (serum 25-hydroxyvitamin D <25 nmol/l) had significant declines on tests of executive functions and general cognition over the study period⁽⁴⁰⁾. Thus, findings from this study present an early link between low levels of vitamin D, cognitive and motor decline in the early stages of neurodegenerative disease.

Inflammation and nutrition

While normal ageing is associated with a low-grade systemic inflammation, previous studies have linked higher levels of inflammatory markers to physical function and mobility impairments in older adults^(26,54,55). A recent review of the influence of nutrition on inflammation indicated that diets low in saturated fats including a high intake of fruit, vegetables and grains are associated with reduced inflammation⁽³⁹⁾. Cross-sectional studies have demonstrated an association between high serum levels of IL-6 and TNF- α with worsening of functional and mobility status^(56–58). However, only elevated serum levels of IL-6 but not TNF- α were associated with increased rates of decline in gait speed when examined prospectively⁽⁵⁹⁾; suggesting that not all inflammatory markers are involved in motoric decline.

In addition to mobility impairments, inflammation is also implicated in the cascade that leads to the development of amyloid neuritic plaques, one of the pathological hallmarks of Alzheimer's disease⁽⁶⁰⁾. Studies have linked cognitive decline to deficiencies in micronutrients such as folates, B₁₂ and vitamin C^(2,45,61), which have been shown to lower levels of inflammation⁽⁶²⁾. Epidemiological studies have identified associations between specific inflammatory markers such as increased IL-6 levels with a decline in the ability to encode new information and recall learned information; aspects of cognition affected early in Alzheimer's disease⁽⁶³⁾.



Vascular diseases, nutrition and cognition

The economic burden of CVD is well known with an estimated 17.3 million people dying annually due to a CVD and over 80% of those deaths being in middle or low-income countries⁽⁶⁴⁾. The cause of this may primarily be due to the increased exposure to risk factors such as smoking and diets that are typically high in saturated fats and sodium⁽⁶⁴⁾. These types of diets have been linked to vascular diseases such as atherosclerosis and hypertension⁽⁶⁵⁾. Moreover, growing evidence suggests that vascular diseases such as hypertension, dyslipidemia, hyperinsulinemia, type 2 diabetes, obesity and subclinical atherosclerosis increase risk for cognitive decline and dementia^(66,67). This has spurred a growing interest in exploring the impact of whole types of foods (e.g., fruit and vegetables) and dietary patterns. The Mediterranean diet, which is high in consumption of fruit, vegetables and grains, and low in saturated fats, has been associated with a decreased risk for CVD, several forms of cancer, mortality and most recently to dementia^(45,68–70). Scarmeas *et al.* found that higher adherence to the Mediterranean diet was associated with lower risk of developing incident MCI and Alzheimer's disease^(44,45). Moreover, these investigators found that seniors who adhered to healthy diet and regular physical activity had a 12% risk reduction of Alzheimer's disease compared with those who did neither⁽⁴⁵⁾. Moreover, a recent review of diet and cognitive decline supported the protective role of the Mediterranean diet in preventing all vascular conditions linked to dementia⁽⁴³⁾.

Vascular diseases, nutrition and gait

In elderly patients, vascular lesions are strongly associated with CVD such as hypertension, diabetes or hyperlipidemia⁽⁷¹⁾, all of which are also associated with poor dietary habits⁽⁴³⁾. The accumulation of vascular structural abnormalities can account for not only cognitive decline^(72–74) but gait abnormalities as well^(20,75,76). The severity of periventricular white matter lesions is associated with a decline in the speed of mental processing⁽⁷³⁾, as well as poorer performance in fluid intelligence measures^(72,74). Subclinical white matter hyperintensities, brain infarcts and brain atrophy predicted a faster rate of decline in gait speed over time⁽⁷⁵⁾. In addition to velocity, Rosano *et al.* demonstrated that a decline in stride length, and an increase in step length variability, was indicative of the presence of brain infarcts and white matter hyperintensities in an elderly population free from stroke, dementia or other neurological diseases^(20,76). Vascular risk factors can lead to cerebral ischaemia secondary to impairment in arterial vasoreactivity, obstruction of small subcortical arterioles or hypoperfusion⁽²⁵⁾. Vascular lesions can be either focal, resulting in lacunar infarctions, seen in the thalamus, basal ganglia, internal capsule or brainstem⁽⁷⁷⁾ or diffuse, affecting the periventricular white matter⁽⁷⁸⁾. The periventricular white matter consists of the ascending thalamocortical and descending corticospinal tracts, which subservise gait and balance functions⁽²³⁾. The frontal–subcortical connections, which control

speed of cognitive processing and executive function, also travel within the periventricular white matter⁽²⁴⁾. Owing to the close proximity of these two circuits, white matter lesions can simultaneously affect motor and cognitive functions, and may be caused by poor nutrition which result in pathologies that are potentially preventable through interventions to improve healthy lifestyle factors.

Interventions

Modifiable lifestyle variables such as diet, physical activity and cognitive interventions may prevent cognitive decline via effects on cardiovascular, stress, inflammation and other pathways. Defining the role of healthy lifestyle factors in dementia may translate into effective preventive interventions.

Physical activity and nutrition-based interventions

Physical activity and good nutrition contribute to healthy ageing and reduces morbidity and mortality⁽⁷⁹⁾. Physical activity has been shown to have protective effects against mortality in patients with chronic diseases such as CVD⁽⁸⁰⁾. Many studies have examined the effect of physical activity on cognitive performance in older individuals. For instance, Baker *et al.* demonstrated an improvement in executive function tests in individuals with normal cognition who underwent a 6-month aerobic exercise programme compared with healthy controls who participated in a stretching regimen⁽⁸¹⁾. The researchers further demonstrated an improvement in executive function after a 6-month aerobic exercise programme in individuals with MCI⁽⁸²⁾. A French study enrolled patients with dementia from a nursing home, half of whom took part in three 60 min exercise sessions per week that strategically focused on improving walking, stamina and equilibrium⁽⁸³⁾. The thirty-one individuals who underwent the physical intervention showed improvement in composite cognitive functions, while the sixteen participants in the usual care control group showed a decline in cognitive functions.

A recent review of the impact of nutrition interventions on health outcomes among community-dwelling older adults reported that interventions that involved active participation in personal nutrition plans were the most effective for positive outcomes for older adults⁽⁸⁴⁾. The findings from several studies revealed that nutritional intervention improved memory and decreased falls⁽⁸⁴⁾. Other studies have not supported the role of nutritional supplements in stroke prevention and treatment^(85,86). A meta-analysis of data of the influence of B-vitamins on stroke patients revealed that the effectiveness of B-complex vitamins as a stroke prevention strategy cannot be established⁽⁸⁵⁾. One randomised control trial indicated that a daily supplement of folic acid and B-vitamins after a stroke was safe, but not effective in reducing the future incidence of stroke⁽⁸⁶⁾. However, investigators on another clinical trial found a significant association between B-vitamins and folic acid

supplements on depression reduction in stroke patients⁽⁸⁷⁾. Although the effect of nutrition interventions on particular health outcomes has not been conclusive in each study, they have all provided evidence for potential benefits of nutrition awareness and improved dietary habits on overall health status^(84,85). Moreover, collectively these studies support the link between gait and cognition by providing evidence that physical exercise and nutrition-based interventions may result in improvements in cognition and physical functioning.

Cognitive remediation and mobility

The reverse relationship between cognitive interventions and their effect on gait are being explored in recent studies. Cognitive remediation approaches using computerised programmes or cognitive training have demonstrated an improvement in attention and executive function as well as memory in cognitively normal older adults. Verghese *et al.*⁽⁸⁸⁾ conducted a pilot study in which twenty-four frail older adults were randomly assigned to either participate in a computerised cognitive remediation programme or were in a usual care group for a 12-week period. The cognitive remediation group showed an improvement in gait velocity during normal walking and during walking while talking conditions compared with their baseline performance. This small study suggests the possibility that cognitive remediation could be a new, non-pharmacological means of modifying gait performance, especially during dual-task conditions.

Participants who received training in dual-tasking have demonstrated improvements in walking abilities^(89,90). Schwenk *et al.* evaluated the efficacy of a 12-week dual-task training programme in seniors with dementia. The participants were randomised to either a dual-task exercise session, involving walking while performing complex motor or cognitive activities, or a low-intensity exercise session⁽⁸⁹⁾. After 12 weeks, the group that received dual-task training performed significantly better on gait in a complex dual-task condition compared with the control group. Mirelman *et al.* examined the efficacy of a treadmill training programme enhanced with virtual reality in patients with Parkinson's disease⁽⁹⁰⁾. After 6 weeks training, gait velocity, stride time and stride length significantly improved in normal and dual-tasking conditions, and gait variability decreased (improved) under the dual-task condition. These preliminary studies support the feasibility and validity of cognitive-based approaches to improve mobility.

Conclusions

Review of the literature suggests that the co-existence of gait and cognitive impairments in older adults are related to common underlying pathologies and are not an age-related phenomenon. Importantly, both mobility and cognitive dysfunctions have been linked to nutritional deficiencies which may have caused or

prolonged deficits in both areas. Further studies need to address the common biological and brain substrates underlying cognitive-motor impairments and identify causal risk factors, such as nutritional deficits, to improve current risk assessment procedures and develop novel interventions to maintain functional independence in older individuals.

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