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Interactions of cognitive and physical ageing

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Introduction

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Introduction

Decline in cognitive and physical performance are striking characteristics of the ageing process. Declining performances are already observed from the third decade of life with a steeper decline from the sixth decade of life^{1,2}. Both cognitive and physical performance are important indicators of quality of life, strongly determining functional abilities and with that the ability to live independently^{3,4}. With increasing life expectancy, the number of elderly people with impaired cognitive and physical performance will grow rapidly, putting a high demand on health care resources⁵. Understanding the age-related changes in cognitive and physical performance and most importantly their interactions is required for the development of preventive and therapeutic paradigms.

However, the temporal order in which age-related changes in cognitive and physical performance occur is still largely unknown; it is unclear whether decline in cognitive performance precedes decline in physical performance, whether this temporal relationship is the other way around or whether they occur at the same time. Current literature is inconclusive showing uni- as well as bidirectional relationships between cognitive and physical performance⁶⁻⁹. Differences in findings between studies using different measures of cognitive and physical performance, i.e. global measures representing functioning on several cognitive or physical domains and domain specific measures, suggest dependence of the temporal relationship on these aspects⁹. Furthermore, it has become more and more evident in recent years that study findings might differ across different age ranges, especially for older populations aged 75 and over^{10,11}. Unfortunately, studies are lacking assessing the temporal relationship between cognitive and physical performance across different age ranges and including various global and domain specific measures. Therefore, important indicators for an effective clinical assessment, development and application of (already existing) interventions are missing as well.

Insights into the interactions between cognitive and physical performance might be suggestive for potential causal mechanisms. The temporal order of the interaction between cognitive and physical performance might indicate whether cognitive and physical performance are in each other's causal pathway or whether their decline has common underlying causes. Such common causes may be illustrated by previous studies showing a potential role for brain pathology or a role for biological aspects of ageing such as increases in the number of senescent cells, i.e. cells with a permanently arrested cell cycle, or the decline of metabolic control¹²⁻¹⁵. These aspects have been shown to be important indicators of biological age reflecting the ageing rate of an individual, which may deviate from its calendar age. However, the association of biological age with cognitive and physical performance is still unknown and with that the potential insight this might give in the ageing process.

For the assessment of physical performance, instrumented measures are increasingly introduced in research and clinical settings to obtain a more refined observation of the individual^{16,17}. These instrumented measures, obtained by e.g. camera-based systems, force plates or body fixed sensors, have been proven to be useful for the early identification and prediction of pathology such as Parkinson's Disease^{16,18}. The additional value of these measures for identification of age-related changes in physical performance and understanding of underlying determinants has not been established.

Aim of this thesis

The aim of this thesis was to enhance our understanding of age-related changes in cognitive and physical performance and their interactions. We focused on global and domain specific measures of cognitive and physical performance and assessed the interactions across different groups of calendar and biological age by including four study populations. Furthermore, instrumented measures of physical performance were introduced to assess their potential additional value.

Study populations

The Leiden Longevity Study

The Leiden Longevity Study (LLS) is a longitudinal cohort of families of at least two long-lived Caucasian siblings of Dutch descent fulfilling the age-criterion of 89 years or older for males and 91 years or older for females¹⁹. In this thesis, we used the middle-aged to older population of offspring of these nonagenarian siblings (n=500, mean age (standard deviation) 66 (6) years), who are enriched for familial factors of longevity, together with their partners as controls of similar age and sharing the same environmental conditions. Cross-sectional data was available on the cognitive domains of memory and executive function and the physical domains of standing balance, sit-to-stand transfers and walking across a 4-meter walk starting from standing position and across a steady-state 25-meter walk, i.e. without an acceleration or deceleration phase, both at usual pace. Thereby, a body fixed sensor positioned at the lower back was used during the performance of each of these physical tasks. This study population was especially used to get more insight into the sensitivity of different cognitive and physical domains to both calendar age and biological age, by comparing offspring of nonagenarian siblings with their partners, and assessing the associations with brain pathology.

The Longitudinal Aging Study Amsterdam

The Longitudinal Aging Study Amsterdam (LASA) consists of a random sample of middle-aged to older adults (n=3107, mean age (standard deviation) 71 (9) years) drawn from the population registers of eleven municipalities in three culturally distinct geographical areas in the Netherlands²⁰. Four repeated measurements on cognitive and physical performance assessed with a time interval of approximately three years were used. Besides domain

specific measures of memory and executive function, global cognitive function was assessed covering several domains like orientation, memory, attention and executive function. Physical domains included handgrip strength used as measure of overall muscle strength and walking speed across a 6-meter walk starting from standing position at maximal pace. This longitudinal study was used to assess the temporal relationship between global and domain specific measures of cognitive and physical performance across different age groups by stratification of the study population.

The Leiden 85-plus Study

The Leiden 85-plus Study includes inhabitants of the city of Leiden, the Netherlands, who all reached the age of 85 years (n=599) and were followed up yearly until the age of 90 years²¹. Global and domain specific measures of cognitive and physical performance that were used were similar to those included in LASA: global cognitive function and memory and executive function, handgrip strength and walking speed. This study population was added to the analyses on the temporal relationship between cognitive and physical performance in LASA, resulting together in an age range from 55 to 90 years.

Elderly outpatients

The cross-sectional study of elderly outpatients consists of community-dwelling elderly (n=299, mean age (standard deviation) 82 (7) years) referred to the geriatric outpatient clinic of a middle-sized teaching hospital (Bronovo Hospital, The Hague, The Netherlands) for a comprehensive geriatric assessment. This assessment included global and domain specific measures of cognitive and physical performance: global cognitive function, standing balance and walking speed across a 4-meter and 6-minute walk starting from standing position and a steady-state 10-meter walk, all at usual pace. Additional to the other three study populations, this particular population was used to assess the cross-sectional association between different cognitive and physical domains in a clinically relevant population giving insight into the possible influence of health status or biological age on this relationship.

Outline

Chapters two and three describe the sensitivity of domain specific measures of cognitive and physical performance to calendar and biological age assessed among the offspring of nonagenarian siblings and their partners of the LLS. In **chapter four**, the cross-sectional relationship between the cognitive and physical domains assessed in the LLS is presented and the influence of brain pathology on these domains as potential common underlying determinant. **Chapters five and six** focus on the cross-sectional relationship between different cognitive and physical domains in elderly outpatients. **Chapter seven** describes the temporal relationship between global and domain specific measures of cognitive and physical performance across different age groups of LASA and the Leiden 85-plus Study. Finally, in **chapter eight**, the main findings are summarized and discussed with a reflection on the clinical implications and future research.

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