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Urbanisation and Cognitive Ageing: An Investigation of Geographical Variations in the Cognitive Health of Older Adults in Ireland.

Marica Cassarino, B.Sc., M.Sc.

Publication-based thesis submitted for the degree of PhD by Research

National University of Ireland, Cork

School of Applied Psychology

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Head of School: Prof. John McCarthy

Primary Supervisor: Dr. Annalisa Setti

Secondary Supervisor: Prof. John McCarthy

To Kamil who made me begin this wonderful journey.

To Lorenzo who made this journey more adventurous.

Table of Contents

Table of Contents **5**

List of Tables **11**

List of Figures **13**

Declaration **15**

Acknowledgements **17**

Abstract **21**

Chapter 1 - Introduction **23**

Chapter 2 – Literature Review **35**

Abstract **35**

Introduction **36**

Environment and Cognition: Historical Perspective **42**

Prevalence of Dementia in Rural vs. Urban Areas **47**

Direct Associations between Environmental Characteristics and Cognition **50**

Environmental restorative properties, visual/auditory complexity and attention 50

Environmental layout, level of clutter and spatial cognition 54

Environmental noise and multisensory stimulation in relation to memory and attention 56

Mediating Factors **58**

Environmental factors associated with socioeconomic status 58

Environmental factors associated with lifestyle: physical activity and social engagement 60

Potential Cognitive Mechanisms Underlying the Association between Physical Environment and Cognition 63

Future Directions 67

Chapter 3 – Operationalisation of Environmental Complexity 71

Abstract 71

Introduction 72

Environmental Measures Linking Complexity to Cognitive Ageing ... 73

Complexity and Cognitive Performance 80

Complexity and Environmental Preference 85

Complexity and Perceived Usability 88

Discussion and Conclusion 90

Chapter 4 – Research Objectives and General Methodology 97

Aim and Focus 97

The Irish Longitudinal Study on Ageing (TILDA) 99

Participants 101

General design 104

TILDA Measures Used in the Project 105

Measures of Place of Residence 105

Cognitive assessments 107

Covariates....112

Chapter 5 - Study One....119

Abstract....119

Introduction....121

Methods....124

Participants....124

Design....127

Explanatory variable....127

Outcome variables....127

Covariates....129

Statistical analyses....130

Results....131

Sample characteristics....131

Regression analyses....138

Interactions between past and current residence....142

Discussion....146

Conclusions....154

Results of Analyses on a Larger Sample....155

Chapter 6 - Study Two....161

Abstract....161

Introduction....162

Methods **165**

Participants 165

Design 165

Population density 165

Cognitive Measures 167

Covariates 168

Statistical analyses 169

Results **170**

Sample characteristics 170

Regression Analyses 178

Discussion **182**

Chapter 7 - Study Three **187**

Abstract **187**

Introduction **188**

Methods **190**

Participants 190

Design 190

Travel Time to Nearest Gateway 190

Cognitive Measures 191

Covariates 192

Statistical analyses 194

Results **195**

Sample characteristics 195

Regression analyses 200

Discussion **203**

Chapter 8 - Study Four **209**

Abstract **209**

Introduction **211**

Methods **214**

Participants 214

Design 215

Place of residence 215

Cognitive Measures 216

Covariates 217

Statistical analyses 219

Results **221**

Sample characteristics at W1 and changes between the two waves 221

Regression analyses 227

Discussion **230**

Chapter 9 - Study Five **233**

Abstract **233**

Introduction **235**

Methods **237**

Participants 237

Design 237

Explanatory measures 238

Outcome measure 240

Covariates 240

Statistical Analyses 242

Results **243**

Descriptive Data 243

Regression Analyses 251

Discussion **254**

Chapter 10 - Discussion **257**

Strengths and limitations **267**

Future directions **270**

Conclusions **272**

References **275**

Appendix 1 ..... **347**

Appendix 2 ..... **349**

List of Tables

Table 2.1.....44

Table 4.1.....103

Table 4.2.....110

Table 4.3.....111

Table 4.4.....115

Table 5.1.....132

Table 5.2.....136

Table 5.3.....140

Table 5.4.....143

Table 5.5.....157

Table 6.1.....167

Table 6.2.....171

Table 6.3.....176

Table 6.4.....179

Table 7.1.....197

Table 7.2.....202

Table 8.1.....223

Table 8.2.....228

Table 8.3.....229

Table 9.1.....243

Table 9.2.....245

Table 9.3.....249

Table 9.4.....252

List of Figures

Figure 2.1 41

Figure 3.1 75

Figure 5.1 126

Figure 5.2 145

Figure 6.1 181

Figure 9.1 253

Declaration

I hereby declare that this thesis is my own work and has not been submitted for another degree, either at University College Cork or elsewhere.

Signed_____

Date_____

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Abstract

Ageing and urbanisation worldwide, and the increasing risk of chronic conditions such dementia and cognitive impairment with higher life expectancy, urge to understand the impact of city or rural living on healthy cognitive ageing. Based on the premise that environmental features influence cognition, my doctoral project investigated whether different levels of urbanisation supported specific cognitive skills in older age.

Firstly, a thorough review of the literature identified environmental characteristics (e.g. urban vs. rural living, perceptual load caused by traffic or noise, presence of green) which could "train" the brain to maintain efficiency and age well. We proposed the concept of complexity to operationalise and measure the dynamic set of physical factors (encompassing a macro, meso and micro level of analysis) that make the lived environment optimally stimulating for cognitive functioning, and which could therefore be key contributors to cognitive-friendly environments.

Using data from The Irish Longitudinal Study on Ageing (TILDA), the PhD project investigated macro (urban-rural living) and meso level (population density and accessibility to urban environments) geographical variations in multiple cognitive domains for approximately 5,000 healthy community-dwelling people age 50+, to test the hypothesis that in Ireland higher urbanisation (i.e., higher environmental complexity) would be associated with better performance. We found a positive association (cross-sectionally, but not longitudinally) between urbanisation and executive functions, a key cognitive skill to interact with the environment, in line with our hypothesis. Healthy lifestyles moderated geographical variations in global cognition, in line with research on cognitive reserve.

This PhD research provides new evidence on the specific cognitive skills amenable to environmental influences, namely executive functions, and stimulates future work to identify neighbourhood characteristics which can ‘train’ executive functions in older age, with implications for the design of usable and cognitively stimulating places for older people.

Chapter 1 - Introduction

Demographic ageing is an increasing trend worldwide. In 2015, more than 900 million people in the world (approximately 11%) were aged 60 and older, and this figure is expected to double by 2050 due to higher life expectancy and reduced fertility rates (Christensen, Doblhammer, Rau, & Vaupel, 2009; Lutz, Sanderson, & Scherbov, 2008; United Nations, 2015; World Health Organization, 2015). A second growing global trend is urbanisation (United Nations, 2015; World Health Organization, 2007): With over half the population worldwide living in cities as of 2015, and a forecasted increase to 60% by 2030, it goes without saying that more and more urban dwellers will be aged over 60 in the next decades.

Ageing and urbanisation worldwide are re-shaping the needs and challenges of our society, urging the scientific community to understand how places can be designed to optimise opportunities for health, security and participation for older people, that is, to be "age-friendly" (Phillipson, 2011; World Health Organization, 2007). This global priority is informed by the need to promote active and healthy ageing (Beard & Petitot, 2010; World Health Organization, 2002, 2015) and to enable older individuals to age in their communities by maintaining independence and quality of life for as long as possible (Wiles, Leibing, Guberman, Reeve, & Allen, 2012), and it falls within the general growing interest in designing sustainable, supportive, and stimulating lived environments ("100 Resilient Cities - Rockefeller Foundation," 2014, "Cities | The Guardian," 2014, "CityLab," 2016, "OPENspace.eca.ed.ac.uk," 2017, "Project for Public Spaces," 2016, "Urbanism and Future Planning | Sustainable Cities Collective," 2014).

Within this global priority, while it is well-established that the built environment determines socio-economic, health and lifestyle inequalities which in turn influence cognitive health in ageing (Kerr, Rosenberg, & Frank, 2012; Lang et al., 2008; Mitchell, Richardson, Shortt, & Pearce, 2015; Renalds, Smith, & Hale, 2010; Winkler, Turrell, & Patterson, 2006), only recently research has begun to explore direct environmental and geographical influences on cognitive functioning in older age (Wu, Prina, & Brayne, 2014), for example in terms of designing built environments that offer an optimal level of stimulation for maintaining health (Giles-Corti et al., 2016; Kleinert & Horton, 2016). This is a new crucial research question given that ageing is the main risk factor for neurodegenerative diseases such as dementia and cognitive impairment, conditions which are increasingly becoming a primary cause of morbidity and mortality (Broe, 2003; Sachs et al., 2011; World Health Organization, 2012). Approximately 35.6 million people aged 60 years and older lived with a form of dementia worldwide in 2010, with a forecasted increase to 115.4 million by 2050 (Prince et al., 2013). A vast majority of these people will be living in urban contexts, therefore it is of paramount importance to understand whether this will represent an advantage for cognition and how to capitalise on city living for preventing cognitive decline and neurodegeneration. Considering the significant impact that these conditions have on wellbeing, independence and quality of life in older age (Ofstedal, Fisher, & Herzog, 2005), and, by consequence, the considerable economic and social costs (Cahill, O'Shea, & Pierce, 2012; Wimo et al., 2011, 2016), capitalising on the lived environment to support cognition is one of the main challenges for the coming years.

To meet this challenge, research needs to exploit the contribution of different disciplines, including Gerontology, Cognitive Sciences, Environmental Psychology,

Geography, Social Sciences and Economics. The availability of longitudinal studies such as The Irish Longitudinal Study on Ageing (TILDA, Kearney et al., 2011; Kenny, 2013) allows to jointly explore some of the multiple factors at play when studying the environmental impact on cognitive ageing, therefore providing evidence for policy making in terms of healthy living for older adults.

The interest in understanding the influence of the environment on human behaviour is not recent: Ecological models of development, for example, focus on the interaction of individuals with their environment (Barker, 1968; Canter & Craik, 1981; Lewin, Heider, & Heider, 1936) and suggest that both social and physical aspects of the environment actively influence human development at multiple levels (physical, cognitive, affective). David Canter (Canter, 1977; Canter, Stringer, & Griffiths, 1976) maintained that the physical arrangement of the lived environment encourages specific patterns of activities and certain psychological processes which enable people to understand, use and create places . The ecological systems theory (Bronfenbrenner, 1979; Bronfenbrenner & Ceci, 1994) proposed environmental influences on the individuals as multiple interactive systems, including not only the close family or the peer group, but also the wider physical and cultural context in which we grow old. Similarly, Gibson (2000) theorised that cognitive development depends on a complex interaction between individuals who perceive their surroundings and the opportunities for action offered by the environment, or *affordances* (Gibson, 1986). Based on the concept of affordances, Clark (1999a) defended his hypothesis of the *extended mind*, according to which cognition is not limited to the brain, but extends to the environment, it is embodied in the external world, and the properties of the environment are vital to individuals to plan actions and strategies to fulfil cognitive tasks. It is intuitive that, when interacting with their

surrounding environments, individuals benefit from the presence of a context which is physically supportive and stimulating, as shown for example in studies on ageing in place in relation to physical improvements to the home environment that support autonomy (Wahl & Oswald, 2010).

Despite the centrality of the physical environment in ecological models of person-environment interactions, however, this tends to be neglected in the study of cognitive processes and behaviour (Dunwoody, 2006).

Cognitive ageing shows significant individual differences (Cabeza, Anderson, Locantore, & McIntosh, 2002; Hedden & Gabrieli, 2004; Lindenberger & Ghisletta, 2009; Wilson et al., 2002), with some old or very old people showing less cognitive deterioration than others (Hedden & Gabrieli, 2004; Schaie, 2005). This is due to a dynamic interaction of genetic, individual and environmental influences across the lifespan (Baltes, Reese, & Lipsitt, 1980; Baltes, 1987; Baltes & Lindenberger, 1988; Boyd, Bee, & Johnson, 2009; Dickens & Flynn, 2001; Tucker-Drob, Briley, & Harden, 2013) which can affect the resilience and adaptability of the brain to age-related structural changes, also defined in terms of *cognitive plasticity* (Baltes & Lindenberger, 1988; Cabeza, 2002; Lövdén, Bäckman, Lindenberger, Schaefer, & Schmiedek, 2010) or as *cognitive reserve* (Stern, 2002, 2009). Cognitive plasticity is the ability of cognitive systems to flexibly adapt to increased internal or external demands by dynamically activating alternative or compensatory neural circuits (Lövdén et al., 2010). Similarly, Stern (2002, 2009) suggested that additional neural resources can be employed by cognitive systems as a source of functional reserve to compensate for brain damage. Both plasticity and reserve have been shown to be affected by environmental factors, such as education and active

lifestyles (Fillit et al., 2002; Hertzog, Kramer, Wilson, & Lindenberger, 2008; Jefferson et al., 2011; Kramer, Bherer, Colcombe, Dong, & Greenough, 2004; Stine-Morrow, Parisi, Morrow, & Park, 2008; Yang, Krampe, & Baltes, 2006). In addition, as it will be described in Chapter 2, animal and human studies on environmental enrichment have shown that environmental stimulation can cause changes in the brain which can contrast age-related decline (Diamond, 1988; Rosenzweig, Krech, Bennett, & Diamond, 1962). However, the direct influence of the design and structure of the built environment on the adaptability of the human brain is still unclear. Importantly, given the multidimensionality and multi-directionality of an individual's cognitive development in the lifespan (Baltes et al., 1980), whether aspects of the lived environment affect specific cognitive skills differently in ageing remains to be established. Research has shown that different cognitive domains follow specific trajectories during the life course, with fluid skills such as problem solving declining over time while knowledge-based crystallised skills (e.g., vocabulary) maintain stable performance until very late in life (Cattell, 1987; Horn, 1982; Horn & Cattell, 1967; Singer, Verhaeghen, Ghisletta, Lindenberger, & Baltes, 2003), and some evidence exists of differential environmental influences on fluid vs. crystallised cognitive skills (Sisco & Marsiske, 2012), which poses the question on which types of environments are more supportive of which cognitive abilities.

In an increasingly urbanised world, cities are complex environments which continue to change in structure and design over time, and their complexity implies both opportunities and challenges for the health of an individual growing old (Phillipson, 2011). Studies on prevalence of dementia and cognitive impairment in different environments have shown that rural areas present higher rates of these conditions (see for a review Cassarino & Setti, 2015; Russ, Batty, Hearnshaw,

Fenton, & Starr, 2012). This evidence provides some support to the hypothesis that different environments are conducive to more positive or negative cognitive ageing. In order to understand the multiple factors underlying this effect and look for further evidence we conducted a review of the existing epidemiological and experimental literature on associations between characteristics of the place of residence and cognitive ageing (presented in Chapter 2) which indicated on one hand lower prevalence and incidence of dementia and cognitive impairment in older populations living in urban rather than rural areas, and on the other hand a higher restorative potential of natural, green, places for cognitive skills such as attention. In addition, epidemiological studies both in Europe and the U.S. suggest an association between variations in health and population density, as well as between health and distance from urbanised and more resourced environments (see Chapter 6 and Chapter 7 for an in depth description of these studies and the research we conducted).

The evidence reviewed in Chapter 2 presents some issues when attempting to interpret the findings in the light of cognitive ageing: (1) epidemiological studies focus mainly on general cognitive impairment rather than multiple cognitive skills, limiting the understanding of whether the lived environment affects some cognitive abilities more than others; (2) most of the epidemiological studies consider patient populations rather than healthy older samples, which fails to inform on variations in cognitive performance in the healthy older population with implications for preventive interventions; (3) studies on cognitive restoration which compare exposure to natural or urban settings have used mainly younger populations, thus not informing on whether the restorative effects of exposure to more or less urbanised environments on cognition occur in a similar way in older people; (4) few or no

studies on variations in health based on population density or on travel time to urban environments have explored cognitive skills.

My doctoral project aimed to address these issues by investigating variations in cognitive performance for a comprehensive set of cognitive skills (global cognition, memory, speed of processing, attention and executive functions) in healthy older adults based on the level of urbanisation of the place of residence, operationalised as urban vs. rural residence (Study One, Chapter 5), levels of population density (Study Two, Chapter 6) and travel time to urban environments (Study Three, Chapter 7). We also explored longitudinally whether urban or rural residence affected cognitive changes over a two-year period (Study Four, Chapter 8).

The research hypothesis that guided this work was that urban environments would be more supportive of cognitive health in older age than rural places because presenting more complex cognitive stimulation to process, which promotes a more efficient cognitive functioning by stimulating attention and executive control. Within this perspective, rural places would present sub-optimal levels of stimulation for cognitive skills because not enough challenging, but at the same time highly urbanised environments would be expected to be daunting for cognitive functioning because presenting such a high level of complexity (e.g., traffic, noise, higher visual clutter) to become too challenging and over-whelming for the ageing mind. One can consider an older adult living in a small town and compare him/her with an older adult living in an urbanised environment: If both individuals are active and do not suffer from physical impairment, they would face very different situations and challenges in their environment when accomplishing simple daily activities such as going grocery shopping. What are these situations and challenges? Based on models

of optimal levels of stimulation for cognitive functioning (Lawton & Nahemow, 1973; Robertson, 2013; Yerkes & Dodson, 1908) and on existing studies on environmental influences on cognitive processing (see Chapter 3), we proposed a framework where environmental complexity is defined at different levels, going from the micro-level of perceptual features of environmental scenes (e.g. colour, clutter), to the meso level of design qualities of neighbourhoods and communities (e.g. legibility, aesthetic appeal), to the macro level of broad geographical areas (i.e., urban vs. rural living).

The studies conducted as part of these project addressed the macro and meso levels of investigation. In addition, we explored whether geographical variations in cognitive performance interacted with the level of engagement in physical activity to test the hypothesis that an active lifestyle could compensate for the cognitive disadvantage of living in a less stimulating environment (Study five, Chapter 9).

The thesis is therefore structured in 10 chapters.

Firstly, a review of the literature on the association between the lived environment and cognition informed the working hypothesis for the doctoral project, proposing that physical characteristics of the lived environment have a direct influence on cognition, and therefore can be optimised to train the ageing brain to age well (Chapter 2).

As no clear operationalisation of environmental measures with a direct impact on cognition is available in the existing literature, we conducted a targeted review and proposed environmental complexity as a key measurable contributor to cognitive ageing which should be investigated at multiple environmental levels (Chapter 3).

Thanks to a collaboration with The Irish Longitudinal Study on Ageing (TILDA), based in Trinity College Dublin (TCD), Ireland, we explored geographical variations in a comprehensive set of cognitive skills for a nationally representative sample of Irish healthy community-dwelling people aged 50 and older. Chapter 4 describes TILDA, the measures used for the doctoral project, and the general methodology employed.

Chapter 5 presents the first cross-sectional study (Study One), in which we explored variations in cognitive performance based on residence in urban places, rural areas, or other settlements. This study indicated a cognitive advantage for urban older dwellers, specifically in terms of executive functions, skills crucial to interact with the surrounding environment successfully.

We then developed these results in Study Two which explored cognitive performance in relation to levels of urbanisation operationalised as population density, a measure obtained by merging the TILDA dataset with the Irish Census, as presented in Chapter 6. This study showed better performance in terms of executive functions for groups living in more urbanised areas.

In the third study (Chapter 7), a collaboration with the All-Ireland Research Observatory (AIRO), Maynooth University, Ireland, made it possible for geocoded information on the area of residence to be linked with the location of residence of TILDA participants. We selected travel time to gateways as a measure of accessibility to urban environments, and found small but significant variations across multiple cognitive domains.

Chapter 8 describes the results of longitudinal analyses on effects of place of residence on changes in global cognition, memory and executive functions (Study Four).

Chapter 9 presents the results of Study Five on the interactions between level of engagement in physical activity and urban/rural residence and their effect on cognition. We found a significant moderation for global cognitive functioning.

Lastly, Chapter 10 presents an overall discussion of the project findings and their implications for future research, together with an account of its strengths and limitations.

Chapters 2, 3 and 5 have been published to peer-reviewed international journals and correspond respectively to the following references:

Cassarino, M., & Setti, A. (2015). Environment as “Brain Training”: A review of geographical and physical environmental influences on cognitive ageing. *Ageing Research Reviews*, *23, Part B*, 167–182. https://doi.org/10.1016/j.arr.2015.06.003

Cassarino, M., & Setti, A. (2016). Complexity as Key to Designing Cognitive-Friendly Environments for Older People. *Frontiers in Psychology*, *7*, 1329. https://doi.org/10.3389/fpsyg.2016.01329

Cassarino, M., O’Sullivan, V., Kenny, R. A., & Setti, A. (2016). Environment and Cognitive Aging: A Cross-Sectional Study of Place of Residence and Cognitive Performance in the Irish Longitudinal Study on Ageing. *Neuropsychology*, *30*(5), 543–557. https://doi.org/10.1037/neu0000253

Chapters 6 and 7 are in review for publication, while Chapter 8 is planned for submission to peer-reviewed international journals.

Preliminary analyses of Chapter 9 were presented at the Irish Gerontological Society 64th Annual and Scientific Meeting "Developing Cultures of Excellence in Ageing and Exploring the Needs of Marginalised Groups", Killarney, Ireland, in September 2016, and published as supplement on the journal Age & Ageing, corresponding to the following reference: Marica Cassarino, & Annalisa Setti (2016). Physical Activity Modulates Geographical Variations in Cognitive Ageing: Results from The Irish Longitudinal Study on Ageing (2016), *Age & Ageing*, *45* (suppl 2): ii13-ii56. doi: 10.1093/ageing/afw159.186.9

Chapter 2 – Literature Review

Environment as "Brain Training": A Review of Geographical and Physical Environmental Influences on Cognitive Ageing.[1]

Abstract

Global ageing demographics coupled with increased urbanisation pose major challenges to the provision of optimal living environments for older persons, particularly in relation to cognitive health. Although animal studies emphasise the benefits of enriched environments for cognition, and brain training interventions have shown that maintaining or improving cognitive vitality in older age is possible, our knowledge of the characteristics of our physical environment which are protective for cognitive ageing is lacking. The present review analyses different environmental characteristics (e.g. urban vs. rural settings, presence of green) in relation to cognitive performance in ageing. Studies of direct and indirect associations between physical environment and cognitive performance are reviewed in order to describe the evidence that our living contexts constitute a measurable factor in determining cognitive ageing.

Keywords: Aging, environment, cognitive reserve, brain training, urban, walkability.

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Introduction

Increased life expectancy (Lutz et al., 2008) and the remarkable economic impact of caring for the older members of our society (Wimo et al., 2011; World Health Organization, 2012) make the support of independent living and ageing in place a global priority (Black, 2008; World Health Organization, 2002, 2012). Cognitive health is a fundamental determinant of independent living and successful ageing (World Health Organization, 2002), and an urgent societal challenge considering the higher risk of cognitive decline and dementia with ageing (Prince et al., 2013; Sachs et al., 2011; World Health Organization, 2012).

The remarkable finding of brain plasticity (Diamond, 1988; Diamond, Krech, & Rosenzweig, 1964; Gibson & Petersen, 1991; Greenwood & Parasuraman, 2010; Lövdén et al., 2010; Pascual-Leone et al., 2011; Pascual-Leone, Amedi, Fregni, & Merabet, 2005; Rosenzweig et al., 1962) supports the idea that our environment can contribute to shape brain structure and functions. Animals and humans exposed to richer environmental stimulation present fewer signs of brain degeneration (Hannan, 2014; Herring et al., 2009; Landau et al., 2012; Robertson, 2013, 2014) and perform better in cognitive tasks than those not exposed to enriched environments (Berardi, Braschi, Capsoni, Cattaneo, & Maffei, 2007; Harati et al., 2011; Jankowsky et al., 2005; Robertson, 2013; Valenzuela & Sachdev, 2009). Animal studies in particular show that enriched environments can trigger morphological changes in the brain through sensory stimulation both in younger and older age (Baroncelli et al., 2012; Engineer et al., 2004; Landers, Knott, Lipp, Poletaeva, & Welker, 2011; Nithianantharajah & Hannan, 2009). These studies are in line with the concept of *cognitive reserve*, which captures the idea that environmental stimulation can build

resilience to cognitive ageing (Steffener et al., 2014; Stern, 2002, 2009; Tucker & Stern, 2014). There are several forms of environmental stimulation: Individuals with higher levels of education, stimulating jobs and more advantaged socioeconomic backgrounds show lower risk of dementia in older age (Sharp & Gatz, 2011; Stern, 2012; Valenzuela & Sachdev, 2006); social engagement and exercise have been shown to benefit cognition in numerous studies (Colcombe & Kramer, 2003; Greenwood & Parasuraman, 2010; Hertzog et al., 2008; Kelly et al., 2014; Lövdén, Ghisletta, & Lindenberger, 2005; Ratey & Loehr, 2011a); lastly, activities which offer mental stimulation influence hippocampal structural changes both in animals and humans (Erickson et al., 2011; Hertzog et al., 2008; Kelly et al., 2014; Kempermann, 2008; Kempermann, Kuhn, & Gage, 1997, 1998; Liu, He, & Yu, 2012; Lövdén et al., 2012; Spalding et al., 2013; Valenzuela, Sachdev, Wen, Chen, & Brodaty, 2008). These kinds of stimulation build cognitive and brain reserve allowing individuals who had ample opportunities for cognitive stimulation early in life to reach the threshold of cognitive pathology at an older age or at a more severe level of underlying brain damage than individuals whose life afforded fewer opportunities (Stern, 2002, 2009, 2012; Tucker & Stern, 2014). At the same time, targeted training interventions aimed to promote cognitive health in older age, defined as *brain training*, have proven effective in modifying the trajectory of cognitive ageing by improving performance in different areas of cognition, such as attention, executive functions and processing speed in a short or mid-term timeframe (Anguera et al., 2013; Ball, Edwards, Ross, & McGwin, 2010; Edwards et al., 2005; Mozolic, Long, Morgan, Rawley-Payne, & Laurienti, 2011; Nouchi et al., 2012; Szelag & Skolimowska, 2012; Toril, Reales, & Ballesteros, 2014; Willis et al., 2006). Brain training is a thriving field of investigation in the area of successful

ageing (Lustig, Shah, Seidler, & Reuter-Lorenz, 2009) and has now reached a broad audience (Aamodt & Wang, 2007); however, further research is needed to understand whether trained cognitive abilities transfer to untrained skills and real life contexts (Green & Bavelier, 2008; Martin, Clare, Altgassen, Cameron, & Zehnder, 2011).

Despite the vast interest in cognitive reserve and brain training as preventative or remediating factors for cognitive decline (Green & Bavelier, 2008; Martin et al., 2011; Valenzuela & Sachdev, 2009), surprisingly little attention has been devoted to quantifying the cognitive benefits of the interaction of individuals with their geographical environment in everyday activities (Dunwoody, 2006; Wu et al., 2014), arguably the most pervasive and complex form of cognitive training or stimulation. For example, for an older person going to the shop, keeping in mind the route and the shopping list, while not being distracted by people and events occurring along the way, is a fundamental means of 'training' the brain, which is presumably performed several times a week. The difficulty of this environmental training depends on where the person lives, and possibly the time of the day and means of transport chosen to reach their destination – an issue explored for example in occupational therapy to maximise opportunities for independent living (Broome, McKenna, Fleming, & Worrall, 2009; Di Stefano & MacDonald, 2003). Similarly, while the effects of dual tasking in ageing have been extensively documented experimentally (Donoghue, Cronin, Savva, O'Regan, & Kenny, 2013; Jain & Kar, 2014; Lindenberger, Marsiske, & Baltes, 2000), it is intuitive that crossing a busy road is a challenging form of multi-tasking, especially considering that older people may have slower walking speed, which makes the task difficult even in the absence of distractors (Romero-Ortuno, Cogan, Cunningham, & Kenny, 2010).

In the present review, we argue that the geographical environment - defined in terms of rurality vs. urbanisation, presence of green, environmental layout and complexity, levels of traffic and noise - can act as a source of brain training and possibly contribute to cognitive resilience in older age, and that, in line with the Yerkes-Dodson law of optimal arousal (1908), environmental stimulation can either facilitate cognitive performance or cause cognitive overload depending on the relationship between levels of stimulation and the individuals' cognitive and physical functionality. Here we review studies which show an association between environmental characteristics and cognition, with a particular emphasis on physical or more broadly geographical aspects of the environment that influence perceptual and cognitive processing. As for any other form of brain training and cognitive stimulation, the challenge is to define the dimensions of the environment which contribute the most to support or hinder cognitive healthy ageing (World Health Organization, 2007), and to understand the association between these dimensions and specific cognitive skills. We acknowledge the important role of factors for cognitive health in older age such as education or occupation, which have been extensively explored in the literature (Albert et al., 1995; Hertzog et al., 2008; Stern, 2009). However, the present work explores measures that could be considered to operationalise the hypothesis of physical environment as a source of brain training/cognitive stimulation for future studies. We firstly discuss evidence of direct environmental influences on cognition drawing from epidemiological studies on urban/rural differences in the prevalence of cognitive impairment, from experimental studies on attention and distractibility in natural vs. urban environments, from the literature on spatial navigation and driving in relation to environmental layouts and visual clutter, and from studies on cognition and environmental noise. We then

discuss mediating factors such as neighbourhood socioeconomic status (for example, neighbourhood affluence) and opportunities for active lifestyles (for example, exercise and walkability in the area of residence), which might moderate an indirect association between physical characteristics of the environment and cognitive health in older age. Figure 2.1 summarises the proposal that both direct (different exposure to, or interaction with, environmental stimuli) and indirect pathways (socioeconomic and lifestyle dimensions) link the environment with cognitive performance. By considering variables at different environmental levels going from broad geographical areas to characteristics of the proximal environment of residence, we aim to address environmental factors for cognitive health beyond simple macro urban/rural categories usually found in the literature. We focus on studies on older adults whenever they are available, otherwise considering studies on younger adults. New research questions and future developments to address this under-explored associations are discussed.

Understanding the influence of our lived environment on cognitive ageing will define strategies to modify or optimise environmental resources which improve cognitive ageing by supporting or even ameliorating specific cognitive abilities, in line with the evidence for environmental sustainability of health (Barton, 2009; Lavin, Higgins, Metcalfe, & Jordan, 2006). Importantly, it will also increase our capability to tailor brain training interventions to users' specific needs and environmental conditions, thus offering specific alternatives where urban planning is not an immediate option.

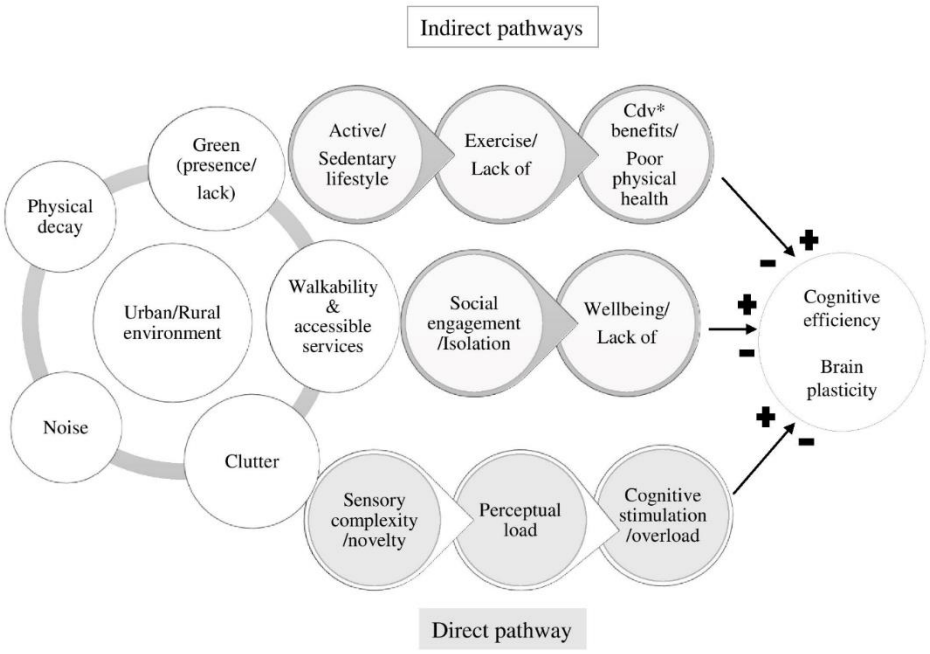


Figure 2.1

Examples of direct and indirect associations between environment and cognition.

* Cardiovascular.

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Environment and Cognition: Historical Perspective

The idea of the environment as a determinant or even a component of our cognition is not new (Clark, 1999a; Gibson, 1986). Ecological models (Bronfenbrenner, 1979; Bronfenbrenner & Ceci, 1994; Canter & Craik, 1981) propose that human behaviour results from a dynamic interplay between individuals and their social and physical environments. The press-competence model proposed by Lawton & Nahemow (1973) emphasises the influence of such interplay on successful ageing: As people age, their competence is reduced due to losses in functionality and therefore they are more subject to environmental demands, a condition defined as 'environmental docility' (Lawton & Simon, 1968). However, older people who live in socio-physical environments which compensate for individual cognitive and physical losses – that is, with reduced environmental press - are more likely to show adaptive behaviours and positive affective responses (Lawton, Brody, & Turner-Massey, 1978). Ecological models have found application in the promotion of ageing in place policies (Black, 2008; Mynatt, Essa, & Rogers, 2000; Wiles et al., 2012) aimed at supporting housing quality and technological aids within the home environment (Oswald & Wahl, 2004, 2005). However, although Lawton's model (Lawton, 1989; Lawton & Nahemow, 1973) and new models of ageing in place (Wahl, Iwarsson, & Oswald, 2012) highlight the psycho-social dimensions of the environmental impact on older individuals, cognitive skills and their neurophysiological bases are not analysed. Moreover, a clearer definition of "place" is needed (Wiles et al., 2012) which encompasses broader spaces, such as neighbourhoods, communities and cities, where older people carry their daily activities, and which addresses cognitive decline and reserve. Within this framework, we analyse the environmental characteristics which can

define ‘place’ in terms of impact on cognition. Table 1 summarises a series of studies which show direct relationships between the environment and specific cognitive skills, with an indication of the geographical level at which the relationship has been studied, ranging from macro (e.g. urban vs. rural environment) to more micro levels (e.g. visual clutter in built environments). The identified environmental factors are analysed hereafter drawing from the literature on ageing when available or from evidence on younger adults. Firstly, factors suggesting a direct association between cognitive performance and environmental characteristics are analysed; we then consider factors which plausibly mediate this association.

Table 2.1

Studies on direct associations between environment and cognition

Environmental factor	Measure of cognition	Geographical level	Results	Study Population	Demographic	Reference
Rurality	Prevalence of cognitive impairment (MMSE, Blessed Dementia Scale)	Urban vs. rural	Higher prevalence of impairment in rural, in interaction with age and presence of vascular risk factors.	Two random samples of community-dwelling adults drawn from health centres registries in urban and rural Portugal.	N = 1146, Age = 55 to 79, 55.5 % female	Nunes et al. (2010)
	Estimated prevalence of dementia	Regional differences	Higher prevalence of dementia in rural regions.	Irish older population with dementia as per Census 2006	N = 41,720, Population age and gender not given	Cahill et al. (2012)
	Risk ratio of dementia	Urban vs. rural	Higher risk of Alzheimer's disease in rural areas.	Community-dwelling older adults in various areas of the world.	Various data as per meta-analysis	Russ et al. (2012)
	Prevalence of Alzheimer and Vascular type of dementia (MMSE, Blessed Dementia Scale)	Urban vs. rural	Higher risk of Alzheimer's disease in rural areas, while higher prevalence of vascular dementia in urban.	Chinese population aged 60+	Various data as per meta-analysis	Zhang et al. (2012)
Presence of green	Sustained and selective attention (Necker Cube Pattern Control task, Search Memory Task)	Urban vs. natural exposure (walk)	Exposure to nature improved attentional performance, but not for urban exposure.	Young adults randomly assigned to experimental groups	N = 112, Mean age = 20.8, 50% female	Hartig et al. (2003)
	Directed attention (backwards digit-span task and Attention Network task)	Urban vs. natural exposure (exp. 1 walk; exp. 2 pictures)	Exposure to nature improved the performance in directed attention tasks.	Convenience sampling	Exp. 1: N = 38 (mean age 22.62, 60% female); Exp. 2: N = 12 (mean age = 24.25, 66% female)	Berman et al. (2008)
	Sustained	Urban vs.	Improvement	Young adults	N = 32,	Berto

	Attention (SART)	natural exposure (pictures)	s in attentional performance after exposure to natural scenes, but not for urban exposure.	randomly assigned to experimental groups	Mean age = 23, 50% female	(2005)
	Executive Attention (backwards digit-span task and Attention Network task)	Urban vs. natural exposure (pictures)	Exposure to natural pictures improves attention in both age groups, with no age differences.	Convenience sampling	N = 56, 26 younger adults (Mean age =20.54), 30 older adults (Mean age = 69.1), Sex not provided	(Gamble, Howard, & Howard, 2014)
	Concentration (Necker Cube Pattern Control Test, Digit Span Forward, Digit Span Backward and Symbol Digit Modalities Test).	Outdoor natural vs. indoor	Elderly people who spent time outside were able to concentrate more than those staying indoor.	Older people living in a care setting.	N = 15, Mean age = 86, 86% women	Ottosson & Grahn (2006)
Topography (city-block or variable)	Spatial navigation (learning to navigate a new environment)	Indoor environment (virtual)	Age-related differences in spatial knowledge, but reduced when older people used a walking support.	Convenience sample from undergraduat e classes and voluntary database.	N = 32, Age groups: 20-30 (n = 16); 60-70(n = 16). 100% male	Lövdén et al. (2005)
Visual clutter	Visual distractibility (Eriksen-type flanker interference)	Urban vs. rural	Urbanised participants were faster, but Himba showed significantly less distractibility.	Convenience sampling of urbanised people and participants from remote rural areas (Himba).	N = 143, 83 Himba (mean age = 25, 55% female), 60 English (mean age = 22.9, 60% female)	de Fockert, et al. (2011)
	Spatial attention and working memory (local selection task)	Urban vs. rural	Traditional more focused than urbanised, but urbanised had better working memory and	Convenience sampling of traditional and urbanised Himba	N = 166, 73 traditional (35 adult, mean age 25; 38 adolescent, mean age 12), 57%	Linnell et al. (2013)

			were as focused as Himba in engaging tasks.		female; 93 urbanised (56 adult, mean age 27; 37 adolescent, mean age 12), 43% female	
	Road signs search (accuracy and speed) in single or dual-task condition while driving	Scenes with low vs. high clutter (number of objects)	High clutter and dual-task impaired both speed and accuracy, and older group worse than young.	Convenience sampling of volunteers from university and community (Calgary, CA)	N= 32, 16 young (mean age 22.6, 68% female), 16 older (mean age 64.2, 43% female)	McPhee et al. (2004)
Visual complexity	Mental workload (reaction time to secondary task while driving in more or less complex environments).	Virtual diving contexts with increased complexity (straight road; intersections, manoeuvres).	Older drivers slower than younger, with significant increase in more complex driving contexts (e.g. overtaking).	Convenience sampling (Laval, CA)/	N = 20, 10 young (mean age 24), 10 older (mean age 69)	Cantin et al. (2009)
	Failure to stop at stop signs while driving	Urban vs. rural living	Rural drivers more likely to fail to stop than urban, probably because used to less traffic and better visibility.	Convenience sampling of older licensed drivers (Maryland).	N = 1,115, Mean age 77.7, 48% female	Keay et al. (2009)

Prevalence of Dementia in Rural vs. Urban Areas

Many studies have explored geographical variations in mental health problems in relation to rural vs. urban living (Andrade et al., 2012; Krabbendam & Os, 2005; Paykel, Abbott, Jenkins, Brugha, & Meltzer, 2000; Roe & Aspinall, 2011; Romans, Cohen, & Forte, 2010; Sundquist, Frank, & Sundquist, 2004). City living has been associated for example with higher prevalence of schizophrenia (Krabbendam & Os, 2005), and with a higher risk of mood and anxiety disorders (Peen, Schoevers, Beekman, & Dekker, 2010; Romans et al., 2010; Sundquist et al., 2004). These associations might be due to maladaptive social stress processing for urban dwellers, as suggested by neuroimaging evidence (Lederbogen et al., 2011) which proposes both urban upbringing and urban living as environmental risk factors for mental health. Geographical variations in dementia and cognitive impairment in older age have been less extensively explored, although some studies have considered cognitive ageing in relation to macro-level distinctions between rural and urban environments (Russ et al., 2012). Nunes et al. (2010) found higher prevalence of cognitive impairment in people aged 55 to 79 years living in rural rather than urban communities of Portugal, arguing that these differences may depend on the fact that living in low-income rural areas is less intellectually-demanding. Rural dwelling was also associated with higher prevalence of cognitive impairment and dementia in different regions of Spain (Contador, Bermejo-Pareja, Puertas-Martin, & Benito-Leon, 2015; Gavrila et al., 2009). Similarly, Cahill et al. (2012) reported higher prevalence of dementia in rural regions of Ireland based on Census data, ascribing this pattern to demographic characteristics of the population such as age groups. Russ et al. (2012), in their systematic review of studies on prevalence and incidence of dementia in relation to geographical factors, identified a strong

association between rurality and Alzheimer's Disease, particularly significant in non-EU countries, and other studies support this association (Bae et al., 2015; Klich-Rączka et al., 2014).

Reaching conclusions on this literature is however difficult for several reasons. Some studies have shown contrasting geographical patterns for different subtypes of dementia (Yaodong Zhang et al., 2012), or no differences between urban and rural dwellers (Chan et al., 2013), and comparisons of different studies are hindered by the lack of a standardised definition of urbanisation and rurality (Hall, Kaufman, & Ricketts, 2006; Hart, Larson, & Lishner, 2005; Russ et al., 2012). Moreover, the majority of studies on the association between cognitive decline and characteristics of the environment of residence focus mainly on the role of socioeconomic factors (Chan et al., 2013; Russ et al., 2012; Yaodong Zhang et al., 2012), while studies on geographical variations in intelligence as measured by standard IQ tests or alternative measures (Gist & Clark, 1938; Jokela, 2014; Lehmann, 1959), suggest specific migration patterns towards cities, possibly because higher IQ individuals would find better opportunities in urban environments (Jokela, 2014), which might determine geographical differences in the prevalence of dementia in older age. Cognitive abilities are influenced by the interaction between genetic and environmental factors (Dickens & Flynn, 2001; Kan, Wicherts, Dolan, & van der Maas, 2013; Molenaar et al., 2013; Scarr & McCartney, 1983), and this could also apply to differences among individuals living in distinct geographical areas (Tucker-Drob et al., 2013). Studies on twins (Lee, Henry, Trollor, & Sachdev, 2010; Petrill et al., 1998), however, despite supporting some heritability of cognitive skills (Pedersen, Plomin, Nesselroade, & McClearn, 1992), suggest an important role of environmental factors for individual differences in cognitive abilities with ageing

(Xu et al., 2015). Research on the Flynn effect (Flynn, 1987, 1999; Neisser, 1998) favours environmental explanations for population gains in intelligence as measured through standardised tests, suggesting, among other possible causes, that increasing urbanisation has provided stimulating environments associated with an enhanced ability to process and manipulate complex visual and abstract information, and thus linked with a growth in fluid cognitive skills (Flynn, 1998, 2007).

Focusing on environmental factors, further issues in the interpretation of geographical variations in cognitive impairment arise based on the evidence that multiple environmental influences can contribute to urban/rural differences. Longitudinal studies, for example, have found associations between cognitive decline and high levels of traffic-related air pollution (Power et al., 2011) or lead in the area of residence (Shih et al., 2006; Weisskopf et al., 2007), as well as long term exposure to particulate matter (Pedata, Grella, Lamberti, & Bergamasco, 2014; Weuve et al., 2012), which are more frequent in urban areas. Other studies suggest better dietary habits for rural dwellers (Huot, Paradis, Receveur, & Ledoux, 2004; Kabagambe, Baylin, Siles, & Campos, 2002; Kun, Liu, Pei, & Luo, 2013; Morgan, Armstrong, Huppert, Brayne, & Solomou, 2000; Santos, Rodrigues, Oliveira, & Almeida, 2014; Scarmeas et al., 2014), with important implications for cognition considering that diet is associated with active lifestyles, cardiovascular health and cognitive benefits in older age (Otaegui-Arrazola, Amiano, Elbusto, Urdaneta, & Martínez-Lage, 2014; Spencer, 2008), as well as involved in mediating the association between vitamin D deficiency and cognitive decline (Buell et al., 2009; Llewellyn et al., 2010; Miller, 2009; Wilkins, Sheline, Roe, Birge, & Morris, 2006), especially in living areas subject to sunlight deprivation (Romero-Ortuno et al., 2011). While acknowledging the importance of air quality and diet in understanding

cognitive ageing, together with the important role of biological and sociocultural intervening factors, the present work focuses on physical characteristics of the environment, e.g. visual or auditory complexity, that may act as training on modifiable and amenable aspects of cognitive performance, such as attention and executive functions (Anguera et al., 2013; Mozolic et al., 2011; Nouchi et al., 2012). These factors are analysed in the following section.

Direct Associations between Environmental Characteristics and Cognition

Environmental restorative properties, visual/auditory complexity and attention

In line with the growing evidence that the availability of green space benefits physical and mental health (Alcock, White, Wheeler, Fleming, & Depledge, 2014; Berto, 2014; Beyer et al., 2014; Irvine, Warber, Devine-Wright, & Gaston, 2013; Richardson, Pearce, Mitchell, & Kingham, 2013), some studies have investigated the impact that green or natural environments, as opposed to the built environment, may have on cognition (Berman, Jonides, & Kaplan, 2008; Berto, 2005; Emfield & Neider, 2013; Gamble, Howard, & Howard, 2014; Hartig, Evans, Jamner, Davis, & Gärling, 2003; Ottosson & Grahn, 2006), in the attempt to test Kaplan's Attention Restoration Theory (ART, Kaplan, 1995), which suggests that natural settings impose less cognitive load, restore attention, and therefore benefit well-being. Studies on younger adults show that even short term exposure to green or natural environments, either in the form of walking in the nature or viewing pictures of natural settings, improves the participants' performance in working memory tasks

such as backwards digit-span and the Attentional Network Test (Berman et al., 2008; Hartig et al., 2003), and in measures of sustained attention (Berto, 2005). Similar results have been found in older adults (Gamble et al., 2014; Ottosson & Grahn, 2006), leading the authors to suggest that exposure to natural settings allows for more attentional resources to be available to carry specific tasks (Berman et al., 2008). Interestingly, improvements in attentional performance have been reported also for exposure to auditory stimuli taken from natural settings (Emfield & Neider, 2013).

It might be argued that natural or green areas are more restorative than busy urban environments because less perceptually complex, and therefore less tiring. Assuming that rural environments have more availability of green spaces and impose lower cognitive and perceptual load, we should expect better attentional performance in rural rather than urban dwellers. This hypothesis finds support in studies on selective attention (Caparos et al., 2012; de Fockert, Caparos, Linnell, & Davidoff, 2011; Linnell, Caparos, de Fockert, & Davidoff, 2013) which compared extremely rural residents (specifically, the Himba semi-nomadic tribe in northern Namibia) with urban individuals (either urbanised Himba or Londoners). In these studies, rural participants were found to be better able than urban residents to focus their attention on target stimuli while ignoring distractors in a visual interference task (de Fockert et al., 2011), and showed a more local processing of the visual field even at low perceptual load (Caparos et al., 2012), that is when the perceptual processing of stimuli is not demanding. Interestingly, rural Himba had overall slower responses than urban residents, although the reaction latencies did not explain the differences in interference (de Fockert et al., 2011). Two possible explanations for these urban/rural differences have been suggested: on one hand, urban living could be

hyper-stimulating and deplete attentional capacity, causing more interference in spatial attention (Berman et al., 2008; Kaplan, 1995); on the other hand, urban or rural living might be associated with different strategic deployments of attentional focus, more spread for urban residents while more focused for rural dwellers (Linnell et al., 2013). The second hypothesis is supported by findings which show that urban/rural differences in interference effects disappeared in a more engaging task with potentially more interesting stimuli, such as discriminating between 'black' or 'white' ethnic group faces, thus increasing focused attention in urban participants (Linnell et al., 2013). Based on these findings, rural individuals, compared with their urban counterpart, should be better able to focus their attention in tasks with low levels of engagement: this advantage, however, should not be found in engaging tasks, as shown by Linnell et al. (2013). Living in an urban environment may contribute to increase cognitive capacity by acting as training of attention, thus enabling urban residents to respond faster and more accurately in focused attention tasks with engaging stimuli (Linnell et al., 2013). However, the frequent exposure to multiple stimulation may cause cognitive load and instigate a broader scanning of the environment in urban individuals, with increased levels of interference, as shown by the observation of higher attention capture by moving stimuli in urban rather than rural participants (Linnell et al., 2013). Linnell et al. (2013) suggest that urbanism may be associated with a tendency to explore the environment rather than focussing on one aspect of it unless that aspect is particularly interesting. This strategy is similar to the one used by expert drivers (Crundall, Chapman, Phelps, & Underwood, 2003; Crundall & Underwood, 1998; Underwood, Chapman, Brocklehurst, Underwood, & Crundall, 2003) and expert soccer players (Vaeyens, Lenoir, Williams, Mazyn, & Philippaerts, 2007; Vaeyens, Lenoir, Williams, &

Philippaerts, 2007), suggesting a possible link between this strategy and expertise in dealing with complex visual scenes. Although the above studies are an extreme example of urban/rural differences due to the fact that they compare an urbanised group with individuals living in remote areas, their core idea can be applied to ageing individuals who live in urban or rural settings because it is intuitive that urban and rural environments offer different levels of cognitive stimulation, and older individuals may be particularly affected by it.

In fact, environments characterised by complex perceptual information, which should be more present in urban contexts, negatively impact attentional resources and interfere with the cognitive control needed to retrieve information from long-term memory in older people. Evidence shows (Wais & Gazzaley, 2014) that the long-term retrieval of previously learned visual information is impaired in older people in the presence of distracting visual or auditory stimuli, as for example pictures of complex scenes such as urban landscapes, or noise from busy environments such as coffee shops; these distractors impose a cognitive load even if non task-related (Wais & Gazzaley, 2014; Wais, Martin, & Gazzaley, 2012). Visual attention to stimulus characteristics is also disrupted in older adults in categorisation tasks in the presence of perceptually complex backgrounds, possibly indicating the difficulty to focus attention on relevant perceptual characteristics to retrieve semantic information from memory (Ashby & Maddox, 2011).

Considering the evidence above on the influence that rural vs. urban settings, or simple vs. complex scenes, may have on *restorativeness* and attentional and executive control, a thorough investigation of levels of visual and auditory

stimulation in the lived environment, starting from broad differences between rural and urban settings down to more specific local settings, is granted.

Environmental layout, level of clutter and spatial cognition

Urban environments are often characterised by high levels of clutter and complex layouts which may affect spatial cognition (Linnell et al., 2013). Spatial cognition, critical to learn, understand, navigate and remember environmental information, depends on the integration of multiple cognitive abilities such as memory, executive functions, and attention (Boccia, Nemmi, & Guariglia, 2014; Chrastil, 2013), and on the interaction between these abilities, cognitive styles, and external factors (Meneghetti, Pazzaglia, & De Beni, 2014; Nori & Giusberti, 2006; Pazzaglia, Cornoldi, & Beni, 2000). The decline of spatial cognition with ageing (Klencklen, Després, & Dufour, 2012; Moffat, 2009) may negatively impact the engagement in outdoor activities (Kirasic, 2000), impair safe driving (Aksan et al., 2013; Dawson, Uc, Anderson, Johnson, & Rizzo, 2010), and increase the risk of falls (M. M. Barrett et al., 2013). Older adults show in fact more difficulties than younger people in learning new environmental layouts (Kirasic, 2000; Liu, Levy, Barton, & Iaria, 2011), as well as longer reaction times and more errors in tasks of visuospatial perception and mental imagery (Klencklen et al., 2012). They are able to remember landmarks, but have more difficulties in remembering their relative position (Moffat & Resnick, 2002). Crucially, the spatial representation of the environment depends also on the characteristics of the environment itself, such as the types of buildings or paths (Lynch, 1960), or the type of spatial information available (Palermo, Piccardi, Nori, Giusberti, & Guariglia, 2012). Older people employ different orientation

strategies - based on general knowledge acquired with experience – than those used by younger people – more dependent on visual information (Lövdén, Schellenbach, Grossman-Hutter, Krüger, & Lindenberger, 2005) - and this may impair their ability to navigate an urban environment which presents higher density of buildings and potential landmarks, potentially impacting mobility itself (K. Z. H. Li, Lindenberger, Freund, & Baltes, 2001; Lindenberger et al., 2000; Schäfer, Huxhold, & Lindenberger, 2006). It has been suggested that older people's worse navigational performance might depend on the combination of a reduced ability to minimise the processing of irrelevant information due to sensory-motor decline (Baltes & Lindenberger, 1997; de Fockert, Ramchurn, van Velzen, Bergström, & Bunce, 2009; Maylor & Lavie, 1998), and the perceptual characteristics of the environment with which they interact (Lövdén, Schellenbach, et al., 2005). These factors influence for example the choice of means of transport (Beirão & Cabral, 2007; Garling, Book, & Lindberg, 1984), and can affect the likelihood that an older person will engage in activities outside home. As urban environments are likely to present higher visual clutter and perceptual complexity than rural landscapes, they might oblige users to engage in a more attentive scan of the background in order to select a given target successfully, thus accounting for higher levels of visual distractibility (de Fockert et al., 2011). So, complex perceptual stimulation may become overwhelming for people with reduced spatial abilities. Evidence for this comes from studies on driving skills in relation to visual clutter (Ho, Scialfa, Caird, & Graw, 2001; McPhee, Scialfa, Dennis, Ho, & Caird, 2004) and visual complexity in the surrounding environment (Cantin, Lavallière, Simoneau, & Teasdale, 2009; Keay et al., 2009; Lambert & Fleury, 1994): Older adults tend in fact to be slower and less accurate in searching road signs in traffic scenes with high clutter, measured as the number of objects in

the visual field (McPhee et al., 2004), and to have increased cognitive workload in complex driving contexts, e.g. overtaking manoeuvres (Cantin et al., 2009). It is possible to envisage that these negative effects of clutter and visual complexity could be contrasted by identifying the environmental elements that provide an optimal level of perceptual and cognitive stimulation, and which enable people to understand and use places (Canter, 1977).

Environmental noise and multisensory stimulation in relation to memory and attention

Urban environments are likely not only to offer more visually complex stimulation than rural environments, but also higher levels of auditory stimulation. Environmental noise may affect cognition both directly, e.g. via perceptual stimulation, and indirectly, for example by influencing cardiovascular health. The role of environmental noise has been studied in relation to cognitive development (Clark & Stansfeld, 2007), showing that children exposed to higher levels of noise, for example traffic or airport noise, have more problems with memory skills and reading comprehension. Environmental noise has also been associated with cardiovascular disease in a recent study in the U.S. which showed that people living near airports, and therefore with higher levels of exposure to aircraft noise, had 3.5% higher hospitals admissions rates due to cardiovascular problems (Correia, Peters, Levy, Melly, & Dominici, 2013). Waist circumference, strongly linked to metabolic syndrome, which is in turn associated with negative cognitive outcomes (Yaffe, Weston, Blackwell, & Krueger, 2009), was also found to be increasingly higher for individuals living near airports in a 10-year study in Sweden (Eriksson et al., 2014). Similar effects of noise on cardiovascular health and diabetes have been shown for exposure to road traffic noise (Selander et al., 2009, 2013; Sørensen et al., 2012). As

cardiovascular health is associated with cognition (Frewen et al., 2013; Frewen, Finucane, Savva, Boyle, & Kenny, 2014; Yaffe et al., 2009), these studies support the hypothesis that noisy environments have a negative impact on cognitive functions. Moreover, environmental noise is associated with higher levels of stress, which negatively affect the regulation of the hypothalamic-pituitary-adrenal axis (Babisch, 2003; Ising & Braun, 2000).

Specific evidence on the direct impact of environmental noise on different cognitive processes can be inferred from the experimental literature on speech processing in the presence of artificial noise, a laboratory situation characterised by stimuli such as white noise or unintelligible speech (babble talk) comparable to having to understand speech in busy places like restaurants or busy roads (Rabbitt, 1968). This literature has provided evidence that increased levels of noise during the encoding of verbal material are associated with a decrease in recall in healthy young adults. In older adults, both episodic retrieval and working memory deficits are more apparent in noisy environments due to the increased attentional effort required (Pichora-Fuller, 1996) and the fact that noise can act as a distractor (Wais & Gazzaley, 2011, 2014); these findings are of relevance considering that older people are more prone to process task-irrelevant background information (Andrés, Parmentier, & Escera, 2006; Hasher & Zacks, 1988; Laurienti, Burdette, Maldjian, & Wallace, 2006). Mobility can also be negatively affected by the cognitive load imposed by environmental auditory stimulation, for example when walking on the road while monitoring the environmental sounds for vehicles or other potentially ‘interesting’ objects, and may place people at an increased risk of falls (Stapleton, Setti, Doheny, Kenny, & Newell, 2014). Environmental noise is however more acceptable when the environment is normally expected to be noisy (Brambilla &

Maffei, 2006a), which may account for an adaptation to environmental demands that could benefit cognitive skills. Older adults can in fact be trained to ignore auditory background information (e.g. playground noise, or city traffic) in laboratory settings, with improvements in selective attention and lower cross-modal distractibility (Mozolic et al., 2011). The discussed studies show that environmental noise can affect cognition both directly and indirectly, making it an important aspect of the environment to consider in the study of cognitive ageing.

Mediating Factors

It is known that individual factors such as socioeconomic status, lifestyle, and health influence cognition in older age (de Frias & Dixon, 2014; Fratiglioni, Paillard-Borg, & Winblad, 2004; Hertzog et al., 2008). Here we consider socioeconomic status at neighbourhood level and environmental resources for active lifestyles as mediators between physical aspects of the environment and cognitive health. These variables can contribute to better understand how the design of lived environments influences behaviour and cognitive ageing.

Environmental factors associated with socioeconomic status

It is widely accepted that socioeconomic status is linked with cognitive performance (Evans & Kantrowitz, 2002; Fors, Lennartsson, & Lundberg, 2009; Hackman & Farah, 2009; Hackman, Farah, & Meaney, 2010; Kaplan et al., 2001; Nguyen, Couture, Alvarado, & Zunzunegui, 2008; Santos et al., 2008), and is therefore an important mediator in the association between environment and cognitive health in older age (Czernochowski, Fabiani, & Friedman, 2008; Jefferson et al., 2011; Roe, Xiong, Miller, & Morris, 2007; Stern, Albert, Tang, & Tsai, 1999).

Several studies have explored this association in relation to the area of residence (Beard & Petitot, 2010; De Deyn et al., 2011; Yen, Michael, & Perdue, 2009), but although it is intuitive that urban and rural areas may have socioeconomic differences (Chan et al., 2013; Russ et al., 2012), research has mainly focused on socioeconomic status in relation to neighbourhoods: Specifically, educational attainment, income, poverty, occupation, and deprivation at neighbourhood level are significantly associated with cognitive performance in older age (Aneshensel, Ko, Chodosh, & Wight, 2011; Lang et al., 2008; Sheffield & Peek, 2009; Wight et al., 2006). It has been suggested that people who live in more socioeconomically deprived neighbourhoods are more subject to health risks due to higher presence of environmental stressors, less availability of physical and social resources, and less cognitively stimulating activities (Sheffield & Peek, 2009). Interestingly, Sisco & Marsiske (2012) reported that neighbourhood socioeconomic status predicted the performance of older participants in vocabulary tasks only. The authors suggested that more advantaged neighbourhoods could promote enhanced sociocultural interactions, with positive effects on knowledge-based abilities, such as vocabulary. Clarke et al. (2012) recently proposed neighbourhood affluence as a source of cognitive reserve for older adults through the mediation of a higher density of institutional resources (for example, schools, libraries and community centres), as well as a higher proportion of older adults, promoting cognitively beneficial activities such as physical activity and peer group interactions. Socioeconomic status of the area of residence represents an important mediator in the impact of the environment on cognitive ageing, thus more research is needed to understand what physical aspects characterise environments with different socioeconomic status, as for example physical decay, accessibility to resources, or environmental stressors

such as noise, and which ones may mediate the link between socioeconomic status of the place of residence and cognition. This is especially important considering that older people are more likely to have lived most of their lives in the same neighbourhood and as a result could be more susceptible to long-term environmental influences (Glass & Balfour, 2003; Oswald & Wahl, 2005).

Environmental factors associated with lifestyle: physical activity and social engagement

Older people can cognitively benefit from engaging in active and healthy lifestyles, especially in the form of physical and social activities (de Frias & Dixon, 2014; Fratiglioni et al., 2004; Hertzog et al., 2008; Kelly et al., 2014; Kramer et al., 2004; Lövdén, Ghisletta, et al., 2005; Scarmeas & Stern, 2003; Shankar, Hamer, McMunn, & Steptoe, 2013). For this reason, there has been a growing interest in identifying aspects of lived environments that can be designed to positively influence healthy behaviours which in turn benefit cognitive health (Badland & Schofield, 2005; Cunningham & Michael, 2004; Dallat et al., 2013; Frank & Engelke, 2001; Jackson, 2003; Kerr et al., 2012; Ramirez et al., 2006; Renalds et al., 2010). Few studies have explored physical activity in relation to the place of residence at a broader geographical scale, although there is some evidence that older people living in urban areas spend more time walking then rural dwellers (Morgan et al., 2000; Parks, Housemann, & Brownson, 2003), and are less sedentary (Martin et al., 2005; Wilcox, Castro, King, Housemann, & Brownson, 2000). In a study conducted on older people in Iceland however, the location of residence promoted domain-specific physical activity: more leisure-oriented for urban dwellers, while more work-related in rural areas (Arnadottir, Gunnarsdottir, & Lundin-Olsson, 2009); these results may however be culture specific. Similarly, a study in Belgium (Van Dyck, Cardon,

Deforche, & De Bourdeaudhuij, 2011) found that, while urban adults were in general more physically active than rural ones, rural participants with higher psychosocial scores had higher levels of physical activity, suggesting that multiple factors contribute to an active lifestyle. When considering the living context at a neighbourhood level, several environmental factors are reported to benefit individuals' engagement in physical activity, particularly in relation to walking (Carlson, Aytur, Gardner, & Rogers, 2012; Heikkinen, 1998): higher residential density, intended as the density of households, activities and services; higher land-use mix, that is, the presence of different types of destinations in the proximal area; higher street connectivity; aesthetic attractiveness and sense of safety; short distance from destinations of interest (Cohen et al., 2007; Handy, Boarnet, Ewing, & Killingsworth, 2002; Kerr et al., 2012; Michael, Green, & Farquhar, 2006; Saelens & Handy, 2008; Saelens, Sallis, Black, & Chen, 2003; Saelens, Sallis, & Frank, 2003; Troped, Saunders, Pate, Reininger, & Addy, 2003). As age-related functional losses may hinder the possibility for some individuals to engage in many outdoor activities (Glass & Balfour, 2003), these dimensions could represent aspects of the environment that support healthy lifestyles (Bauman et al., 2012; Gidlow, Cochrane, Davey, Smith, & Fairburn, 2010) with a positive repercussion on cognition.

In terms of social engagement and its association with environmental factors, some studies suggest that people living in rural areas experience wider social networks than urban dwellers (Paúl, Fonseca, Martín, & Amado, 2003; Wanless, Mitchell, & Wister, 2010), as well as higher social involvement (Greiner, Li, Kawachi, Hunt, & Ahluwalia, 2004). The factors influencing these differences might lie in a stronger sense of belonging and more accessible social networks in rural areas, which in turn show positive associations with self-rated health. Social support

may also be more important in rural settings because the scarcity of services in rural places might lead people to rely more on family and friends for assistance (Wanless et al., 2010). It has been suggested that urbanisation is associated with worse social behaviour, for example related to traffic noise (Korte & Grant, 1980; Korte, Ypma, & Toppen, 1975), as well as social isolation in relation to neighbourhood deprivation (Buffel, Phillipson, & Scharf, 2013). However, living in urban areas with walkable neighbourhoods enhances social capital, defined as the number of an individual's social networks and interactions (Leyden, 2003; Wood et al., 2008), while having easy access to green areas in the city increases social integration (Kweon, Sullivan, & Wiley, 1998; Maas, van Dillen, Verheij, & Groenewegen, 2009). Urban environments are also likely to provide higher chances for engagement in social and leisure activities which offer intellectual stimulation (Kearns & Parkinson, 2001), fostering cognitive reserve and mitigating the negative effects of ageing on cognition (Fratiglioni et al., 2004; Schooler, Mulatu, & Oates, 1999; Stine-Morrow et al., 2008; Wang, Karp, Winblad, & Fratiglioni, 2002). Going beyond urban/rural differences, environmental measures such as the geographical distance from family or friends (Dewit, Wister, & Burch, 1988; Gillespie & van der Lippe, 2015; Smith, 1998; Yiduo Zhang, Engelman, & Agree, 2013), the lack of transportation options (Locher et al., 2005; Lucas, 2012), or even living in deprived areas (Chappell, Monk-Turner, & Payne, 2011), contribute to differences in social support or participation, which in turn can have potential impact on health (Berkman & Glass, 2000; Hays, Steffens, Flint, Bosworth, & George, 2001; Shankar, McMunn, Banks, & Steptoe, 2011), and indirectly influence cognitive outcomes in older age (Cacioppo & Hawkley, 2009; Lövdén, Ghisletta, et al., 2005; Shankar et al., 2013). Environmental factors such as residential proximity to the family, which promote or hinder the

engagement in healthy and socially rewarding lifestyles, could represent indirect predictors of cognitive health in older age, especially for lower socioeconomic status individuals who may have fewer opportunities for mobility (Cook & Swyngedouw, 2012).

Potential Cognitive Mechanisms Underlying the Association between Physical Environment and Cognition

Evidence from animal models shows that enriched and stimulating environments produce plastic changes in the brain (Leggio et al., 2005; Nithianantharajah & Hannan, 2006). When an environment presents the optimal amount of cognitive challenge, this can have protective effects against brain pathology (Berardi et al., 2007; Herring et al., 2009), although reverse causality between cognitive advantage and enriched social environmental stimulation has also been proposed (Gow, Corley, Starr, & Deary, 2012). Environmental challenges could operate on the brain in a similar way to other kinds of challenges, such as education and stimulating job conditions, which are linked to increased cognitive reserve and diminished incidence of brain pathology (Stern, 2012; Valenzuela & Sachdev, 2009). Current evidence reviewed above (Keay et al., 2009; Linnell et al., 2013; Russ et al., 2012) favours the hypothesis that urban environment offers an advantage in terms of cognitive stimulation. However, different environments may provide different levels and/or kinds of challenges, which can offer optimal or sub-optimal stimulation depending on the characteristics of the individual. For the ageing individual a cognitively demanding environment may provide excessive challenge (Lövdén et al., 2010; Lövdén, Schellenbach, et al., 2005; Moffat, 2009), influencing,

as a result, the capacity to compensate for underlying brain damage and reduced processing efficiency, aspects of paramount relevance in order to maintain an acceptable level of cognitive performance in older age (Cabeza et al., 2002); conversely, an environment not sufficiently rich in stimulation may co-cause cognitive deficits directly or indirectly (Robertson, 2013). A similarity with the effects of physical exercise on health can be drawn: In evolutionary terms, humans are supposed to be physically active (Bortz II, 1985; Proper, Singh, van Mechelen, & Chinapaw, 2011; Vaynman & Gomez-Pinilla, 2006), as shown by a host of studies on the health damage due to modern sedentary lifestyles (Lakka et al., 2003; Proper et al., 2011; Saris et al., 2003; Tremblay, Colley, Saunders, Healy, & Owen, 2010); on the other hand, strenuous exercise is associated with increased risks for health (O'Keefe et al., 2012; Patil et al., 2012). We argue that the same occurs for environmental stimulation. The optimal threshold for older individuals in terms of environmental challenge may depend on individual characteristics such as current level of cognitive health, personality, or alternative sources of stimulation as for example profession, hobbies, and social networks. Further research is needed on the interplay of these factors in relation to environmental impact on cognitive health.

Environmental challenges can be quantified in terms of social and lifestyle opportunities afforded (Carlson et al., 2012; Kerr et al., 2012; Wood et al., 2008), i.e. the indirect pathway in Figure 2.1, and in terms of sensory processing, the direct pathway in Figure 2.1. In terms of sensory processing, cities provide a highly perceptually stimulating environment, often if not always requiring the processing of information from multiple sensory modalities. However, older adults are more prone to process irrelevant sensory information (Andrés et al., 2006; Laurienti et al., 2006) and are more susceptible to multisensory interactions than younger adults (Setti,

Burke, Kenny, & Newell, 2011). This enhanced multisensory processing on one hand can be beneficial if the information is congruent (for example, when seeing a green traffic light and hearing the beep sounds signal that one can cross the road), while on the other hand it can be daunting if incongruent (Laurienti et al., 2006). Indeed multisensory processing can impact balance and is linked to falls (Setti et al., 2011; Stapleton et al., 2014), especially in case of sensory impairment, e.g. poor vision or hearing, which is common in older adults (Pichora-Fuller, 1996). Moreover, living in a complex environment is plausibly more likely to be associated with completing a task (e.g. walking) while at the same time doing something else (e.g. reading signs, hearing noises), and dual tasking is more difficult for older adults (Wais & Gazzaley, 2011).

Whether these environmental effects are mainly occurring on specific cognitive skills or they are more broad remains to be established. From the studies presented above, attention and executive functions emerge as key cognitive processes influenced by the environment: The presence of green benefits attentional processes by reducing visual complexity (Berman et al., 2008), while urbanisation seems to influence attentional engagement and perceptual processing biases (Linnell et al., 2013). Visual complexity negatively impacts spatial navigation (Klencklen et al., 2012), possibly due to a decreased ability to inhibit distracting stimuli (de Fockert et al., 2011), and studies on noise show that older adults are less efficient in complex noisy environments because less able to multi-task (Clapp, Rubens, Sabharwal, & Gazzaley, 2011). On the other hand, it has been suggested that complex environments like cities offer cognitive challenges which may actually benefit attention (Linnell et al., 2013) by activating neural networks involved in

alertness, sustained attention, response to novelty and self-monitoring - functions which are crucial to cognitive reserve (Robertson, 2014).

Identifying which aspects of our living environments can act as a source of optimal cognitive stimulation represents a new opportunity to better understand ageing processes in context. For example, when considering the association between physical exercise and walkability reported above (Carlson et al., 2012), the possibility that geographical environments afford different kinds of exercise remains understudied (Arnadottir et al., 2009), and by consequence it is difficult to advance hypotheses on whether the effects of the environment on cognition mediated by physical exercise are general, e.g. of cardiovascular nature, or specific, as shown in studies on attention (Kelly et al., 2014).

Interestingly, a recent study by Stine-Morrow et al. (2014) has for the first time contrasted directly the effects of two types of environmental stimulation - social engagement training vs. targeted cognitive training (through games and puzzles) - on cognitive enrichment in older age, measured as reasoning and problem solving. The results showed that both types of intervention improved specific cognitive abilities, but only in the engagement training baseline levels of openness and social engagement moderated the outcomes by influencing participants' ability to respond effectively to environmental complexity. This study suggests that environmental benefits can be quantified, but they may be effective only for specific groups of people - in this case people more open to social interaction. Importantly, it shows that both the manipulation of the environmental stimulation and targeted cognitive interventions could be viable alternatives to improve cognitive performance depending on specific individual characteristics and needs.

Future Directions

From this discussion it is clear that several research questions need to be addressed by future studies on the association between stimulation in the lived environment and cognitive ageing.

Firstly, it is currently not known how to operationalise measures of cognitive stimulation in the physical environment. We propose that this operationalisation should consider different geographical levels, going from broad urban/rural differences to characteristics of the neighbourhood such as visual complexity, physical layout, presence of green and its restorative qualities for attention. Quantifiable measures of urbanisation (e.g. through population density and sprawl) should be used for example to provide new epidemiological evidence of geographical variations in cognitive impairment (Russ et al., 2012). In addition, physical characteristics of proximal environments should be directly or indirectly manipulated experimentally in ecological or virtual settings to better address the complexity underlying urban/rural differences. Studies on urban planning have already proposed ways to quantify key environmental features for healthy behaviours, such as walkability (Lwin & Murayama, 2011), and tools to explore the mental benefits of exposure to natural vs. urban environments have been created (Han, 2003; Korpela & Hartig, 1996; Laumann, Gärling, & Stormark, 2001); moreover, general guidelines on the factors that make an environment user-friendly for older people have been produced by the WHO (World Health Organization, 2007). However, these indices have not been exploited yet to understand cognitive ageing, especially in relation to contextual measures of the environment of residence independent of socioeconomic factors (Wu et al., 2014). Although studying an association between environment and cognitive performance presents considerable

methodological difficulties in terms, for example, of control of confounders in real world studies or generalizability of results obtained by employing virtual environments techniques (Lövdén, Schellenbach, et al., 2005; Moffat, 2009), technological advancements, in the form for example of geographic information systems (GIS), may enable to quantify environmental measures in unprecedented ways (Coulton, 2012; Mehl, Pennebaker, Crow, Dabbs, & Price, 2001), potentially offering the possibility to test whether different environments provide different levels (and kinds) of stimulation, and whether this stimulation relates to cognitive ageing. This analysis, in combination with the exploration of socioeconomic and lifestyle factors for successful ageing which are associated with characteristics of the built environment (Clarke et al., 2012; Dallat et al., 2013; Kerr et al., 2012; Sisco & Marsiske, 2012), may provide a multicomponent tool for the investigation of how the environment shapes cognition in ageing, and can inform projects of environmental optimisation as well as targeted brain training programs.

Secondly, this new operationalisation of the environment could contribute to the literature on the interaction between genetic and environmental factors for cognitive health in older age (Lee et al., 2010; Xu et al., 2015) by incorporating an analysis of the physical environment in studies on the cognitive performance of reared apart twins, in order to isolate the environmental contribution to cognitive differences. It has been suggested that individuals with specific characteristics may tend to seek for different environments (Dickens & Flynn, 2001; Jokela, 2014; Scarr & McCartney, 1983), thus it is important to explore which factors, not only socioeconomic but also physical, make an environment more appealing than others. In line with this, and in order to address human migration and residential mobility (Oishi, 2010; Skeldon, 2014), new research should be dedicated to study cognition in

relation to geographical patterns of migration, mobile populations, the influence of childhood living circumstances for migrated individuals, as well as cognitive adaptation strategies of people migrating later in life (Walters, 2002). These studies should take into account the changing structure of families whereby family members, for example children and grandchildren, may not live in the proximity of the ageing individual, creating novel scenarios in terms of social networks and social support in older age. It is known that self-perceived social isolation, i.e. loneliness, is associated with negative cognitive outcomes (Cacioppo & Hawkley, 2009), and this suggests that distance from family and geographical barriers are relevant factors for cognitive ageing together with moderating factors such as technology (Winstead et al., 2013).

Third, and following up on the second point, we know that increasing urbanisation and the growing interest in building user-friendly environments (Gehl, 2010; Gehl & Svarre, 2013) are changing the physical organisation of living contexts, but little is known on the cognitive effects of these changing environments, especially in relation to new forms of environments such as mega-cities. By conducting longitudinal research on the cognitive performance of people living in areas with increasing levels of urbanisation, it will be possible to better address the pathways through which changing environments affect healthy ageing.

Lastly, animal models of cognitive impairment could further inform on the causal pathways of environmental enrichment and sensory stimulation by manipulating environmental modifications based on the measures operationalised in human studies. While it is known that novel stimulation triggers brain plasticity (Veyrac et al., 2008), new research pathways include studying the cognitive effects of modifications such as creating a more challenging path to reach a goal, or a more

natural environment, or providing different living spaces with variations of accessibility, affordances, and rewards. Rewards in particular have been shown to strongly contribute to the effectiveness and generalisation of brain training programs (Anguera et al., 2013; Smith et al., 2009) and therefore the trade-off between cognitive environmental challenge and kind/entity of reward needs further exploration.

To conclude, we propose that studying the environment as a source of cognitive stimulation and brain training has the potential to significantly contribute to better understand successful ageing as well as ageing in place, and to create new ecological and cost-effective interventions for cognitive enhancements tailored to individuals' personal resources and needs.

Chapter 3 – Operationalisation of Environmental Complexity

Complexity as Key to Designing Cognitive-Friendly Environments for Older People.[2]

Abstract

The lived environment is the arena where our cognitive skills, preferences and attitudes come together to determine our ability to interact with the world. The mechanisms through which lived environments can benefit cognitive health in older age are yet to be fully understood. The existing literature suggests that environments which are perceived as stimulating, usable and aesthetically appealing can improve or facilitate cognitive performance both in young and older age. Importantly, optimal stimulation for cognition seems to depend on experiencing sufficiently stimulating environments while not too challenging. Environmental complexity is an important contributor to determine whether an environment provides such an optimal stimulation.

The present paper reviews a selection of studies which have explored complexity in relation to perceptual load, environmental preference and perceived usability to propose a framework which explores direct and indirect environmental influences on cognition, and to understand these influences in relation to ageing processes. We identify ways to define complexity at different environmental scales, going from micro low-level perceptual features of scenes, to design qualities of

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proximal environments (e.g.: streets, neighborhoods), to broad geographical areas (i.e.: natural vs. urban environments).

We propose that studying complexity at these different scales will provide new insight into the design of cognitive-friendly environments.

Keywords: environmental complexity, cognition, perceptual load, usability, preference, aging.

Introduction

With ageing, the experience we have of the environment is reshaped both by physical, sensory, and cognitive changes, and by modifications of the perceived affordances offered by the environment. At the same time, the environment, in terms of architecture and sensory/cognitive stimulation provided, also shapes cognition and can be more or less supportive of independent living in older age. Thus, one could envisage a virtuous circle whereby the environment can provide an optimal level of stimulation to the older individual, so that she/he can maintain independence and, in turn, experience the environment in a positive and supportive way. Conversely, an environment which does not offer optimal stimulation can be detrimental for cognitive ageing, unsupportive, and, likely, less pleasant for older people, to the detriment of their quality of life. In this targeted review we propose that the concept of complexity can provide a route to studying interactions between ageing individuals and their environment, starting from sensations and perception, and including the lived experience of older adults in the environment.

Environmental Measures Linking Complexity to Cognitive Ageing

Lived environments offer both opportunities and challenges for healthy living (Boyko & Cooper, 2011; Corburn, 2015; Galea, Freudenberg, & Vlahov, 2005; Jackson, 2003; Vlahov & Galea, 2002). The extensive evidence that person-environment interactions influence human behaviour (Barker, 1968; Bronfenbrenner, 1979; Bronfenbrenner & Ceci, 1994; Lawton & Nahemow, 1973; Wahl et al., 2012), and that characteristics of the built environment contribute to physical and mental health (Badland & Schofield, 2005; Dallat et al., 2013; Kerr et al., 2012; Ramirez et al., 2006; Renalds et al., 2010), has urged to reconsider environmental planning and design as more user-centred (Gehl, 2010; Gehl & Svarre, 2013) and, in the light of global ageing and urbanisation (Beard & Petitot, 2010; World Health Organization, 2007), more facilitating for ageing individuals, or "age-friendly" (World Health Organization, 2002, 2007, 2012). Understanding how lived environments are experienced by older people has received growing interest in research (Buffel, Phillipson, & Scharf, 2012; Phillipson, 2011), and given the crucial role of cognitive health in maintaining autonomy and quality of life in older age (World Health Organization, 2002), many studies have explored the beneficial influence of factors such as social activities and lifestyle on cognitive ageing (Fillit et al., 2002; Hertzog et al., 2008; Stern, 2009, 2012; Stine-Morrow et al., 2008). However, only recently research has started to systematically address the influence of physical and perceptual characteristics of the environment on cognitive functioning in older age (Cassarino & Setti, 2015; Wu et al., 2014).

The present paper argues that trajectories of cognitive ageing as well as day-to-day cognitive performance of older people can be affected by environmental factors which make places more or less complex, and that environmental complexity

could represent an important and measurable contributor to cognitive functioning (Davidson & Bar-Yam, 2006; Rapoport, 1990; Rapoport & Hawkes, 1970; Rapoport & Kantor, 1967). Effectively, environmental complexity could be a potentially measurable contributor to cognitive reserve (Stern, 2009): Animal studies have shown that exposure to enriched, complex environments, presenting elements of novelty, can have a direct impact on brain structure and cognition (Cassarino & Setti, 2015; Diamond, 2001; Rosenzweig, Bennett, & Diamond, 1972). Enriched environments may also promote an active lifestyle, e.g. physical activity, which in turn is associated with better cognitive performance in older age (Cassarino & Setti, 2015).

The purpose of the present work is to explore links between cognitive ageing and existing measures of environmental complexity by considering studies on perceptual stimulation, environmental preference, and perceived usability of lived environments at different environmental scales (Cassarino & Setti, 2015; Jackson, 2003; Saehoon Kim, Park, & Lee, 2014), going from visual and/or auditory micro-characteristics of scenes (micro scale), to design qualities of streets and neighborhoods (meso scale), to broad forms of environmental exposure (macro scale: urban vs. natural).

Figure 3.1 synthesises a framework based on measures of complexity which are directly or indirectly associated with cognitive health at different environmental scales, as well as the links between these measures. In the framework, some links have been already explored in the literature in relation to ageing (indicated by solid lines in Figure 3.1), while other links (indicated by dashed lines in Figure 3.1) are suggested/inferred and need empirical exploration.

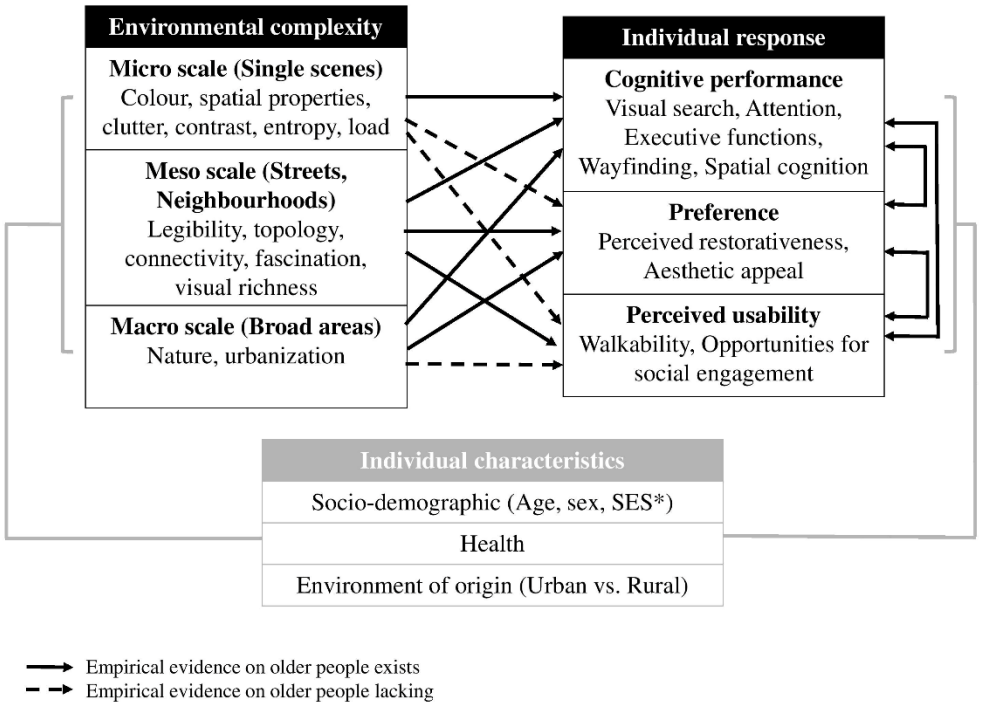


Figure 3.1

Links between environmental complexity and cognition

Proposed framework to study the association between environmental complexity (defined at multiple environmental scales) and cognitive performance in ageing. Solid lines indicate established associations (e.g. environmental perceptual stimulation can be associated with cognitive performance in older age directly in relation to cognitive load). Dashed lines indicate associations related to ageing processes which need to be explored by future research. Individual characteristics (in grey) mediate the association.

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The framework is based on the assumption that cognition is situated (Clark, 1999a, 1999b), embedded in the environment. The literature on learning environments (Brown, Collins, & Duguid, 1989; Choi & Hannafin, 1995) and ecological models of development (Bronfenbrenner, 1979; Gibson, 2000; Gibson, 1986) suggest that the successful fulfilment of cognitive tasks depends on how individuals interact with their surroundings. This interaction can be explored in relation to three types of environmental influences:

(a) the direct environmental impact on cognitive functioning based on the amount/type of perceptual information (Berman et al., 2008; Lavie, 1995; Lavie, Hirst, de Fockert, & Viding, 2004; Linnell et al., 2013);

(b) the mediating role of environmental qualities which influence affective responses such as environmental preference (Kaplan and Kaplan 1989; Kaplan 1995), as well as

(c) the "affordances" or "presses" which affect the perception of usability and, as a consequence, the likelihood of using the environment (Gibson 1986; Lawton and Nahemow 1973).

We argue that defining complexity in relation to these different dimensions may provide insights into studying the environmental impact on cognitive ageing, especially considering that the evidence for the impact of these dimensions on cognition is abundant.

The plausibility of a direct environmental impact on cognition has been supported by animal studies (Engineer et al., 2004; Hannan, 2014; Herring et al., 2009), as well as recent epidemiological evidence on geographical variations of

cognitive functioning in ageing when socio-economic and lifestyle factors were controlled for (Cassarino et al. 2015; Wu et al. 2015). Experimental evidence on environmental restorativeness for cognitive skills, i.e. the potential for natural, green environments to restore depleted attentional capacities as described within attention restoration theory (ART, Berman et al., 2008; Hartig et al., 2003; Kaplan, 1995; Kaplan & Kaplan, 1982), also suggests a direct link between environment and cognition in older adults (Gamble et al., 2014). Specifically, ART suggests that exposure to nature helps to restore humans from attentional fatigue and stress (Berto, 2014) due to the presence of perceptual stimulation that engages bottom-up attention (or involuntary attention) without causing a burden on top-down attentional resources (defined as directed or voluntary attention) which can be used for other cognitive tasks, such as for example successfully navigating a novel environment. This hypothesis has recently received support from neuroimaging studies showing that exposure to environments with high restorative potential, such as natural scenes, or urban scenes including vegetation, activates brain areas involved in involuntary attention (Martínez-Soto, Gonzales-Santos, Pasaye, & Barrios, 2013), including the middle frontal gyrus, middle and inferior temporal gyrus, insula, inferior parietal lobe, and cuneus.

User's environmental preference can further inform on environmental influences on cognition because it is related to how, and based on which factors, people perceive the surrounding environment as pleasant (Lynch, 1960; Quercia, O'Hare, & Cramer, 2014; Zambaldi, Pesce, Quercia, & Almeida, 2014). Studies on environmental restorativeness have in fact shown that cognitive skills such as voluntary attention and executive functions are positively associated with preference ratings of lived environments (Kaplan & Berman, 2010; Kaplan & Kaplan, 1982).

Moreover, the aesthetic appeal of the environment can influence lifestyle, such as transportation choices (Ding et al., 2014; Kerr et al., 2012).

Lastly, the design of the built environment influences its perceived usability, for example in terms of opportunities for physical exercise, and therefore the engagement in active lifestyles (Carlson et al., 2012; Ewing & Handy, 2009; Guo, 2009; Kerr et al., 2012), which in turn benefit cognitive health, especially in older age (Abbott et al., 2004; Ble et al., 2005; Erickson et al., 2011; Fillit et al., 2002; Fratiglioni et al., 2004; Weuve et al., 2004). For example, the successful navigation of an environment (e.g.: a city) for an older individual depends not only on the person's visuo-spatial skills, but also on the opportunities for navigation present in that environment (e.g.: accessible pedestrian areas), and on the aesthetic appeal which promotes positive psychological states (e.g.: presence of green, see Berto, 2014).

The relationship between environmental complexity and the ageing individual's cognitive skills may influence whether the person is able to use the environment finding it easy to use, pleasant and conducive to an active lifestyle. In turn, such a positive relationship with the environment may promote healthy cognitive ageing. Environmental complexity could represent a key factor to identify an optimal level of environmental stimulation for cognitive functioning in older age, however it is difficult to provide a definition of complexity that could be studied in relation to all the above dimensions, and inform cognitive ageing in relation to different types of environment. In fact, there is no commonly accepted operationalisation of complexity in the literature (Cannon & John, 2007), although

recent studies have attempted to operationalise the construct (Berto, Barbiero, Pasini, & Pieter, 2015).

Looking at micro features of scenes, for example, measures of visual complexity include (but are not limited to, see Cavalcante et al., 2014, Gunawardena et al., 2015 for a review): clutter, defined by Rosenholtz et al. (2005) as an excessive amount of distractors in a scene, determined either objectively through statistical techniques (Jingling & Tseng, 2013; Rosenholtz, Huang, Raj, Balas, & Ilie, 2012) or subjectively via participants judgments (Ho, Scialfa, Caird, & Graw, 2001; McPhee, Scialfa, Dennis, Ho, & Caird, 2004; spatial frequency, defined as a measure of the repetition of sinusoidal components of a structure per unit of distance (Cavalcante et al., 2014); contrast, defined in vision as the difference in luminance or colour that makes an object or display distinguishable from others (Cavalcante et al., 2014; Rosenholtz et al., 2005); fractal dimension, a measure of how well an object fills the space in which it lies, with higher fractal dimension indicating higher visual complexity (Mandelbrot, 1977).

Moving onto the meso scale of qualities of the built environment, complexity has been measured in terms of richness and variety of information in urban design (Ewing & Handy, 2009; Kaplan, Kaplan, & Brown, 1989), while studies on space syntax use network connectivity as a measure of layout complexity (Slone, Burles, & Iaria, 2016).

Moreover, macro scale environments such as cities tend to be considered in research as more perceptually complex than rural and/or natural settings (Berman et al., 2008; Kaplan & Kaplan, 1989; Linnell, Caparos, & Davidoff, 2014; Linnell et al., 2013).

These different measures are due to the specific characteristics of each field of investigation. However, numerous definitions of complexity make it difficult to operationalise this construct for a broad empirical examination of the environmental influence on cognition, justifying the need for a framework which synthesizes different measures of complexity to identify the links between cognition and the environment. This would allow to explore whether environmental complexity is associated with cognitive performance, preference and usability at each environmental scale (micro, meso, and macro), or whether the association at one scale may impact the association at another scale.

To this end, we discuss in the following sections a selection of studies on specific measures of complexity associated with cognitive performance, environmental preference, and perceived usability for each environmental scale as described in Figure 3.1. Although ageing individuals are the population of interest of the present review, little research in this area has been carried on older people, therefore inferences on implications for studying cognitive ageing are proposed where evidence on young populations is the only available. We then discuss suggestions for future research.

Complexity and Cognitive Performance

At a micro scale, the association between complexity and cognitive performance has been investigated in terms of low-level perceptual features of images which influence visual search, showing, for example, that scenes high in complexity in terms of clutter (measured either objectively or subjectively) or crowding of distractors, impact negatively on reaction times and accuracy when trying to detect a target stimulus (Ho et al., 2001; Jingling & Tseng, 2013; McPhee

et al., 2004; Plainis & Murray, 2002; Rosenholtz et al., 2005). These results may depend on the fact that visual complexity affects scanning strategies, as shown by Wu and colleagues (Wu, Anderson, Bischof, & Kingstone, 2014) whom, by examining temporal dynamics of eye movements, reported less structured, and therefore more exploratory, scanning strategies for scenes with high complexity (measured in terms of fractal dimension and clutter) in young participants, while reduced complexity was associated with more structured fixations around specific objects. Davidson & Bar-Yam (2006) reported however positive associations between visual complexity, operationalised as a combination of possible spatial positions (a measure of entropy) and internal features of objects, and the cognitive performance of older adults measured through the Mini Mental State Examination (MMSE). One might then ask whether there is a linear association between increased visual complexity and worse perceptual and voluntary attentional processing. Neurophysiological studies (Hansen, Johnson, & Ellemberg, 2012) have shown that, in young adults, an increase in visual complexity actually stimulates enhanced responses by the visual system (measured through evoked potentials), but up to a certain threshold after which saturation is reached, supporting a detrimental effect on visual search for scenes which are perceptually too complex (Cavalcante et al., 2014; Hansen et al., 2012).

According to load theory (Lavie, 1995; Lavie et al., 2004; Lavie & Tsal, 1994), susceptibility to distractors depends on the level of perceptual load caused by an attended scene: higher perceptual load, associated with higher complexity, for example number of objects or colours, reduces the awareness for distractors. While this reduced distractibility indicates improved selective attention, it also implies lower visual and auditory awareness of stimuli which could be important in real-life

situations, as for example the presence of unexpected events while driving (Murphy & Greene, 2015). Given age-related changes in visual processing (Fiorentini, Porciatti, Morrone, & Burr, 1996; Porciatti, Burr, Morrone, & Fiorentini, 1992; Sokol, Moskowitz, & Towle, 1981; Tobimatsu, Kurita-Tashima, Nakayama-Hiromatsu, Akazawa, & Kato, 1993), one could expect an even higher dependence of the visual system on visual complexity with ageing. In fact, older age exacerbates the interference effects associated with visual complexity, as found for example in studies on simulated driving in different conditions of clutter or contrast (Cantin et al., 2009; Ho et al., 2001; McPhee et al., 2004), and is associated with higher susceptibility to distractors (de Fockert et al., 2009; Maylor & Lavie, 1998), meaning that low-level perceptual features which make the environment less complex could facilitate its successful exploration or navigation for an older person.

Considering complexity at the meso scale of global qualities of proximal environments (e.g. streets, neighborhoods), fascination (Kaplan 1995; Kaplan and Berman 2010) is a subjective quality of environments proposed by ART to elicit involuntary attention and therefore reduce the burden on directed (voluntary) attention, improving selective attention, for example measured through an attention orienting task (Berto, Baroni, Zainaghi, & Bettella, 2010), as well as promoting a less effortful visual search measured via eye movements (Berto, Massaccesi, & Pasini, 2008). In addition, topographic factors are relevant to understand the burden of the structure of the environment on cognition, given the evidence that navigational skills can decrease with age (Klencklen et al., 2012; I. Liu et al., 2011; Lövdén, Schellenbach, et al., 2005). Legibility, defined by Lynch (1960) as the extent to which a place can be easily read to be navigated, has been shown to affect wayfinding in outdoor environments both in healthy individuals (Li & Klippel, 2014;

Long & Baran, 2012) and in patients with dementia and cognitive impairment, for example in relation to the presence of landmarks and architectural features (Mitchell & Burton, 2006; Mitchell, Burton, & Raman, 2004). Moreover, complex topology has been associated with worse visual sampling in older patients with Parkinson's Disease when navigating environments with turning points rather than straight paths (Galna et al., 2012). In line with this evidence, Barton and colleagues (Barton, Valtchanov, & Ellard, 2014) found impaired navigation skills (measured in terms of speed and accuracy when reaching a target) in environments with low intelligibility, which they operationalised as the correlation of connectivity (the number of potential routes connected to a specific path in a network) and integration (the average number of turns required to change path in the network). The results were independent of familiarity with the environment or accessibility to visual information. Similarly, Slone et al. (2015) compared the wayfinding performance of young participants in two virtual indoor environments by manipulating plan complexity, a measure of network connectivity defined as the average number of connections at each decision point or terminal corridor, and found that the more interconnected (more complex) environment caused more errors and longer completion times to reach a target, although performance improved with familiarity. In a following study (Slone et al., 2016) using functional magnetic resonance imaging (fMRI) the authors found that varying the network connectivity (and thus the complexity) of an environment not only influenced navigational performance, but also modulated the activity of brain areas associated with successful navigation (e.g. hippocampus, precuneus, cerebellum and prefrontal cortex). Thus, legibility and topology are distinct but both associated with environmental complexity, and, importantly, with cognitive performance in terms of navigation skills.

Lastly, at a macro scale, different studies based on ART have reported the cognitive benefits of exposure to nature (both for real environments and pictures) in young and older people, in terms of visual search (Sandry, Schwark, Hunt, Geels, & Rice, 2012), as well as voluntary attention and executive functions (Berman et al., 2008; Berry, Sweeney, Morath, Odum, & Jordan, 2014; Berto, 2005; Gamble et al., 2014; Hartig et al., 2003; Kaplan & Berman, 2010; Laumann et al., 2001). Berman et al. (2012) also found improvements in memory span after a walk in nature for patients with depressive disorders. If a short exposure to urban or natural environments affects cognition, one might argue that different perceptual and top-down attentional strategies could be influenced by the environment of residence, which could therefore be considered as a form of long-term exposure. Studies which compared perceptual biases and attentional engagement of individuals living in remote rural areas to a highly urbanized group (Bremner et al., 2016; Caparos et al., 2012; de Fockert et al., 2011; Linnell et al., 2014, 2013) have shown that people living in urbanized areas (i.e. Londoners), when compared to remote individuals, had a more global perceptual bias and more unfocused selective attention, which would indicate more disengaged and exploratory visual strategies. The authors suggested that these differences were due to a higher level of visual clutter (in terms of number of objects) in urban environments, which would cause an increase in intrinsic alertness and would prioritize exploration over focused attention (Linnell et al., 2014). This effect, according to the authors, was independent of cultural or social influences because even a brief exposure (two visits) of remote people to an urbanized environment changed the perceptual bias (measured through susceptibility to the Ebbinghaus Illusion) from local to global (Caparos et al., 2012). In line with these results, Chapman & Underwood (1998) reported shorter fixations for drivers in

urban rather than rural environments, suggesting more exploratory scanning strategies for complex environments. In our recent work (Cassarino et al., 2016), we showed that urban healthy older people had better executive functions than people living in rural areas after controlling for socio-economic, health, and lifestyle confounders, further indicating that different environments could be associated with distinct perceptual and cognitive abilities. Although the study did not manipulate environmental complexity directly, the results suggest a direct association between living in a complex environment and cognitive functioning in older age.

Complexity and Environmental Preference

Low-level colour and spatial properties of scenes have been associated with preference for environments which present elements of nature (Berman et al., 2014; Kardan et al., 2015). Specifically, Berman and colleagues (Berman et al., 2014) showed that properties including lower density of straight edges, lower hue level (i.e.: high prevalence of yellow-green content), and higher diversity in colour saturation were more likely to be found in scenes of nature, and were significantly associated with positive ratings of environmental preference; the authors speculated that, in line with ART, these properties could explain preference for natural environments rather than urban scenes because less taxing on voluntary attentional resources. These results were replicated by Kardan et al. (2015), who showed that scenes of environments which presented varying edges, diverse levels of saturations, and yellow-green colour tones significantly contributed to positive preference ratings in younger adults. Similarly, Quercia, O'Hare & Cramer (2014) reported positive aesthetic judgments of beauty, quiet and happiness for environmental scenes with

green colour, a higher density of vertical edges (a measure related to the structure of buildings), and a higher density of visual points of interest. In addition, Forsythe (Forsythe, Nadal, Sheehy, Cela-Conde, & Sawey, 2011) showed that images of natural environments with high complexity, measured through fractal dimension, were judged as the most beautiful when compared to images of man-made environments as well as images of abstract art, and the objective complexity matched well with the subjective perception of complexity (defined in this study as "the amount of detail and intricacy"). However, despite the evidence that older people prefer natural environments (Berto, 2007), perceptual features of scenes associated with environmental preference have not been tested in older populations, thus representing an interesting area for future investigation. It is also to note that architectural micro features of urban streetscapes can influence environmental ratings, as found by Lindal & Hartig (2013) who associated higher architectural entropy, measured as variation in silhouette and surface attributes of buildings, with positive judgments of preference and likelihood of restoration, suggesting that different types of perceptual features can influence users' appeal depending on the specific type of environment.

Studies on urban design (Ewing & Handy, 2009; Ewing, Handy, Brownson, Clemente, & Winston, 2006; Purciel et al., 2009; Rapoport, 1990; Rapoport & Hawkes, 1970; Rapoport & Kantor, 1967) inform on perceived qualities associated with users' environmental preference at a meso scale. Among other qualities, complexity defined as visual richness in colours, architectural styles, buildings and activities is a factor significantly influencing positive affective responses to places (Ewing & Handy, 2009; Purciel et al., 2009; Rapoport & Kantor, 1967). Similarly, Kaplan hypothesised that complexity, defined as richness of environmental

information, is a predictor of environmental preference because promoting exploration (Kaplan et al., 1989), and studies on the preference for urban landscapes seem to support Kaplan's hypothesis, indicating natural elements as a key modulator for positive ratings of urban environments (Abkar, Kamal, Maulan, & Davoodi, 2011; Hernández & Hidalgo, 2005; Herzog, 1992; Martínez-Soto, Gonzales-Santos, Barrios, & Lena, 2014; Pazhouhanfar, Davoodi, & Kamal, 2013; Twedt, Rainey, & Proffitt, 2016). Along this line, richness and variety in environmental information have been suggested as key design factors for dementia-friendly environments (Mitchell & Burton, 2006).

More broadly, natural environments have been associated with positive judgments of preference (Abkar et al., 2011; Hernández & Hidalgo, 2005; Herzog, 1992; Laumann et al., 2001; Martínez-Soto et al., 2014; Pazhouhanfar et al., 2013; Twedt et al., 2016). A limitation of comparing broad environments such as green areas and urban contexts is the potential influence of confounders, which calls for a more in-depth analysis of these environments. A recent study (Staats, Jahncke, Herzog, & Hartig, 2016) addressed this issue by comparing judgments of preference and restoration likelihood for four urban scenarios (city park, cafe, shopping mall, busy street): The results showed that busy street scenarios were the least preferred, although these results were moderated by social factors (being in company or alone). Interestingly, the findings were moderated by the country of residence, which highlights the importance of broad contextual factors for environmental perception.

Complexity and Perceived Usability

Gibson's ecological theory of perception (Gibson, 1986) suggests that perceptual characteristics of the environment can act as "affordances" which inform users on opportunities for action, and which facilitate usability depending on how well they fit individuals' abilities. Importantly, environments that are perceived as usable have the potential to promote health-related behaviour, such as physical activity, or walkability (Adkins, Dill, Luhr, & Neal, 2012; Cohen et al., 2007; Leyden, 2003; McCormack, Rock, Toohey, & Hignell, 2010; Wood et al., 2008). Thus, identifying perceptual affordances in the environment can inform on strategies to foster active lifestyles which benefit cognitive health in older age. For example, street characteristics such as slopes or zebra crossings have been reported to be perceived by older people as more attractive for walking (Borst, Miedema, de Vries, Graham, & van Dongen, 2008). Moreover, traffic lights can facilitate older people to cross the street, but if the lights do not allow enough time for older pedestrians to cross (Lachapelle & Cloutier, 2017; Romero-Ortuno, Cogan, Cunningham, & Kenny, 2010), they can negatively impact on mobility, especially if the older person finds it difficult to use perceptual information for decision-making (Lobjois & Cavallo, 2009). These features can be considered measures of complexity which inform on the accessibility of the environment for older people. However, while environmental measures to reduce complexity for enhanced usability have been to some extent implemented in studies on universal design in relation to accessibility for individuals with physical or cognitive impairment, for example in terms of street layout, (Crews & Zavotka, 2006; Iwarsson & Ståahl, 2003; Mace, 1997; Mynatt et al., 2000), an account linking low-level perceptual features with the experience and the use of the environment in normal ageing is still lacking. One could expect that

the same perceptual features of the environment that influence top-down attentional control and environmental preference, such as clutter or colour properties, would affect its perceived usability, but to our knowledge no studies have explored this association, especially in relation to ageing, which stimulates further research in this area, as suggested by Wu et al. (2014).

Complexity at a meso scale, defined as richness of information, can also promote the use of the environment (Ewing, Hajrasouliha, Neckerman, Purciel-Hill, & Greene, 2015; Ewing & Handy, 2009; Rapoport & Hawkes, 1970). For example, in relation to walking, Ewing et al. (2015) found a significant positive association between the number of street furniture (an indicator of urban complexity in terms of visual richness) and the number of pedestrians encountered in a given block, although they didn't record the age of the pedestrians. Nonetheless, studies on environmental design for physical activity in older people suggest that elements of attractiveness and interest increase perceived walkability (Kerr et al., 2012; Michael et al., 2006). On the other hand, however, perceptions of walkability are influenced by design qualities which make environments more accessible, such as legible topography or increased network connectivity (Adkins et al., 2012; Guo, 2009). These qualities have been in fact associated with positive perceptions of usability and walkability both in healthy older individuals (e.g. in relation to street connectivity and accessibility to services; see (Kerr et al., 2012; Rosso, Auchincloss, & Michael, 2011), and in patients populations (Joseph & Zimring, 2007; Mitchell & Burton, 2006; Mitchell et al., 2004).

At a macro scale, in a previous review on environmental influences on ageing processes (Cassarino & Setti, 2015), we compared urban and rural environments in

relation to physical exercise and social engagement, showing how each type of environment was associated with both perceived opportunities and challenges for active and engaged lifestyles (e.g.: some studies reported higher level of instrumental walking in rural areas, but more recreational walking in urban areas). Assuming that rural environments are less perceptually and structurally complex than urban contexts, and based on the evidence that environmental measures related to health-related behaviour in ageing can be area-specific (Cleland et al., 2015; Levasseur et al., 2015), one could argue that different environments afford different types of usability. While urban-rural dichotomies can be too simplistic to address usability, studies on nature highlight that the use of green areas (which are supposedly more available in rural environments) benefits physical and mental health (Barton, Griffin, & Pretty, 2011; Barton & Pretty, 2010; Berman et al., 2012; Beyer et al., 2014; Dallat et al., 2013), in turn promoting cognitive health as well as restoring attention, as previously discussed.

Discussion and Conclusion

The discussed literature indicates properties and qualities which make lived environments more or less complex, and how they may impact cognitive performance either directly or indirectly. Importantly, while measures of complexity have been discussed over three environmental scales (i.e., micro, meso, and macro), these need to be considered not as distinct, but as interconnected and interdependent levels of a continuum of environmental influences.

Considering different operationalisations of complexity at a micro scale, cognitive functioning in older age can be affected by properties that make scenes less

perceptually complex, such as reduced clutter or presence of distractors, which have been shown to facilitate visual search and voluntary attention. Colour and spatial properties which can be found in natural (and supposedly less complex) settings are more appealing to users, and ART suggests that environmental preference may depend on the restorative potential of nature for voluntary attention, drawing a link between affective and cognitive responses to the environment based on perceptual complexity which deserves further exploration in relation to ageing. These properties could in fact potentially serve as affordances for the use of the environment (e.g.: by promoting navigation).

Studies on measures of complexity at a meso scale further support the hypothesis that environments which are legible, or easy to "read", facilitate cognitive skills such as attentional control and navigational skills in older age, as well as promoting usability and engagement in health-related behaviour. However, environments need to provide some level of cognitive stimulation to avoid boredom (Rapoport & Kantor, 1967), as shown by the findings that exposure to environments with high fascination and visual richness enhances environmental preference (Kaplan et al., 1989), in turn positively associated with improved selective attention and visual search (Berto et al., 2010, 2008). It is to note that Kaplan (Kaplan et al., 1989) suggested complexity (a measure of the visual richness of a scene) and legibility (indicating how easy an environment can be read) as two distinct environmental qualities predicting judgments of preference and perceived restorativeness of environments. This conceptualization seems to contradict our suggestion that legibility could be a potential measure of environmental complexity based on the discussed studies on wayfinding, but we need to distinguish between different levels of operationalisation of complexity considering also the role of

coherence, another predictor of environmental preference which measures the level of order and organization of an environmental scene (Kaplan et al., 1989): Environments with low legibility are intuitively less coherent, and therefore more complex for perception and cognition, but not necessarily poor in terms of richness of stimulation (or complexity according to Kaplan). On the other hand, an environment can be rich in terms of variation of elements, but still legible and coherent, as in the case of nature. Therefore, both legibility and information-richness inform on the amount of perceptual stimulation received from the environment, and a balance between these two qualities could be a key indicator of cognitively optimal environments.

Lastly, at a macro scale, while exposure to natural (and less complex) settings has the potential to enhance voluntary attention both in young and older samples, and positively impact environmental preference and perceived usability, studies suggest that environments with different levels of structural complexity (e.g.: rural vs. urban) can offer different types/levels of stimulation for cognitive health, supporting the role of micro and meso level environmental measures of complexity in influencing cognitive performance both directly and indirectly.

The discussed evidence suggests that environmental complexity can be a key contributor to design living contexts which support and stimulate cognitive health in older age. However, what determines an optimally stimulating environment for older people remains to be established, although the existing measures of complexity support the hypothesis that factors which on one hand facilitate action, and on the other hand stimulate interest could contribute to an optimal level of environmental

complexity. This hypothesis should be tested in the context of cognitive ageing. Based on the discussed studies, specific suggestions for future research emerge.

Firstly, the most suitable environmental measures to quantify an optimal level of environmental complexity for cognitive performance need to be identified by empirical work. Future experimental studies could manipulate the discussed measures both cross-sectionally to identify correlations with cognitive performance, and longitudinally to highlight causal effects.

The relations between different measures of complexity at different environmental scales should be explored, in terms of understanding whether complexity at a micro scale (e.g.: perceptual load) is correlated with complexity at a meso scale (e.g.: neighborhood legibility), or whether cognitive abilities engaged at different scales are correlated (e.g. visual search in a cluttered scene and visual search in spatial navigation), or whether the cognitive load required at different scales is associated with preference and, possibly, lifestyle (in terms of use of the environment). Therefore, an analysis of the lived environment could consider, for example, the level of perceptual complexity and restorativeness of specific scenes in the local surroundings (Berto, 2014), the network complexity of the main paths connecting the individual with focal points such as shops, amenities, or parks (Joseph & Zimring, 2007; Slone et al., 2015), as well as the quality of these paths in terms of attentional load and more broadly in terms of aesthetic appeal and perceived usability. This kind of empirical work could then inform both on the mechanisms behind the relationship between environmental complexity, cognition, usability and preference, and on which environmental characteristics can be modified to make the lived environment more optimal for the ageing individual.

Importantly, although many studies on environmental complexity have focused on the visual domain, environments offer multisensory experiences which may impact cognitive processing as well as affective responses and behaviour (Brambilla & Maffei, 2006b; Emfield & Neider, 2013; Marin & Leder, 2013; Wais & Gazzaley, 2011), and because the processing of information from different sensory modalities changes with age, showing for example a more facilitating effect on attentional performance of multisensory stimuli (Laurienti et al., 2006; Setti et al., 2011), future studies should take into account multiple sensory domains when studying the interaction of older people with their environment.

Both objective and subjective measures of complexity should be tested to identify potential inconsistencies and to attempt a comprehensive operationalisation. Long & Baran (2012), for example, found significant correlations between objective intelligibility and perceived legibility of neighborhoods. Moreover, Kim et al. (2014) highlighted the importance of using both objective and subjective measures of the built environment to identify environmental influences on human behaviour at multiple environmental scales. The development of surveys and questionnaires could help to assess both objective and subjective environmental factors for cognition, as for example done for the assessment of the pedestrian environment (Clifton, Livi Smith, & Rodriguez, 2007), for identifying qualities of residential environments for ageing well (Burton, Mitchell, & Stride, 2011; Dunstan et al., 2005; World Health Organization, 2007), or for ratings of preference (Hartig, Korpela, Evans, & Gärling, 1997; Laumann et al., 2001).

Lastly, other potential factors should be included in this investigation. For example, the role of coherence (Kaplan et al., 1989) in modulating the relationship

between the legibility and the richness of information of an environment should be taken into account when looking at urban design. In addition, familiarity has been shown to influence wayfinding skills (Klencklen et al., 2012; Slone et al., 2015) as well as preference (Berto, 2007), and experience improves driving performance even in complex environments (Patten, Kircher, Östlund, Nilsson, & Svenson, 2006; Underwood, 2007; Underwood et al., 2003).

The purpose of this work was to provide evidence from the literature that environmental complexity serves as a unifying concept for the multiple environmental influences on cognition, and for studying healthy ageing in place from a cognitive perspective, in line with the existing literature on environmental influences on behaviour and health (Beard & Petitot, 2010; Brownson, Hoehner, Day, Forsyth, & Sallis, 2009; Carlson et al., 2012; Clarke & George, 2005; Kerr et al., 2012; Renalds et al., 2010). The evidence of associations between environmental complexity and cognitive ageing is currently fragmentary or inferred from studies on young populations, therefore this targeted review aimed to provide some insights for future research on a topic which is of increasing relevance given global demographic changes (World Health Organization, 2007).

The literature on ageing in place (Black, 2008; Mynatt et al., 2000; Wiles et al., 2012) points out the importance of developing effective forms of environmental support which enhance usability, for example through technology (Mynatt et al., 2000; Rantz, Skubic, Miller, & Krampe, 2008). Importantly, environmental support needs to be addressed not only in terms of what can be afforded by individuals with impairments such as poor vision or hearing, but also in terms of how everyday cognition can be optimized in relation to the environment - an aspect explored, for

example, in research on human-computer interaction (Hollan, Hutchins, & Kirsh, 2000; Preece et al., 1994; Preece, Sharp, & Rogers, 2015; Zander & Kothe, 2011). Understanding cognitive ageing in place is a current priority given the increasing need for supportive and enabling environments for ageing individuals (World Health Organization, 2007). We argue that studying complexity will advance the knowledge on the factors which make the built environment optimally stimulating for cognition, usable and pleasant, and a first step in this direction is to consider different measures of complexity and their relationships at micro, meso and macro environmental scales. Complementarily, it is crucial to develop instruments to capture how the individual perceives the cognitive load when interacting with the environment and what strategies are adopted to minimise it, for example in case of physical limitations. These instruments should take into account objective measures and the subjective experience of the lived environment.

The proposed framework hopes to stimulate interdisciplinary research on perception, cognition, subjective preference, and usability to better understand environmental influences on cognition, especially in relation to ageing, and therefore to inform urban design and planning on strategies to make environments cognitive-friendly for older people, where with “friendly” we intend environments which are facilitating but at the same time optimally stimulating.

Chapter 4 – Research Objectives and General Methodology

Aim and Focus

The present project focused on exploring whether urban or rural environments are more cognitive-friendly, that is, more supportive of cognitive functioning in older age. Considering the literature discussed in the previous chapters, animal models tells us that exposure to a physically enriched and stimulating environment can cause positive changes both at a neurophysiological and behavioural level which benefit cognitive ageing. In addition, epidemiological and experimental studies suggest differences in attention, executive functions and general cognitive health based on exposure to, or residence in, more or less urbanised environments. Using this evidence, we proposed a model built from a cognitive perspective to investigate the lived environment as a direct source of cognitive stimulation (as described in Chapter 2). Physical factors such as noise or visual richness, for example, can make the environment more or less complex to perceive and interact with. Given higher susceptibility to environmental stimulation in older age (Lawton, 1989a), we can expect that the efficiency of an older adult's cognitive skills such as attention or executive functions can be influenced by being exposed to high or low levels of environmental complexity. We use the concept of complexity as it has been utilised at different levels of analysis from visual perception (Cavalcante et al., 2014) to urban design (Rapoport & Hawkes, 1970), and it serves the purpose of paradigmatic concept in the present work. Thus, in order to understand what makes an environment cognitive-friendly in older age, our model proposes to identify the environmental factors that offer an optimal level of

complexity for cognitive processing. To this end, we synthesised existing measures of complexity associated directly or indirectly with cognitive outcomes in a framework, and proposed three environmental levels of analysis, going from the micro scale of perceptual features of scenes, such as colour or clutter, to the meso level of design qualities of streets or neighbourhoods, as for example legibility, to the macro level of broad urban or rural environments (see Chapter 3). This approach aims to go into progressively more depth in understanding the influence of the environment at these different scales.

The empirical studies conducted as part of the doctoral project focused on the macro and meso levels of investigation and explored geographical variations in multiple cognitive skills (global cognition, memory, speed of processing, attention, and executive functions) for a large sample of healthy Irish individuals aged 50 and older. The variations were based on the level of urbanisation of the place of residence, assuming urbanisation as a proxy of environmental complexity.

This type of investigation was chosen for multiple reasons. Firstly, exploring whether variations in cognitive performance exist at a broad geographical scale (macro level) is an important initial step to clarify the broad impact of urbanisation on cognition and to guide subsequent research investigating environmental factors intervening at smaller geographical scales. Secondly, as explained in the Introduction (Chapter 1), epidemiological studies have mainly focused on patient populations and general cognitive impairment; as a consequence, it is unclear whether variations in cognitive performance can be highlighted already in healthy adult populations and whether the place of residence impacts specific cognitive domains differently. Third, experimental studies investigating environmental influences on specific cognitive

skills (e.g., attention, executive functions) have focused mainly on young populations, leaving unanswered the question on whether similar associations can be observed in older samples. The studies presented in the following chapters aim therefore to add to the literature on geographical variations in cognitive health in older age by looking at a healthy adult sample and at multiple cognitive domains.

Based on existing models considering individual responses to varying levels of environmental stimulation (Berlyne, 1970; Lawton & Nahemow, 1973; Rapoport & Hawkes, 1970; Yerkes & Dodson, 1908), we hypothesised a nonlinear association between levels of urbanisation and cognitive performance. Specifically, we would expect better performance in urban rather than rural participants, especially in relation to executive functions, because urban places offer a more complex and more stimulating environment. On the other hand, however, we would expect poor performance in highly urbanised areas based on studies which suggest that a highly urbanised environment can become too complex and challenging for an older person (Buffel et al., 2012; Phillipson, 2011).

The availability of data collected in The Irish Longitudinal Study on Ageing (TILDA, Trinity College Dublin) represented an excellent opportunity to test our hypothesis at a population level. Details of TILDA are provided in the following section.

The Irish Longitudinal Study on Ageing (TILDA)

This doctoral project included analyses of geographical variations in cognitive performance in older age by using data collected in The Irish Longitudinal Study on Ageing (TILDA). TILDA (Kearney et al., 2011; Kenny et al., 2010; Kenny, 2013; Whelan & Savva, 2013) is a nationally representative prospective

cohort study which began in 2009 and is conducted every two years to explore the health, well-being and socioeconomic circumstances of approximately 8,000 healthy community-dwelling Irish individuals aged 50 and older. Participants in TILDA are asked to complete a computer-assisted personal interview (CAPI) and a self-completion questionnaire (SCQ) in their homes which collect demographic data and information on health status, social circumstances, financial conditions, and well-being. In addition, a comprehensive physical and cognitive health assessment conducted every four years investigates physical and cognitive functioning (Cronin et al., 2013). TILDA is harmonised with other international and cross-national longitudinal studies (Savva, Maty, Setti, & Feeney, 2013), including the Health and Retirement Study (HRS) in the United States (Juster & Suzman, 1995), the English Longitudinal Study on Ageing (Marmot, Banks, Blundell, Lessof, & Nazroo, 2003) and the Survey of Health, Ageing and Retirement in Europe (Börsch-Supan, Hank, & Jürges, 2005), offering therefore comprehensive data on older people.

The information collected in TILDA is made available to the scientific community in an anonymised format free of charge. Researchers interested in using TILDA data may access it from the following sites: Irish Social Science Data Archive (ISSDA) at University College Dublin http://www.ucd.ie/issda/data/tilda/; Interuniversity Consortium for Political and Social Research (ICPSR) at the University of Michigan http://www.icpsr.umich.edu/icpsrweb/ICPSR/studies/34315.

Thanks to the large sample size, the wealth of information about cognitive, health and socioeconomic circumstances, and the availability of geocoded information of participants' place of residence, using TILDA data would enable to

test the macro and meso level of analysis of our model by exploring variations in cognitive performance on a large population and across different geographical areas

In order to conduct the analyses of the TILDA sample, an active collaboration with the TILDA research team was sought to have access to the data and to merge the TILDA information with measures of place of residence available in other datasets or repositories (see for details "Measures of Place of Residence" section, pp.105-107).

Participants

A total of 8,175 people aged 50 and older took part in the first wave of TILDA, with 5,898 of these completing the health assessment. The doctoral project focused on the health assessed sample as most of the cognitive assessments were collected in the health assessment. Table 4.1 includes participants' demographic, health, and social circumstances. The sample (mean age = 62.92, standard deviation = 8.84; 54.12% female) appeared to be overall healthy, well-educated and socially integrated. Over one third of the sample was still employed at the interview (37.84%), while 36% of participants were retired. Approximately 26% of the sample was unemployed either because looking after the house or for health reasons. In terms of place of residence, almost half of the participants (46.55%) lived in a rural area at the time of the interview and 80% of these indicated to have lived in a rural area up to the age of 14, whereas 70% of those currently living in urban places had also had an urban childhood. Over 90% of the sample was born in Ireland, and over 82% of participants had lived in the same county for 30 years or more, suggesting a general pattern of low migration. While a full account of these characteristics for the general Irish population aged 50 and older is not available in the Irish Census,

sampling weights and preliminary checks were employed by the TILDA research groups to ensure the representativeness of the sample to the general population, and details of these are available elsewhere (Cronin, O'Regan, Finucane, Kearney, & Kenny, 2013; Kenny et al., 2010; Whelan & Savva, 2013). The sample varies slightly across the analyses presented in the thesis based on the specific inclusion criteria used in each study.

Table 4.1

Participants' characteristics

Characteristic	TILDA health assessed sample (*N* = 5,898)
Demographic	
Place of residence, n (%)	
Urban (Dublin)	1,532 (26.00)
Other settlements	1,618 (37.46)
Rural	2,743 (46.55)
Irish native, n (%)	5,346 (90.64)
Lived in the same county 30+ years, n (%)	4,878 (82.82)
Female, n (%)	3,192 (54.12)
Age, mean (*SD*)	62.92 (8.84)
Education, n (%)	
None/Primary	1,544 (26.19)
Secondary	2,419 (41.03)
Third/Higher	1,933 (32.78)
Social class, n (%)	
Professional/managerial	1,440 (25.48)
Non manual	742 (13.13)
Manual	1,200 (21.23)
Farmers	334 (5.91)
Self-employed (not specified)	442 (7.82)
Unemployed	1,494 (26.43)
Employed, n (%)	2,232 (37.84)
Retired, n (%)	2,171 (36.81)
Health	
BMI, mean (*SD*)	28.66 (4.96)
Number of chronic conditions, mean (*SD*)	1.95 (1.66)
Disabilities, n (%)	682 (11.56)
Depressive symptoms, n (%)	
None/mild	4,253 (73.16)
Moderate	1,031 (17.74)
Severe	529 (9.10)
Social engagement and lifestyle	
Cohabiting, n (%)	4,715 (79.94)
Social connectedness Index, n (%)	
Mostly isolated	375 (6.37)
Moderately isolated	1,507 (25.58)
Moderately integrated	2,407 (40.86)
Mostly integrated	1,602 (27.19)
Engagement in physical activity, n (%)	
Inactive/low	1,769 (30.24)
Moderate	2,056 (35.15)
Vigorous	2,024 (34.60)
Childhood circumstances	
Father's social class, n (%)	

Professional/managerial	815 (14.40)
Non manual	479 (8.46)
Manual	2,551 (45.08)
Farmers	1,397 (24.69)
Unemployed	417 (7.37)
Rural childhood, n (%)	3,455 (58.60)
Childhood self-rated health, good/excellent, n (%)	5,509 (93.44)

General design

The project included three cross-sectional studies (Study One, Two and Three) exploring variations in cognitive performance (global cognition, memory, speed of processing, attention, and executive functions) based on the geographical location of TILDA participants' place of residence, plus one longitudinal study on changes over time in cognitive performance for some measures (global cognition, memory and verbal fluency) based on urban/rural residence (Study Four), and one cross-sectional study exploring variations in global cognitive functioning based on interactions between urban/rural residence and engagement in physical activity (Study Five). Regression analyses controlled for a comprehensive set of socio-demographic, health, and lifestyle covariates (see the "Covariates" section below). Sampling weights were applied: these were calculated for each participant in TILDA as the inverse of the probability that an individual in the Irish older population selected at random with same age, sex and educational attainment would have completed the health assessment (Kearney et al., 2011; Kenny et al., 2010), with participants from groups less likely to participate having a higher weight. Attrition weights were used in Study Four. As the public releases of the first and second waves of TILDA did not include attrition weights, we requested and were accepted by the TILDA management a project proposal to calculate *ad hoc* attrition weights to

conduct longitudinal analyses of changes in cognition between the two waves by using the TILDA hot desk.

Detailed information on the type of statistical analyses conducted are presented separately in each study.

TILDA Measures Used in the Project

The following sections describe measures of place of residence, cognitive performance, and the covariates used in general in the project. Specific measures used in each of the studies are described in the Methods section of each subsequent chapter.

Measures of Place of Residence

In Study One (Chapter 5), place of residence was defined as urban areas, other settlements, or rural areas, in line with the epidemiological literature on geographical variations in the incidence of dementia. The "other settlements" category was used to account for areas with intermediate levels of urbanisation between rural and urban places (see details on the operationalisation of this variable at p.127). This measure was accessed via the anonymised public release of the first wave of TILDA (version 1.2).

In Study Two (Chapter 6), levels of urbanisation were defined at a meso level of analysis in terms of population density (number of inhabitants per hectare) averaged at the level of the electoral division (see Chapter 6 for details). Special permission was granted from TILDA to merge the first wave of TILDA with data on the population density of TILDA participants' place of residence: The measure of population density was derived from the Irish Census 2006 collected by the Irish Central Statistics office (www.cso.ie). Data analysis was conducted on one the hot

desks available in TILDA in Trinity College Dublin after liaising with the TILDA data management in order to maintain data confidentiality.

In Study Three (Chapter 7), a collaboration with the All-Ireland Research Observatory (AIRO) Maynooth University, Ireland, made it possible for geocoded information on the area of residence captured via geographic information systems (GIS) to be linked with the geocoding of location of residence of TILDA participants'. We selected travel time to gateways as a measure of accessibility to service infrastructure and stimulating activities, mainly clustered in urban centres. This measure was captured at the level of Small Areas (see Chapter 7 for details), and enabled to explore the place of residence at a meso level of analysis. Analyses on this measure were conducted on the TILDA hot desk.

In Study Four (Chapter 8), we used the same measure of environment of residence used in Study One (urban, other settlements, rural) to study changes in cognition between the first and second wave of TILDA.

Lastly, in Study Five (Chapter 9) we explored interactions between lifestyle (i.e., the level of engagement in physical activity measured through the International Physical Activity Questionnaire (IPAQ) short form, and environment of residence coded as urban, other settlements, and rural.

The above measures of place of residence were used to capture broad variations in cognitive health, checking whether better performance was clustered in more or less urbanised areas. In addition, population density and travel time to gateways were employed to capture the potential impact of urbanisation (i.e., a more or less densely populated environment and a higher or lower accessibility to urban environments) at the level of the local place of residence. Investigating urbanisation at different environmental levels allows for a comprehensive examination of how the

environment of residence can impact cognitive functioning. However, the long procedure required to have access to information on TILDA participants' place of residence while maintaining data confidentiality, the scarce availability of environmental measures available for the Irish national territory, and the fact that funding for the project was bound to working with TILDA, limited opportunities to explore meso scale characteristics such as presence of usable green, or micro level features impacting cognitive processing. Nonetheless, exploring macro and meso levels of urbanisation offers observational data on whether broad variations in cognitive health exist.

Cognitive assessments

The cognitive variables for the study included assessments of cognitive performance collected during the CAPI interview and the health assessment in TILDA (Kenny et al., 2010) and are related to global cognition, memory, speed of processing, attention, and executive functions (see Table 4.2). Measures of global cognition included the Montreal Cognitive Assessment Test (Nasreddine et al., 2005) and the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975). Memory was measured in terms of: immediate and delayed recall of a list of 10 words based on the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery (Morris et al., 1989; Welsh et al., 1994), derived from the Health & Retirement Study and used across several longitudinal studies (Shih, Lee, & Das, 2011); recall and recognition in a Picture Memory Test taken from the Cambridge Mental Disorders of the Elderly Examination, or CAMDEX (Roth et al., 1986); and prospective memory (reminding the reviewer to do a certain thing after occurrence of a specific event) based on the Rivermead Behavioural Memory Test (Wilson, Cockburn, & Baddeley, 1991). Speed of processing was assessed through the

cognitive mean reaction time (in seconds) for the Choice Reaction Time Test, and through the mean completion time (seconds) for the Colour Trail Making Test Part 1 (CTT 1), while attention was assessed through self-rated frequency of absentmindedness (coded as 0 = "Sometimes/Never", 1 = "Most of/All the time"), and the Sustained Attention to Response Task (SART) (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) in terms of reaction time (milliseconds, SART RT), standard deviation from the mean reaction time (a measure of variability of performance, SART SD), number of commission errors (responding when not needed, SART Commissions), and number of omissions (not responding when needed, SART Omissions). Lastly, measures of executive functions included a verbal fluency test asking to name as many animals as possible (Lezak, 2004), a 6-items test of visual reasoning from the CAMDEX (Roth et al., 1986), the mean completion time (seconds) for the Colour Trail Making Test 2 (CTT 2, D'Elia, Satz, Uchiyama, & White, 1996), and the mean change in completion time from CTT 1 to CTT 2 (CTT Δ), this last considered a measure of executive function adjusted for biases due to differences in visuo-motor functioning (Ble et al., 2005). CTT errors were not analysed due to the very low error rate, equal to less than 10% for one error and less than 2% for two or more errors (Cavaco et al., 2013).

All cognitive measures were explored in relation to the place of residence in the cross-sectional studies except for the longitudinal analyses in Study Four, which focused on MMSE, immediate and delayed recall, prospective memory and verbal fluency because these were the only measures of cognition which were assessed in the second wave of TILDA as part of the CAPI, and for Study Five (see Chapter 9) which explored the moderating effect of lifestyle on geographical variations in MoCA scores emerged in Study One (Chapter 5).

Correlations between cognitive measures for the health assessed sample (excluding observations with missing cases, N = 5,262) are shown in Table 4.3.

Table 4.2

List and Operationalisation of Cognitive Assessments

Cognitive dimension	Measure	Operationalisation
Global cognition	Montreal Cognitive Assessment Test (MoCA)	Mean total score (0 to 30)
	Mini Mental State Examination (MMSE)	Mean total score (0 to 30)
Memory	Immediate recall (10-words list learning)	Mean number of recalled words (0 to 10)
	Delayed recall	Mean number of recalled words after delay (0 to 10)
	Picture Memory Test (PIC) – Recall	Number of recalled objects (0 to 6)
	Picture Memory Test (PIC) – Recognition	Number of identified objects (0 to 6)
	Prospective memory	Success/failure (0, 1) in reminding the interviewer to do something at a certain time.
Speed of processing	Choice Reaction Time Test – Cognitive score (CRT)	Mean cognitive reaction time (milliseconds)
	Colour Trail Making Test Part 1 (CTT 1)	Mean completion time (seconds)
Attention	Sustained Attention to Response Task (SART)	Mean response time (milliseconds) (RT)
		Standard deviation of response time (milliseconds) (*SD*)
		Number of omissions (0 to 142)
		Number of commissions (0 to 23
	Self-rated absentmindedness	Frequency of absentmindedness (0=sometimes/never, 1=most/all times)
Executive Functions	Verbal fluency	Mean number of animal names provided
	Colour Trail Making Test Part 2 (CTT 2)	Mean completion time (seconds)
	CTT Δ	Increase in completion time from CTT 1 to CTT 2 (seconds)
	Visual reasoning	Number of correct answers (0 to 6)

Table 4.3

Correlations between cognitive assessments

	MoCA	MMSE errors	Immediate recall	Delayed recall	Picture recall	Picture recognition	Prospective memory	CRT
MoCA								
MMSE errors	-0.63							
Immediate recall	0.48	-0.42						
Delayed recall	0.45	-0.37	0.68					
Picture recall	0.26	-0.22	0.24	0.24				
Picture recognition	0.26	-0.19	0.21	0.22	0.23			
Prospective memory	0.26	-0.24	0.29	0.26	0.15	0.12		
CRT	-0.31	0.26	-0.25	-0.22	-0.17	-0.21	-0.16	
CTT 1	-0.44	0.41	-0.37	-0.32	-0.21	-0.25	-0.22	0.37
SART RT	-0.23	0.19	-0.19	-0.14	-0.09	-0.09	-0.13	0.26
SART SD	-0.37	0.33	-0.31	-0.25	-0.17	-0.18	-0.19	0.33
SART Omissions	-0.38	0.34	-0.31	-0.25	-0.16	-0.18	-0.18	0.34
SART Commissions	-0.35	0.33	-0.27	-0.24	-0.16	-0.16	-0.16	0.25
Absentmindedness	-0.08	0.09	-0.11	-0.07	-0.07	-0.04	-0.07	0.06
Fluency	0.38	-0.29	0.37	0.36	0.16	0.13	0.21	-0.21
CTT 2	-0.54	0.47	-0.42	-0.38	-0.24	-0.29	-0.25	0.41
CTT Δ	-0.41	0.34	-0.31	-0.28	-0.17	-0.21	-0.17	0.28
Visual reasoning	0.43	-0.37	0.31	0.29	0.14	0.16	0.15	-0.21

Table 4.2 (Continued)

Correlations between cognitive assessments

	CTT 1	SART RT	SART SD	SART Omis.	SART Commis.	Absentmindedness	Fluency	CTT 2	CTT Δ
SART RT	0.29								
SART SD	0.41	0.55							
SART Omissions	0.41	0.39	0.73						
SART Commissions	0.32	0.26	0.65	0.61					
Absentmindedness	0.07	0.03	0.07	0.06	0.05				
Fluency	-0.28	-0.16	-0.26	-0.25	-0.22	-0.06			
CTT 2	0.76	0.32	0.46	0.46	0.38	0.08	-0.35		
CTT Δ	0.25	0.22	0.33	0.32	0.28	0.06	-0.26	0.81	
Visual reasoning	-0.34	-0.17	-0.28	-0.27	-0.26	-0.06	0.24	-0.39	-0.29

Covariates

Covariates for statistical models included measures selected *a priori* based on the evidence in the literature of an association both with cognitive ageing and of geographical variations. These included socio-demographic measures, physical and mental health, lifestyle and social connectedness, and childhood circumstances (a detailed operationalisation is provided in Table 4.4).

In initial analyses (Study One), socio-demographic data included sex, age, educational attainment, employment status, and household income (log-transformed to inform on the percentage of increase).

Physical and mental health was assessed in terms of body mass index (BMI), self-rated hearing problems, presence of disabilities in activities of daily living (ADL) and/or instrumental activities of daily living (IADL), use of polypharmacy, clinical symptoms of depression measured through the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977), and number of chronic conditions. This was a composite variable informing on the presence of one or more among the following: high blood pressure or hypertension, angina, heart attack, congestive heart failure, diabetes or high blood sugar, stroke, mini-stroke or transient ischemic attack (TIA), high cholesterol, heart murmur, abnormal heart rhythm, other heart trouble, chronic lung disease, asthma, arthritis, osteoporosis, cancer or malignant tumour, Parkinson's disease, emotional/nervous/psychiatric problem, alcohol or substance abuse, stomach ulcers, varicose ulcers, cirrhosis or serious liver damage.

Social engagement and lifestyle included household composition (i.e., cohabiting or not) and participation in clubs taken from the Berkman-Syme Social

Network Index (Berkman & Syme, 1979), participation in lifelong learning, level of engagement in physical activity as measured through the International Physical Activity Questionnaire (IPAQ) short form (Craig et al., 2003), and smoking habits.

Lastly, childhood circumstances included father social class coded as per Irish Census, childhood urban or rural residence, and self-rated childhood health.

After completion of Study One (Chapter 5), we modified some of the covariates both for theoretical and methodological reasons. The following changes were applied: we used age as a continuous rather than a categorical measure (removing "age groups" from the analyses); the variable household income was replaced with current social class (see Table 4.4 for a detailed categorisation) to have a more accurate and long-term measure of socioeconomic status and to gain a bigger sample size (the variable income had over 1,000 missing observations); employment status was removed because of collinearity with social class; self-rated vision was introduced to give a better account of perceptual processing together with self-rated hearing; presence of disability was recoded into a dummy variable with values 1 = "Yes" (including ADL and/or IADL) and 0 = "No" (No disabilities) to have a more balanced number of observations in each category and to reduce the risk of perfect prediction; perceived frequency of loneliness (1 = "Rarely or never"; 2 = "Some of the time"; 3 = "Moderate amount/All the time") was introduced to give a better account of perceived social integration, and the Berkman-Syme Social Network Index (Berkman & Syme, 1979) was added to have a standardised composite measure of social connectedness based on household composition, participation in clubs, participation in religious events, and presence of close friends and/or relatives (1 = "Mostly isolated", 2 = "Moderately isolated", 3 = "Moderately integrated", 4 =

"Mostly integrated"); lastly, the category "Unknown" in the variable father social class was removed and those observations coded as missing. These changes were applied to validity checks of the analyses presented in Study One (Chapter 5), and to studies Two, Three, Four (Chapters 6-8).

Table 4.4

List and Operationalisation of Covariates Used in the Project

Dimension	Measure	Operationalisation
Socio-demographic	Sex	1 = Male 2 = Female
	Age group [a]	1 = 50-64 2 = 65-74 3 = 75+
	Age [b]	Range: 50 to 80+
	Educational attainment	1 = None/Primary 2 = Secondary 3 = Third/Higher
	Employment status	1 = Working 2 = Retired 3 = Other (not working, not retired)
	Household income [a]	Euro, range: 0 to 14.51
	Social class [b]	1 = Professional/managerial 2 = Non manual 3 = Manual 4 = Farmer/Self-employed not specified 5 = Unemployed
Physical and mental health	Body Mass Index	Kg/cm^2, range: 18 to 45
	Self-rated hearing	0 = Poor/Fair 1 = Good/Very good
	Self-rated vision [b]	0 = Poor/Fair 1 = Good/Very good
	Number of chronic conditions	Range: 0 to 10
	Use of polypharmacy (more than 5 medications)	0 = No 1 = Yes
	IADL and/or ADL disabilities	0 = Not disabled 1 = IADL only 2 = ADL only 3 = IADL and ADL
	Clinical symptoms of depression (CES-D)	0 = None/mild (0-7) 1 = Moderate (8-15) 2 = Severe (16-70)
Social engagement	Household composition	0 = Not cohabiting 1 = Cohabiting (spouse or others)
	Participation in social clubs or groups [a]	0 = Not participating 1 = Participating
	Berkman-Syme Social Network Index [b]	1 = Mostly isolated 2 = Moderately isolated

		3 = Moderately integrated 4 = Mostly integrated
	Perceived frequency of loneliness	1 = Rarely or never 2 = Some of the time 3 = Moderate amount/All the time
Lifelong learning	Participation in courses, education or training	0 = Not participating 1 = Participating
Behavioural health	Physical exercise (IPAQ short form)	0 = None 1 = Moderate 2 = Vigorous
	Smoking habits	1 = Never 2 = Current 3 = Past
Childhood circumstances	Father social class	1 = Professional/managerial 2 = Non Manual 3 = Manual 4 = Farmer 5 = Unemployed
	Childhood residence	0 = Urban residence 1 = Rural residence
	Childhood self-rated health	0 = Poor/Fair 1 = Good/Excellent

Note. [a]. These measures were removed from the analyses following Study One.
[b] These measures were included in the analyses following Study One.

The main rationale for choosing these covariates was the association with cognitive health in older age. Socio-demographic influences on cognition have extensively been reported in the literature, especially in relation to the protective role of higher educational attainment and socio-economic status on late-life cognition (Jefferson et al., 2011; Stern, 2012). Also well-established are the cognitive detrimental effects of poor physical and mental health: increases in BMI, in cardiovascular conditions and in the use of polypharmacy (more than five medications) have been reported to have a negative impact on cognition in older age (Hilmer & Gnjidic, 2009; Onder et al., 2013; Profenno, Porsteinsson, & Faraone,

2010; Siervo, Harrison, Jagger, Robinson, & Stephan, 2014; Yaffe et al., 2009). Problems with hearing and vision have been suggested as determinants of cognitive impairment via low-level perceptual mechanisms (Baltes & Lindenberger, 1997; Lin et al., 2013; Rogers & Langa, 2010; Toner et al., 2012) and depressive symptoms have also been linked to worse cognitive functioning in older age (Lyketsos et al., 2002; Modrego & Ferrández, 2004). Controlling for measures of social engagement and lifestyle was justified by extensive literature on cognitive reserve which has long established how engaging in social, intellectual and physical activities protects from cognitive decline both through psychological and cardiovascular mechanisms (Fratiglioni et al., 2004; Hertzog et al., 2008; Kelly et al., 2014; Zhu, Qiu, Zeng, & Li, 2017). Lastly, we controlled for childhood socio-economic, environmental and health circumstances to account for potential long-term moderating effects on cognitive ageing as suggested in the literature (Case, Fertig, & Paxson, 2005; Contador et al., 2015; Fors et al., 2009; Santos et al., 2008).

Importantly, these measures, particularly in relation to health and lifestyle, can show geographical variations based on the level of urbanisation as well as physical, social and economic characteristics of the place of residence, for example in terms of social capital, walkability, or accessibility to health services or healthy food (Ewing et al., 2006; Kerr et al., 2012; Layte et al., 2011; Leyden, 2003), further justifying their use in our analyses.

Chapter 5 - Study One

Environment and Cognitive Ageing: A Cross-Sectional Study of Place of Residence and Cognitive Performance in the Irish Longitudinal Study on Ageing.[3]

Abstract

Objectives - Stimulating environments foster cognitive vitality in older age. However, it is not known whether and how geographical and physical characteristics of lived environments contribute to cognitive ageing. Evidence of higher prevalence of dementia in rural rather than urban contexts suggests that urban environments may be more stimulating than rural places either cognitively, socially or in terms of lifestyle. The present study explored urban/rural differences in cognition for healthy community-dwelling older people while controlling for a comprehensive spectrum of covariates.

Methods – The cognitive performance of 3,765 healthy Irish people aged 50+ participating in the first wave of The Irish Longitudinal Study on Ageing was analysed in relation to current location of residence – urban places, other settlements, or rural areas – and its interaction with childhood residence. Regression models controlled for socio-demographic, health, and lifestyle factors.

Results – Urban residents showed better performance than the other two residence groups for global cognition and executive functions after controlling for

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covariates. Childhood urban residence was associated with a cognitive advantage especially for currently rural participants.

Conclusions – Our findings suggest higher cognitive functioning for urban residents, although childhood residence moderates this association. Suggestions for further developments of these results are discussed.

Keywords: cognitive ageing, executive functions, environment, urbanisation, childhood

Introduction

Global ageing, coupled with increasing urbanisation, poses the challenge to create lived environments promoting successful ageing, or ageing well (World Health Organization, 2007). The association between the socio-physical environment and ageing processes has long been investigated in Environmental Gerontology (Barker, 1968; Bronfenbrenner, 1979; Lawton & Nahemow, 1973; Wahl et al., 2012), promoting attempts to help older people to live in their communities in autonomy for as long as possible, such as "ageing-in-place" initiatives (Black, 2008; Oswald & Wahl, 2004).

Although multiple factors influence ageing well (Baltes & Baltes, 1993), maintaining cognitive health is crucial to live independently and efficiently for as long as possible (World Health Organization, 2007). It is therefore a priority to identify individual and environmental influences on cognitive ageing, both in terms of protective factors against the increasing prevalence of dementia and cognitive impairment (Sachs et al., 2011; World Health Organization, 2012), and in terms of opportunities to enhance cognitive vitality and capitalise on brain plasticity in older age (Fillit et al., 2002; Hertzog et al., 2008). There is evidence that lived environments can influence social interactions and promote active lifestyles which in turn benefit cognition (de Frias & Dixon, 2014; Hertzog et al., 2008; Kelly et al., 2014; Kramer et al., 2003). The neuropsychological underpinning of these environmental effects could relate to the functional and structural brain enhancing properties of enriched environments shown in both animals and humans (Diamond, 1988; Nithianantharajah & Hannan, 2006), suggesting that the lived environment can impact cognition not only indirectly, for example through lifestyle, but also directly via cognitive and sensory stimulation (Engineer et al., 2004; Kempermann, 2008;

Nithianantharajah & Hannan, 2009; Wells, 2009). This is in line with extensive literature showing environmental effects on cognitive reserve - the ability of cognitive systems to function in spite of brain damage (Stern, 2002, 2009, 2012).

Despite the plausibility of the association between physical aspects of the environment and cognition, this topic is understudied (Dunwoody, 2006), possibly due to methodological difficulties (Wu et al., 2014). Nonetheless, epidemiological studies report geographical variations in dementia and cognitive impairment (Bae et al., 2015; Cahill et al., 2012; Contador et al., 2015; Gavrila et al., 2009; Iyer et al., 2014; Klich-Rączka et al., 2014; Nunes et al., 2010; Russ et al., 2012), with better cognitive performance for older urban than rural dwellers, suggesting that urban environments may be more stimulating either cognitively, socially or in relation to lifestyle. Robertson (2013, 2014) for example, linked novelty in the environment (more likely to be found in urban environments) with enhanced cognitive reserve through the activation of the noradrenergic brain system. In turn, rural dwelling seems to be associated with a cognitive disadvantage in relation to both current and childhood residence (Gupta et al., 2011; Nguyen et al., 2008).

On the other hand, experimental studies report poorer cognitive outcomes in association with urban living (Caparos et al., 2012; Linnell et al., 2013), suggesting that environments with complex visual and auditory stimulation may impose higher cognitive load (Wais & Gazzaley, 2011) and become too challenging for older adults (Baltes & Baltes, 1993; Baltes & Lindenberger, 1997; de Fockert et al., 2009; Singer et al., 2003), potentially impairing cognitive function. Attentional or executive processing (Linnell et al., 2013; Wais & Gazzaley, 2011, 2014), speech processing (Pichora-Fuller, 1996), and spatial navigation (Cantin et al., 2009; Lövdén,

Schellenbach, et al., 2005) decline in older age, especially in noisy and complex environments which require some form of dual tasking. In fact, there is evidence that exposure to natural, green settings (more likely to be found in rural environments) restores attentional resources both in young and older individuals by imposing fewer demands on visual or auditory processing (Berman et al., 2008; Berto, 2005; Gamble et al., 2014; Hartig et al., 2003; Ottosson & Grahn, 2006). Based on these studies, it might be argued that urban and rural environments contribute differently to cognitive stimulation, particularly in older age when fluid cognitive skills are in decline (Hedden & Gabrieli, 2004; Schneider & Kathleen, 2000; Singer et al., 2003). However, little is known about which aspects of the built environment act as a source of optimal cognitive stimulation for older people, and which specific cognitive benefits are associated with urban or rural living, given current contrasting evidence from epidemiological studies on dementia and experimental studies on attention and executive functions.

To address this issue, the present study aimed to explore urban/rural differences for a wide range of cognitive processes in community-dwelling people aged 50 and over residing in the Republic of Ireland, while considering the role of socioeconomic, health, and lifestyle factors known to be strongly associated with enhanced cognitive health in ageing (Hertzog et al., 2008; Kelly et al., 2014). To our knowledge, this is the first study that allows for such a broad assessment of cognition while taking into account relevant confounding factors. In the light of the existing literature on cognitive functions, the study tested the hypothesis that, if urban environments are more stimulating and engaging than rural areas, urban older dwellers would show better cognitive performance than rural dwellers, especially in terms of executive functions (Robertson, 2014) when confounding factors are

accounted for. Vice versa, if urban environments are over-stimulating and impose cognitive load in older age (Linnell et al., 2013), urban older people should have poorer cognitive performance than rural dwellers. Moreover, based on the evidence that early life residence circumstances can influence late-life cognition (Contador et al., 2015; Fors et al., 2009; Hall, Gao, Unverzagt, & Hendrie, 2000; Nguyen et al., 2008; Zhang, Gu, & Hayward, 2008), the present study explored whether interactions between current and childhood location of residence influenced cognitive scores.

Methods

Participants

Data were obtained from The Irish Longitudinal Study on Ageing (TILDA), a large cohort study on the health, well-being and socioeconomic circumstances of approximately 8,000 healthy Irish residents aged 50 and over (Kearney et al., 2011; Kenny, 2013) which began in 2009 and is conducted every two years. Participants in TILDA are asked to complete a computer-assisted personal interview (CAPI) and a self-completion questionnaire (SCQ) in their homes, as well as a physical and cognitive health assessment conducted by trained study nurses in one of two dedicated health centres or at home (Cronin et al., 2013). The present study analysed data from the first wave of TILDA, conducted between July 2009 and June 2011. A flow chart of the population included in the analyses is shown in Figure 5.1: 8,175 participants aged 50 and over participated in Wave 1, and 5,898 of these who underwent health assessment were included. Of these, 5 participants were excluded because no information on current location of residence had been recorded during

data collection, and 636 were excluded because of missing data in one or more of the considered cognitive measures. Further 1,492 observations were excluded from the analyses in order to have a fixed sample size for all statistical models, leaving a final sample of 3,765 observations (Figure 5.1). The final sample size was heavily influenced by the missing data for covariates such as income, which had around 1,400 missing values. While this variable was initially kept in the analyses despite the high level of non-response to have a measure of socioeconomic status, it was then removed in follow-up analyses (see p.155) and substituted with social class (as explained in Chapter 4) to have a larger sample size. Specific sampling methodology and sampling weights based on the distribution of socio-demographic characteristics at population level (Kearney et al., 2011; Kenny et al., 2010; Whelan & Savva, 2013) were used to ensure the representativeness of the TILDA sample. The sampling weights were applied to the analyses in the present study to ensure the representativeness of our subsample (see Statistical analyses section for further details). Moreover, the distribution of participants per area of residence (the explanatory variable in our study) in the sample included in this study did not differ significantly from that of participants taking part in the health assessment, further supporting the representativeness of the subsample. Further details on the design and methodology of TILDA in relation to representativeness of the sample are available elsewhere (Cronin et al., 2013; Kenny et al., 2010; Whelan & Savva, 2013), and comparability with other longitudinal studies has been demonstrated (Savva, Maty, Setti, & Feeney, 2013).

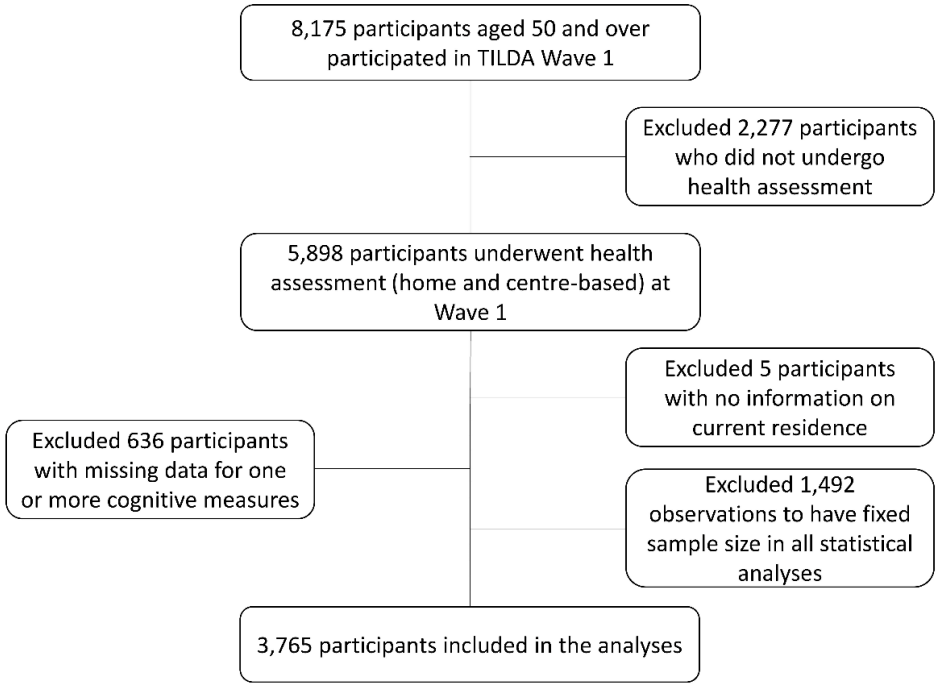


Figure 5.1

Flowchart of participants included in study one.

Design

Cross-sectional analyses were conducted on measures of cognitive performance in relation to current location of residence, while controlling for socio-demographic circumstances, health and lifestyle. An anonymised version of the dataset for the First Wave released by TILDA (see http://www.ucd.ie/issda/data/tilda/) was used in order to maintain confidentiality and data protection. Ethical approval was obtained at the beginning of the data collection, and all respondents provided signed informed consent before participation (Kenny et al., 2010) excluding individuals with severe cognitive impairment (Whelan & Savva, 2013).

Explanatory variable

The independent variable for this study was the geographical location of residence of the respondent at the time of the interview as assessed by the interviewer according to three categories: (a) Urban; (b) Other settlements; (c) Rural areas. Based on the Irish Census 2011 (http://www.cso.ie/en/census/census2011boundaryfiles/), the "Urban" category refers to the Dublin area, which is the only urban settlement with more than one million inhabitants in the Republic of Ireland, while the category "Other settlements" include five Cities, five Boroughs, and 75 Towns with a population ranging from 1,500 to less than 200,000 inhabitants; lastly, rural areas are settlements with a population of less than 1,500.

Outcome variables

The dependent variables for the study included measures of cognitive performance collected during the CAPI interview and the health assessment in

TILDA (Kenny et al., 2010), and are related to global cognition, memory, speed of processing, attention, and executive functions. Measures of global cognition included the Montreal Cognitive Assessment Test (MoCA) (Nasreddine et al., 2005) and the Mini Mental State Examination (MMSE) (Folstein et al., 1975). Memory was measured in terms of: immediate and delayed recall of a list of 10 words based on the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery (Morris et al., 1989; Welsh et al., 1994), derived from the Health & Retirement Study and used across several longitudinal studies (Shih et al., 2011); recall and recognition in a Picture Memory Test taken from the Cambridge Mental Disorders of the Elderly Examination, or CAMDEX (Roth et al., 1986); prospective memory based on the Rivermead Behavioural Memory Test (B. A. Wilson et al., 1991). Speed of processing was assessed through the cognitive mean reaction time (in seconds) for the Choice Reaction Time Test, and through the mean completion time (seconds) for the Colour Trail Making Test Part 1 (CTT 1), while attention was assessed through self-rated absentmindedness, and the Sustained Attention to Response Task (SART) (Robertson et al., 1997) in terms of reaction time (milliseconds, SART RT), standard deviation from the mean reaction time (a measure of variability of performance, SART SD), number of commission errors (SART Commissions), and number of omissions (SART Omissions). Lastly, measures of executive functions included a verbal fluency (animal naming) test (Lezak, 2004), a 6-items test of visual reasoning from the CAMDEX (Roth et al., 1986), the mean completion time (seconds) for the Colour Trail Making Test 2 (D'Elia et al., 1996), and the mean change in completion time from CTT 1 to CTT 2 (CTT Δ), this last considered a measure of executive functions adjusted for biases due to differences in visuo-motor functioning (Ble et al., 2005). CTT errors were not

analysed due to the very low error rate (less than 10% for one error and less than 2% for two or more errors) (Cavaco et al., 2013).

Covariates

Covariates for statistical analyses (see details in Table 4.2 p.115) included variables associated in the literature with changes in cognitive outcomes in older age and with different geographical distributions in terms of place of residence: socio-demographic data, including sex, age, educational attainment, employment status, and household income; physical and mental health, in terms of Body Mass Index, self-rated hearing problems, presence of disabilities in activities of daily living (ADL) and/or instrumental activities of daily living (IADL), number of chronic conditions, use of polypharmacy, and clinical symptoms of depression measured through the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977); social engagement and lifestyle measured through household composition, participation in clubs, participation in lifelong learning, exercise measured through the International Physical Activity Questionnaire (IPAQ) short form (Craig et al., 2003), and smoking habits; lastly, childhood circumstances, including father social class as per Irish Census, childhood urban or rural residence, and self-rated childhood health. Household composition and participation in clubs, two components from the Berkman-Syme Social Engagement Index (Berkman & Syme, 1979) together with attendance at religious events and the presence of at least two close friends or relatives, were the only two components to be significantly associated with cognitive scores for this sample, and were thus included in the analyses, while the global Index itself and its other two components were excluded.

Statistical analyses

Statistical analyses were performed using Stata version 12 (StataCorp LP, Texas). Survey data analyses were conducted by applying sampling weights which provided estimates correcting for distribution of socio-demographic characteristics at national level, and for differential responses to the health assessment (A. Barrett et al., 2011). Descriptive statistics and regression models explored differences in cognitive performance among the three categories of current residence. Linear regression models were used for continuous variables (MoCA, MMSE, immediate recall, delayed recall, CRT, CTT 1, SART RT, SART SD, SART omissions, SART Commissions, fluency, CTT 2, and CTT Δ), Poisson regression for count variables (Picture recall and recognition, visual reasoning), and Chi-square test and logistic regression for categorical variables (prospective memory, absentmindedness). Nonparametric analyses for continuous variables were conducted as validity checks (data not shown). Regression analyses included two models, where Model 1 explored the association between current residence and cognitive performance in univariate analyses, while Model 2 consisted of multivariate analyses including all covariates.

We also looked at the interaction between current and childhood location of residence in regression models which controlled for all covariates, in order to explore a possible moderation of childhood residence on the association between environment and cognitive outcomes.

Results

Sample characteristics

Participants' characteristics for the total sample and based on area of residence are shown in Table 5.1. In this sample (Mean age 62.5, *SD* = 8.81; median age = 61, interquartile range = 69-55; 48.5% female), 24.9% lived in urban areas at the time of data collection, 26.8% in other settlements, and 48.2% in rural areas.

[4]No differences of statistical relevance emerged between participants living in urban areas and those in other settlements in terms of socio-demographic circumstances, health or lifestyle. Participants living in rural areas were slightly younger than participants in the urban group (reference category), slightly less educated and less likely to be retired. In terms of health, despite the total sample was overall healthy, rural participants had slightly higher BMI, but fewer chronic conditions and fewer disabilities than urban dwellers. In addition, they were more likely to cohabit and engage in exercise, but currently smoking and less involved in lifelong learning. In terms of childhood circumstances, both rural participants and those living in other settlements were more likely than the urban group of having a father who had worked as a farmer or had been unemployed, and both groups were also more likely to have lived in a rural place up to the age of 14.

[4] This paragraph is not part of the published paper.

Table 5.1

Descriptive analyses: Estimates of Socio-demographic, Health and Lifestyle Characteristics for Total Sample and Current Residence

Characteristic	Total sample (n = 3,765)	Urban (n = 980, 24.94%)	Other settlements (n = 1,021, 26.85%)	Rural (n = 1,764, 48.21%)	*P*-value (effect size)
Sex, n (%)					.83
Male	1,841 (51.5)	500 (52.1)	490 (50.9)	851 (51.5)	
Female	1,924 (48.5)	480 (47.9)	531 (49.1)	913 (48.5)	
Age, mean (*SD*)	62.5 (8.81)	63.3 (9.21)	62.5 (8.97)	62.0 (8.46)*	.049 (0.04)
Age group, n (%)					.07
50-64	2,391 (63.2)	585 (58.7)	642 (62.9)	1,164 (65.6)	
65-74	981 (23.2)	272 (25)	269 (23.4)	440 (22.1)	
75+	393 (13.6)	123 (16.3)	110 (13.6)	160 (12.3)	
Education, n (%)					<.000 (0.08)
Primary	902 (34.9)	233 (35.9)	223 (31.9)	446 (36)	
Secondary	1,539 (44.4)	322 (36.9)	447 (47.9)**	770 (46.3)	
Third/Higher	1,324 (20.7)	425 (27.2)	351 (20.2)	548 (17.7)**	
Employment, n (%)					<.000 (0.08)
Employed	1,540 (39.5)	386 (36.9)	386 (35.7)	768 (42.8)	
Retired	1,350 (34.9)	416 (42.1)	391 (38.4)	543 (29.2)***	
Unemployed	875 (25.6)	178 (21)	244 (25.9)	453 (28)	
Household income, mean (*SD*)	10.05 (1.17)	10.13 (1.29)	10.09 (1.01)	9.9 (1.19)	.08
BMI, mean (*SD*)	28.7 (4.55)	28.4 (4.66)	28.4 (4.54)	28.9 (4.49)**	.002 (<0.01)
No. chronic conditions, mean (*SD*)	1.94 (1.66)	2.08 (1.75)	1.97 (1.69)	1.84 (1.61)**	.01 (<0.01)
Polypharmacy, n (%)					.08
No	3,075 (80.2	793 (78.7)	814 (78.4)	1,468 (81.8)	
Yes	690 (19.9)	187 (21.3)	207 (21.6)	296 (18.2)	
Self-rated hearing, n (%)					.92
Poor/Fair	518 (15.1)	130 (14.8)	145 (14.8)	243 (15.4)	
Good/Excellent	3,247 (84.9)	850 (85.2)	876 (85.2)	1,521 (84.6)	
Disabilities, n (%)					<.001 (0.06)
None	3,401 (89.4)	886 (88.4)	903 (87.4)	1,612 (90.8)	
IADL	93 (2.9)	32 (4.7)	31 (3.5)	30 (1.7)***	

ADL	179 (4.9)	45 (5.1)	59 (6.1)	75 (4.2)	
ADL + IADL	92 (2.8)	17 (1.7)	28 (2.9)	47 (3.2)	
Depressive symptoms, n (%)					.16
None	2,806 (74)	729 (73)	744 (72.4)	1,333 (75.4)	
Moderate	645 (17.4)	170 (18.5)	173 (17.1)	302 (17.1)	
Severe	314 (8.6)	81 (8.6)	104 (10.5)	129 (7.5)	
Cohabiting, n (%)					<.000 (0.11)
No	814 (22.4)	231 (24.7)	274 (28.3)	309 (18)	
Yes	2,951 (77.6)	749 (75.3)	747 (71.7)	1,455 (82)**	
Participating in clubs, n (%)					.07
No	1,768 (49.9)	422 (46.3)	490 (51.5)	856 (50.9)	
Yes	1,997 (50.1)	558 (53.7)	531 (48.5)	908 (49.1)	
Lifelong learning, n (%)					.006 (0.06)
No	3,178 (86.9)	789 (83.9)	856 (86.2)	1,533 (88.9)	
Yes	587 (13.1)	191 (16.1)	165 (13.8)	231 (11.1)**	
Exercise, n (%)					.006 (0.05)
None	1,104 (30.3)	274 (29.3)	299 (30)	531 (30.9)	
Moderate	1,340 (34.8)	388 (39.3)	378 (36.9)	574 (31.4)*	
Vigorous	1,321 (34.9)	318 (31.4)	344 (33.1)	659 (37.7)	
Smoking status, n (%)					.009 (0.05)
Never	1,676 (43.1)	421 (40.5)	424 (40.5)	831 (45.7)	
Current	603 (17.4)	155 (18.5)	194 (20.6)	254 (15.2)*	
Past	1,486 (39.5)	404 (41)	403 (38.9)	679 (39.1)	
Father social class, n (%)					<.000 (0.22)
Professional	520 (10.7)	188 (15.2)	148 (11.5)	184 (7.9)	
Non Manual	303 (6.99)	127 (11.9)	98 (8.6)	78 (3.5)**	
Manual	1,674 (47.7)	477 (54.7)	498 (52.5)	699 (41.5)*	
Farmer	844 (22.7)	94 (8.1)	168 (15.6)***	582 (34.1)***	
Unemployed	272 (7.7)	41 (4.7)	63 (6.6)*	168 (9.8)*	
Unknown	152 (4.2)	53 (5.2)	46 (5.1)	53 (3.1)	
Childhood residence, n (%)					<.000 (0.46)
Urban	1,572 (40.1)	690 (71.4)	525 (50.8)	357 (18)	
Rural	2,193 (59.9)	290 (28.6)	496 (49.2)***	1,407 (82)***	
Childhood self-rated health, n (%)					.05
Poor/Fair	235 (6.5)	56 (6.1)	78 (8.4)	101 (5.7)	

Good/Excellent	3,530 (93.5)	924 (93.9)	943 (91.6)	1,663 (94.3)

Note. *SD* = standard deviation; BMI = Body Mass Index; ADL = activities of daily living; IADL = instrumental activities of daily living. P-values correspond to a Wald test of the hypothesis that estimates across areas of residence were equal. Effect sizes are shown for variables with significant differences between areas of residence, and are expressed as R^2 for continuous variables and Cramer's V for categorical variables. Data are weighted.

Significant differences between Other settlements and Urban or Rural and Urban are indicated at the level * p <.05, ** p < .01 and *** p < .001.

The distributions of cognitive scores among the three categories of current residence (see Table 5.2) showed poorer performance for rural than urban participants in relation to measures of global cognition, memory (except the recall score in the Picture Memory test and prospective memory), absentmindedness, and all measures of executive functions, but no significant differences emerged for speed of processing (CRT and CTT 1). Urban participants had slower responses in the SART RT, but no significant differences were found for SART SD, Omissions or Commissions. Participants living in other settlements had poorer performance than urban dwellers for global cognition, recognition score in the Picture Memory test and for some measures of executive functions, while they were slightly faster in the SART.

Table 5.2

Descriptive Analyses: Estimates of Cognitive Performance for Total Sample and Current Residence

Cognitive measure	Total sample (n = 3,765)	Urban (n = 980, 24.94%)	Other settlements (n = 1,021, 26.85%)	Rural (n = 1,764, 48.21%)	P-value (Effect size)
Global cognition					
MoCA, mean (*SD*)	24.7 (3.36)	25.4 (3.26)	24.7 (3.27)***	24.4 (3.38)***	<.000 (0.02)
MMSE, mean (*SD*)	28.4 (1.81)	28.7 (1.73)	28.4 (1.75)**	28.2 (1.84)***	<.000 (0.02)
Memory					
Immediate recall, mean (*SD*)	6.6 (1.52)	6.7 (1.55)	6.8 (1.48)	6.5 (1.51)*	.002 (<0.01)
Delayed recall, mean (*SD*)	5.9 (2.25)	6.15 (2.33)	6.15 (2.32)	5.7 (2.15)**	<.001 (<0.01)
Picture recall, median (IQR)	3 (4-3)	3 (4-3)	3 (4-3)	3 (4-3)	.38
Picture recognition Picture recall, median (IQR)	6 (6-5)	6 (6-6)	6 (6-5)**	6 (6-5)***	<.001 (<0.01)
Prospective memory, success, n (%)	3,075 (79.5)	792 (78.5)	815 (76.9)	1,464 (81.5)	.07
Speed of processing					
CRT[a] (ms), mean (*SD*)	522.1 (159.48)	518 (160.69)	522.5 (169.83)	523.5 (152.88)	.81
CTT 1[a] (sec), mean (*SD*)	57.8 (.53)	57.2 (1.2)	58.1 (1.02)	57.9 (.70)	
Attention					
SART RT[a] (ms), mean (*SD*)	384.2 (101.31)	392.2 (107.27)	379.3 (101.35)*	382.8 (97.95)*	.044 (<0.01)
SART SD[a] (ms), mean (*SD*)	126.8 (77.43)	122.8 (76.19)	124.0 (78.65)	130.4 (77.14)	.06
SART Omissions[a], mean (*SD*)	8.5 (10.96)	7.87 (10.65)	8.46 (11.24)	8.97 (10.93)	.12
SART Commissions[a], mean (*SD*)	4.44 (4.36)	4.27 (4.59)	4.28 (4.18)	4.6 (4.33)	.13

Absentmindedness, most times/always, n (%)	298 (8.4)	48 (1.27)	82 (2.18)*	168 (4.95)***	<.001 (0.07)
Executive functions					
Verbal fluency, mean (*SD*)	20.6 (6.78)	22.2 (7.65)	20.3 (6.56)***	20.1 (6.31)***	<.000 (0.02)
CTT 2 (sec)[a], mean (*SD*)	115.1 (43.57)	109.9 (42.15)	114.6 (45.01)	118.2 (43.16)***	<.001 (<0.01)
CTT Δ[a], mean (*SD*)	57.3 (29.15)	52.7 (27.99)	56.4 (30.45)*	60.3 (28.62)***	<.000 (0.02)
Visual reasoning, median (IQR)	3 (4-2)	3 (4-2)	3 (4-2)*	3 (4-2)**	.006 (<0.01)

Note. *SD* = standard deviation. *P*-values correspond to a Wald test of the hypothesis that estimates across areas of residence were equal. Effect sizes are shown for variables with significant differences between areas of residence, and are expressed as R^2 for continuous variables while Cramer's V for categorical variables. Data are weighted.

[a] Higher values for these measures indicate worse performance.

Significant differences between Other settlements and Urban or Rural and Urban are indicated at the level * p <.05, ** p < .01 and *** p < .001.

Regression analyses

The results of regression analyses in Model 1 (univariate analyses) and Model 2 (adjusted for all covariates) are shown in Table 5.3, where the cognitive scores of participants living in other settlements or rural areas were compared to those of urban dwellers, the reference category. Regression models are not presented for Picture recall, prospective memory, CRT, CTT 1, SART SD, Omissions and Commissions, as these did not show significant differences in the descriptive analyses (see Table 5.2). In the regression models, unstandardized b coefficients are shown as differences in score between urban dwellers and each of the other two categories of residence for continuous variables, while absentmindedness was analysed in terms of Odds Ratios (O.R.) of being absentminded most or all the time for participants in other settlements or rural areas as compared to urban residents. Lastly, Picture recognition and Visual reasoning were analysed in terms of Incident Rate Ratios (I.R.R.) of success in the task.

After controlling for all covariates, rural dwelling, as compared to urban residence, was significantly associated with poorer cognitive performance in terms of global cognition (MoCA b = -0.44, $p < .01$; MMSE b = -0.28, $p < .001$), verbal fluency (b = -1.83, $p <. 001$), completion time for the CTT 2 (b = 3.94, $p < .05$), and increase in completion time from CTT part 1 to part 2 (CTT Δ, b = 5.38, $p < .001$); in addition, rural participants reported higher likelihood of being absentminded (O.R. = 2.15, $p < .001$) and showed worse scores in the Picture Memory recognition task (I.R.R. = 0.98, $p < .05$). On the other hand, rural dwellers showed faster reaction times than urban participants at the SART (b = -11.12, $p < .05$). Participants living in other settlements showed significant worse performance than urban residence in the

MMSE (b = -0.22, $p < .001$), Picture recognition (I.R.R. = 0.98, $p < .01$), absentmindedness (O.R. = 1.56, $p < .05$), verbal fluency (b = -1.64, $p < .001$), and CTT Δ (b = 2.92, $p < .05$), but faster response time in the SART RT (b = -12.56, $p < .05$).

[5]A post-estimation Wald test of differences in estimates between participants in other settlements and rural participants in Model 2 indicated that participants in other settlements were significantly better than the rural group in terms of immediate recall ($p = .005$). It is to note that the "other settlements" had higher scores that the urban group in this task, but the differences did not reach statistical significance.

Interactions of current environment of residence with social and lifestyle covariates were not significant except for a moderating effect of the level of engagement in physical activity (measured through the IPAQ) on MoCA scores, which might indicate a compensatory role of modifiable lifestyle factors on geographical variations in general cognitive health. Follow-up analyses of this interaction are presented in Study Five (see Chapter 9).

[5] This and the following paragraphs are not part of the published paper.

Table 5.3

Regression Analyses: Estimates of Cognitive Scores for Current Residence ("Other settlements" and "Rural" as compared to "Urban") in Model 1 (univariate analysis) and Model 2 (all Covariates accounted for).

Cognitive measure	Current residence (Ref: Urban)	Model 1			Model 2		
		Estimate [95% CI]	*p*-value	R^2	Estimate [95% CI]	*p*-value	R^2
Global cognition							
MoCA[a]	Other settlements	-0.65*** [-1.01, -0.29]	<.000	0.02	-0.38** [-0.66, -0.11]	.004	0.24
	Rural	-1.01*** [-1.34, -0.67]			-0.44** [-0.72, -0.17]		
MMSE[a]	Other settlements	-0.32*** [-0.51, -0.12]	<.000	0.02	-0.22** [-0.39, -0.05]	.003	0.21
	Rural	-0.49*** [-0.67, -0.32]			-0.28*** [-0.45, -0.12]		
Memory							
Immediate recall[a]	Other settlements	0.08 [-0.09, 0.26]	.002	<0.01	0.14 [0.0002, 0.28]	.02	0.24
	Rural	-0.21* [-0.36, -0.04]			-0.06† [-0.21, 0.07]		
Delayed recall[a]	Other settlements	0.005 [-0.27, 0.28]	<.001	0.01	0.14 [-0.11, 0.38]	.11	0.21
	Rural	-0.42*** [-0.66, -0.17]			-0.11 [-0.32, 0.11]		
Picture recognition[b]	Other settlements	0.98** [0.97, 0.99]	<.001	<0.01	0.98** [0.97, 0.99]	.02	<0.01
	Rural	0.97*** [0.96, 0.98]			0.98* [0.97, 0.99]		
Attention							
SART RT[a]	Other settlements	-12.84* [-23.13, -2.55]	.04	<0.01	-12.56** [-21.87, -3.25]	.02	0.11
	Rural	-9.32* [-18.53, -0.11]			-11.12* [-20.14, -2.10]		
Absentmindedness[c]	Other settlements	1.65* [1.12, 2.42]	<.001	<0.01	1.56* [1.04, 2.35]	.002	0.08
	Rural	2.14*** [1.49, 3.06]			2.15*** [1.44, 3.19]		
Executive functions							

Verbal fluency[a]	Other settlements	-1.96*** [-2.97, -0.95]	<.000	0.02	-1.64*** [-2.56, -0.72]	<.001	0.16
	Rural	-2.23*** [-3.21, -1.26]			-1.83*** [-2.81, -0.85]		
CTT 2[a]	Other settlements	4.68 [-0.24, 9.61]	<.001	<0.01	2.62 [-0.81, 6.04]	.05	0.35
	Rural	8.26*** [4.01, 12.52]			3.95* [0.75, 7.14]		
CTT Δ[a]	Other settlements	3.75* [0.73, 6.77]	<.000	0.01	2.92* [0.27, 5.57]	<.001	0.16
	Rural	7.58*** [4.98, 10.17]			5.38*** [2.84, 7.93]		
Visual reasoning[b]	Other settlements	0.95* [0.91, 0.99]	.006	<0.01	0.97 [0.94, 1.01]	.37	0.03
	Rural	0.93** [0.89, 0.97]			0.98 [0.95, 1.02]		

Note. N = 3,765. CI = confidence interval. P-values correspond to a Wald test of the hypothesis that estimates of cognitive performance between areas of residence were equal. Reference category for predictor: Urban. Effect sizes are shown as R^2 for linear regression and pseudo-R^2 for Poisson and logistic regression. Model 2 includes all demographic, health, social, lifestyle, and childhood covariates. Data are weighted.

[a] Unstandardized b coefficients are shown for linear regressions.

[b] Incident Rate Ratios shown based on Poisson regressions.

[c] Odds Ratios shown based on Logistic regressions.

* p <.05, ** p <.01, *** p <.001.

† indicates statistically significant differences between the rural and the "other settlements" group.

Interactions between past and current residence

The percentage of participants currently living either in urban, other settlements, or rural areas differed significantly by childhood residence, $\chi^2(2, 3{,}765) = 799.95$, $p < .001$ (see Table 3), and the regression models controlling including all covariates indicated that participants with rural rather than urban childhood had significantly worse cognitive performance for most cognitive measures (see Table 5.4). Analyses of interactions between childhood and current residence were therefore conducted to explore potential moderating effects of childhood environment on the association between current place of residence and cognitive outcomes.

Table 5.4

Regression Analyses: Estimates of Cognitive Scores for Childhood Residence in Model 2 (all Covariates accounted for).

Cognitive measure	Childhood residence (Rural as compared to Urban)	
	Estimate [95% CI]	R^2
MOCA[a]	-0.88*** [-1.13,-0.64]	0.04
MMSE[a]	-0.34*** [-0.49,-0.17]	0.02
Immediate recall[a]	-0.25*** [-0.37,-0.14]	0.02
Delayed recall[a]	-0.53*** [-0.71,-0.35]	0.03
PIC recall[b]	0.98 [0.96,1.01]	<0.01
PIC recognition[b]	0.97*** [0.96,0.98]	<0.01
Prospective memory[c]	1.38* [1.09,1.76]	<0.01
CRT[a]	21.59** [8.72,34.45]	<0.01
CTT 1[a]	5.52*** [3.46,7.58]	0.02
SART RT[a]	3.78 [-4.39,11.96]	<0.01
SART SD[a]	10.40*** [4.53,16.27]	0.01
SART Omissions[a]	1.55*** [0.72,2.35]	0.01
SART Commissions[a]	0.32 [-0.024,0.67]	<0.01
Absentmindedness[c]	1.29 [0.95,1.78]	<0.01
Verbal fluency[a]	-0.91** [-1.47,-0.34]	0.02
CTT 2[a]	9.48*** [6.34,12.64]	0.03
CTT Δ[a]	3.97** [1.57,6.36]	0.02
Visual reasoning[b]	0.92*** [0.88,0.95]	<0.01

Note. N = 3,765. CI = confidence interval. Estimates indicate differences in cognitive scores between urban (Reference) and rural childhood. Model 2 includes all covariates. Data are weighted.
[a] Unstandardized b coefficients are shown for linear regressions.
[b] Incident Rate Ratios shown based on Poisson regressions.
[c] Odds Ratios shown based on Logistic regressions.
* p <.05, ** p <.01, *** p <.001.

After controlling for covariates, we found that participants who were currently rural but with an urban childhood showed a cognitive advantage with similar scores than those of participants currently residing in urban areas, while participants with rural residence both currently and in childhood showed the worst performance for MoCA (b = 0.52, p < .05, Figure 5.2a), verbal fluency (b = 1.16, p < .05, Figure 5.2b), and CTT 2 (b = 6.84, p < .05, Figure 5.2c). Moreover, participants in the 'other settlements' group but with a rural childhood had significant lower rate of success than urban residents (I.R.R. = 0.97, p < .05) or rural participants (I.R.R. = 0.96, p < .01) in the Picture recognition task (Figure 5.2d).

MMSE showed independent main effects for childhood and current residence without interactions, with an advantage for urban childhood as well as urban current residence. Main effects of current residence with no interactions were maintained for CTT Δ, absentmindedness, and SART RT, with significantly poorer performance of rural participants as compared to urban residents in CTT Δ (b = 4.08, p < .05) and absentmindedness (O.R. = 2.24, p < .01), but slightly faster RTs in the SART (b = -14.77, p < .05). Main effects of childhood residence with no interactions, with significantly lower scores for rural than urban childhood, emerged for immediate recall (Urban b = -0.32, p < .01; Other settlements b = -0.29, p < .01; but no differences for rural) and delayed recall (Urban b = -0.34, p < .05; Other settlements

b = -0.53, $p < .01$; Rural b = -0.67, $p < .001$), and visual reasoning (Urban I.R.R. = 0.94, $p < .05$; Other settlements I.R.R. = 0.93, $p < .01$; Rural I.R.R. = 1.06, $p < .05$).

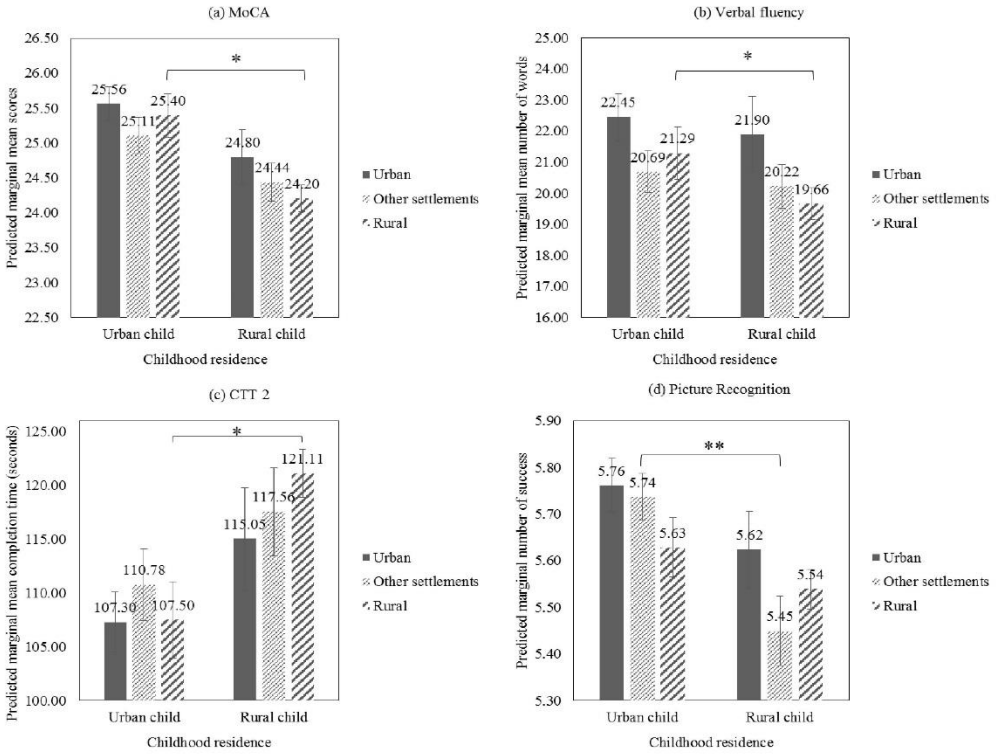


Figure 5.2

Predicted cognitive performance for interaction between childhood and current residence. Errors bars represent 95% confidence intervals. All covariates are controlled for. Predicted mean scores shown for MoCA (a) and verbal fluency (b), while predicted mean completion time is shown for the Colour Trail Making Test Part 2 (c), and predicted Incident Risk Ratios of Success are shown for the Picture Recognition Task (d).

Discussion

Our results suggest that residing in a highly urbanised area was associated with better cognitive performance than living in less urbanised or rural areas in terms of global cognition and executive functions. Specifically, participants living in highly urbanised places (i.e. Dublin area) had higher scores than those living in less populated (other settlements) or rural areas in terms of MoCA, MMSE and verbal fluency. On the other hand, the results for the CTT 2 and CTT Δ showed a more gradual pattern, with participants in other settlements having a poorer performance than those in the urban (Dublin) group, but better than rural dwellers. Analyses of speed of processing and attention did not show clear patterns for this sample. The association between current place of residence and cognitive scores was moderated by childhood residence for some of the explored measured (MoCA, verbal fluency, CTT 2, and picture recognition).

The results on global cognition (MoCA and MMSE) are broadly in line with epidemiological studies which report an association between higher prevalence of dementia and cognitive impairment in older age and rural residence, either current (Bae et al., 2015; Cahill et al., 2012; Gavrila et al., 2009; Klich-Rączka et al., 2014; Nunes et al., 2010; Russ et al., 2012) or past (K. S. Hall et al., 2000; Nguyen et al., 2008; Z. Zhang et al., 2008). It is to note that while these studies attribute urban/rural differences to socio-demographic factors such as education and income (except Hall et al., 2000), in our study geographical differences were maintained even after controlling for a comprehensive set of covariates including education, occupation, income, and father social class, considered to be the main indicators of socio-demographic inequalities. While analyses of MoCA scores showed significant interactions for current and childhood location of residence, the MMSE did not show

significant interactions: this result might be due to differences between the two tests in the sensitivity to specific cognitive measures (e.g. executive functions) which have been reported in the literature (Dong et al., 2010; Nasreddine et al., 2005; Zadikoff et al., 2008).

Measures of executive functions which showed significantly higher scores for urban residents as compared to participants living in other settlements or rural areas were verbal fluency and CTT Δ (increase in completion time from CTT Part 1 to CTT Part 2). In addition, urban/rural differences emerged in the CTT 2 (completion time in CTT Part 2), where again, rural participants with rural childhood had significantly poorer performance. An association between poorer verbal fluency and rural living has been suggested in studies on older people (Chávez-Oliveros et al., 2014), while Gupta and colleagues (2011) reported urban/rural differences in executive functions and fluency in a sample of Chinese middle-aged participants, differences which however disappeared after controlling for self-rated academic skills. On the contrary, such differences remained significant in our study after controlling for educational attainment, a discrepancy possibly due to the older age of our sample.

The results on global cognition and executive functions are in line with the hypothesis that people living in highly urbanised areas such as Dublin may be accustomed to higher levels of perceptual and cognitive stimulation due to traffic, intense noise, and increased visual complexity (Cantin et al., 2009; Linnell et al., 2013; Stansfeld, Haines, & Brown, 2011), which stimulate high-level cognitive abilities such as executive functions, involving skills like shifting between multiple tasks, updating and monitoring mental representations of our surroundings, paying

attention to important stimuli, and inhibiting maladaptive or wrong responses (Miyake et al., 2000; Repovš & Baddeley, 2006). Highly urbanised environments such as Dublin might therefore offer a level of complexity which stimulates executive functions independently of socio-economic and lifestyle circumstances, and its effects could even be long-term for those who lived in urban areas early in life but are currently living in less urbanised environments (as shown in our interactions). It is interesting to note that the MoCA test includes several tasks involving executive functions, as for example, a version of the CTT 2 and verbal fluency; although the available dataset for this sample reported no scores for the subtests of MoCA, it might be argued that the differences in MoCA scores between urban participants and the other two residence groups depend on differences in executive functions, an argument supported by the fact that group differences for MoCA and MMSE in our sample were not equal. The MoCA test has been reported to have higher sensitivity to cognitive impairment related to executive functions (Dong et al., 2010; Nasreddine et al., 2005; Zadikoff et al., 2008), thus the differences between MoCA and MMSE scores might actually reflect performance differences in terms of executive functions. Moreover, scores in the CTT 2, CTT Δ and verbal fluency in this study explained 33.7% of the variance in MoCA scores but 23% of the variance in MMSE scores, further supporting our hypothesis. Therefore, differences in scores between groups of residence in verbal fluency, CTT Δ, CTT 2 and MoCA are plausibly due to more efficient executive functions in people who live or have lived in urban contexts.

In contrast, immediate and delayed recall showed an association only with childhood residence when analysing current/childhood residence interactions. These results may indicate that memory is more influenced by past circumstances than

current place of residence, possibly due to the fact that current urban living does not impose a specific load on memory, or in other words it does not, to a certain extent, stimulate memory directly, but indirectly via stimulation of executive functions emerged in our analyses. Studies on distractibility and recall in older adults (Wais & Gazzaley, 2011, 2014; Wais, Rubens, Boccanfuso, & Gazzaley, 2010) showed in fact that retrieval of verbal information is impaired in the presence of task-irrelevant visual or auditory distractors, and suggested that these distractors impacted frontal control processes which in turn affected recall. Associations between current living circumstances and cognitive performance in older age might thus be more evident for executive and control processes. On the other hand, verbal abilities such as recall may be more associated with learning circumstances which affect cognition mainly during childhood (Deary & Brett, 2015; Manly, Touradji, Tang, & Stern, 2003).

Although our results do not provide information on causality of the effects or the direction of the interaction between childhood and current residence, they emphasise the relevance of considering changes in the environment of residence across the lifespan to understand cognitive outcomes later in life. While exploring patterns of migration at different points in time could be more informative than comparing childhood with older age, our analyses are in line with other studies which have compared childhood and current environment of residence to explore health and cognitive outcomes later in life (Contador et al., 2015; Fors et al., 2009; Nguyen et al., 2008). Our findings may be interpreted as an association between migration and enhanced cognitive performance, in line with studies (Gist & Clark, 1938; Jokela, 2014; Lehmann, 1959; Tucker-Drob et al., 2013) which propose that higher cognitive abilities, as measured through IQ, predict migration in the sense that people with higher IQ would create more opportunities for themselves to move to

stimulating environments. However, the interpretation of the interaction between childhood and current residence along those lines needs caution because the absence of measures of childhood cognitive performance or IQ in the present study, together with the cross-sectional nature of the analyses, limits the possibility to isolate the influence of environmental stimulation on cognitive health from potential genetic predisposition. Therefore, while urbanisation has been suggested as a potential cause for gains in intelligence (Flynn, 1998, 2007), we are not in the position to draw conclusions in this regard from our analyses. Nonetheless, current and past environment of residence in the present study were differently associated with executive functions and memory when controlling for educational attainment and other socioeconomic factors, both in childhood and in older age. Considering that these covariates are strongly associated with IQ in the literature (Crawford, Stewart, Garthwaite, Parker, & Besson, 1988; Rindermann, Flores-Mendoza, & Mansur-Alves, 2010), this might suggest that environmental factors could play a specific role in stimulating cognitive functions. Moreover, our models controlled for self-rated childhood health, which has been reported in the literature as a good predictor of morbidity later in life (Blackwell, Hayward, & Crimmins, 2001), and of socioeconomic and health circumstances in adulthood (Case et al., 2005). Self-rated childhood health, despite the limitations related to self-reports, might be indicative of a health status early in life which may also have hypothetically impacted the possibility to migrate or change environment.

Interestingly, some significant differences in cognitive performance were found between urban dwellers and participants living in other settlements for MMSE, SART RT, CTT Δ, verbal fluency, absentmindedness and Picture recognition: These differences might suggest a dose-response relationship between

levels of urbanisation and cognitive health, in the sense that living in a large metropolitan area or in a relatively smaller city seems to make a difference in cognitive performance, which deserves further exploration. However, Dublin is relatively small compared to bigger metropolises in other areas of the world, therefore cross-national investigations are needed to fully clarify which level of urbanisation is optimal for cognitive performance in adult age. It is also to note that the category "Other settlements" defined by the Irish Census includes areas with varying population which might actually show intra-variations in cognitive performance as well as different environmental effects. This limits the interpretation of comparisons of the "Urban" and "Other settlements" groups, and urges further exploration using variables such as population density as well as measures related to meso level characteristics of the area of residence (e.g.: neighbourhood). It is plausible that characteristics of the environment of residence at a meso level, such as in the neighbourhood or proximal community, may contribute to the macro-differences in cognitive performance between individuals living in urban areas or other settlements found in the study (Cassarino & Setti, 2015; Wu et al., 2014). Moreover, environmental characteristics at a meso level could better address the differences in cognitive performance between urban and rural areas, which, given the gap in their population size, might not be equivalent to urban/rural differences in other countries. Specific environmental effects need therefore further exploration in relation to variables that have already been reported to influence geographical variations of health in older age, such as population density (Russ et al., 2012), presence of green areas (Alcock et al., 2014; Gamble et al., 2014), noise (Babisch, 2003; Correia et al., 2013; Selander et al., 2009, 2013), walkability (Neckerman et al., 2009), or accessibility to services (Charreire et al., 2010), and diet (Inagami,

Cohen, Finch, & Asch, 2006; Layte et al., 2011; D. M. Santos et al., 2014; Winkler et al., 2006).

In addition, a meso level analysis could address the potential limitation that the association found between environment and cognition is due to a bias in the selection of individuals with different cognitive abilities living in different areas, as well as allowing for a more precise assessment of the impact of geographical variations in cognitive health associated with exposure to environmental toxins, disease risk, diet, socio-economic status and opportunities for social interaction (see for a review Cassarino & Setti, 2015). While acknowledging the limitations of the broad environmental categories used in the present study, we note that our analyses controlled for a set of covariates in line with the literature on urban/rural differences in mental health (Gavrila et al., 2009; Klich-Rączka et al., 2014; Lederbogen et al., 2011; Russ et al., 2012). Education, income and occupational status were used as measures of socioeconomic status, while BMI was controlled for as a measure of obesity, which is influenced by a poor diet and unhealthy lifestyle (Hu et al., 2001; Mozaffarian, Hao, Rimm, Willett, & Hu, 2011), and associated with cognition both directly or indirectly (Łojko et al., 2014; Profenno et al., 2010; G. Wang et al., 2014). No data were available for exposure to risk factors for disease or environmental toxins within the sample, but our analyses controlled for health conditions which could be related both to environmental exposure and to a higher risk of disease, and these did not alter our findings. In addition, the Irish Environmental Protection Agency has reported no geographical variations in air quality, radiation, or soil contamination in Ireland, and the general Irish environmental quality is within the standards set by the European Commission

(reports from 2013 are available at http://www.epa.ie/pubs/reports/http://www.epa.ie/).

The selection of a small final sample size due to the high number of missing data for the covariate income (around 1,400 missing observations) is a potential limitation for the study because it might have caused biased estimates in our models, despite the use of sampling weights which ensured representativeness. Although we are aware that such a loss of observations might have affected our results, adding this variable to our analyses was in our opinion crucial because income is a measure of socioeconomic status which has been shown in the literature to correlate strongly with cognitive outcomes in older age (Fors et al., 2009; Glymour & Manly, 2008).

The present study suggests urban/rural differences in the cognitive performance of healthy community-dwelling older people in relation to global cognition and executive functions. Although the cross-sectional design does not inform causality, our results suggest an association between environment of residence and cognitive functioning in older age after controlling for socio-economic, health and lifestyle factors, and causal pathways will be tested when longitudinal data is available. Effect sizes of place of residence were relatively small (around or below 2%), which is to be expected given the healthy and relatively young sample (i.e., less susceptible to environmental influences) and the well-established important role of socio-demographic and health circumstances on cognitive performance. Demographic covariates in particular (age, educational attainment, social class) explained most of the variance for some cognitive measures in our final models. Nonetheless, our results are of interest because show that even taking into account individual-level factors, living in a more or less urbanised

environment is associated with small but significant differences in cognitive performance which might become of clinical relevance with increasing age. These findings advance the knowledge on the association between environment and cognition, which is still under-explored (Dunwoody, 2006), encourage further research to explore environmental factors for cognitive health, and have policy implications supporting the identification of environmental resources that can be modified or optimised to promote cognitive health in older age and to protect against cognitive decline. As urbanisation is changing the places in which we live (World Health Organization, 2007), understanding whether cities or rural environments are more supportive of cognitive ageing is crucial to identify contextual resources which make an age-friendly community from a cognitive perspective.

Conclusions

Demographic changes and urbanisation worldwide pose a challenge to identify lived environments which support healthy ageing (World Health Organization, 2007), particularly in relation to protective factors for the risk of dementia and cognitive impairment. The present study represents a first step in understanding the factors through which the environment contributes to cognitive ageing in a representative sample of older people in the Republic of Ireland.

Results of Analyses on a Larger Sample[6]

At a later stage of the project, we re-conducted the same analyses on a larger sample (*N* = 4,892) as an extra validity check. This sample was obtained by removing the income covariate, which had over 1,400 missing observations, and including current social class as a more stable measure of socioeconomic status, together with some minor changes to other covariates as explained in Chapter 4, "Covariates" section p. 112. In addition, we used the following types of regression analyses to better address the psychometric characteristics of cognitive assessments: linear for MoCA, CRT, CTT 1, SART RT and *SD*, fluency, CTT 2, and CTT Δ; Poisson for MMSE recoded in terms of number of errors (30 – participant's score), immediate and delayed recall, Picture recall and recognition, and visual reasoning; negative binomial for SART omissions and SART commissions; logistic for prospective memory and absentmindedness.

The regression analyses on this sample (mean age = 62.44, *SD* = 8.71; 51.28% female) confirmed the results of the data on the smaller sample, with significant variations based on place of residence for global cognition, Picture recognition, absentmindedness and executive functions (except visual reasoning) as shown in Table 5.5. Significance differences in immediate recall emerged between the "other settlements" group and both the rural group ($p < .001$) and the urban group ($p < .05$), with the "other settlements" group showing better performance than the other two groups.

[6] This section is not part of the published paper and it is related to analyses conducted at a later stage of the doctoral project.

Analyses of interactions between childhood and current residence for the larger sample confirmed the previous results in relation to CTT 2, with rural participants with rural childhood being slower than those with urban childhood (b = 10.92, Wald test $F(2, 620) = 10.09$, $p < .000$), and in relation to Picture recognition, with participants currently residing in other settlements and with rural childhood having 3% lower probability of success than those with urban childhood (IRR = 0.97, Wald test $F(2, 620) = 4.24$, $p = .02$). Interactions for MoCA and verbal fluency were not confirmed, while significant interactions emerged for delayed recall, with participants currently rural who reported a rural childhood having 8% lower probability of recalling all the words than those with urban childhood (IRR = 0.92, Wald test $F(2, 620) = 3.94$, $p = .02$), and for CTT Δ, with rural participants who had reported a rural childhood showing 7 seconds higher increase in completion time between CTT 1 and CTT 2 than those with urban childhood (b = 7.07, Wald test $F(2, 620) = 5.07$, $p = .006$).

Overall these new analyses confirmed that geographical variations in cognitive performance pertain executive functions especially, with a robust indication of better performance in verbal fluency and Trail Making Test, as well as measures of global cognition (MoCA and MMSE).

Table 5.5

Regression Analyses: Estimates of Cognitive Scores for Current Residence ("Other settlements" and "Rural" as compared to "Urban") in Model 1 (univariate analysis) and Model 2 (all Covariates accounted for)

Cognitive measure	Current residence (Ref: Urban)	Model 1			Model 2		
		Estimate [95% CI]	*P*-value	R^2	Estimate [95% CI]	*P*-value	R^2
Global Cognition							
MoCA[a]	Other settlements	-0.57** [-0.91, -0.24]	<.000	0.02	-0.37** [-0.62, -0.12]	<.001	0.23
	Rural	-1.01*** [-1.31, -0.69]			-0.48*** [-0.72, -0.24]		
MMSE errors[b]	Other settlements	1.21** [1.06, 1.38]	<.000	<0.01	1.17** [1.05, 1.31]	.001	0.12
	Rural	1.35*** [1.19, 1.52]			1.21*** [1.09, 1.35]		
Memory Immediate recall[b]	Other settlements	1.01 [0.98, 1.04]	<.000	<0.01	1.02* [1.001, 1.04]	.002	0.02
	Rural	0.96** [0.94, 0.98]			0.98† [0.96, 1.002]		
Delayed recall[b]	Other settlements	1.02 [0.97, 1.06]	<.000	<0.01	1.04 [0.99, 1.07]	.02	0.04
	Rural	0.93*** [0.90, 0.97]			0.98 [0.95, 1.01]		
Picture recall[b]	Other settlements	0.98 [0.95, 1.01]	.38	<0.01	0.98 [0.95, 1.01]	.32	<0.01
	Rural	0.99 [0.96, 1.02]			0.99 [0.97, 1.03]		
Picture recognition[b]	Other settlements	0.98** [0.97, 0.99]	<.000	<0.01	0.98** [0.98, 0.99]	.008	<0.01
	Rural	0.97*** [0.96, 0.98]			0.98* [0.98, 0.99]		
Prospective memory[c]	Other settlements	1.03 [0.81, 1.30]	.37	<0.01	1.13 [0.88, 1.45]	.006	0.08
	Rural	1.16			1.48**		

		[0.93, 1.46]			[1.16, 1.90]		
Speed of processing							
CRT[a]	Other settlements	10.96 [-4.06, 25.98]	.23	<0.01	4.38 [-8.94, 17.71]	.78	0.12
	Rural	9.74 [-2.46, 21.94]			0.42 [-11.87, 12.71]		
CTT 1[a]	Other settlements	0.61 [-2.08, 3.29]	.22	<0.01	-0.07 [-2.04, 1.91]	.77	0.32
	Rural	1.96 [-0.48, 4.42]			0.53 [-1.38, 2.44]		
Attention							
SART RT[a]	Other settlements	-9.69* [-18.84, -0.55]	.55	<0.01	-8.61 [-17.24, 0.02]	.02	0.10
	Rural	-9.42* [-17.6, -1.28]			-11.97** [-20.32, -3.62]		
SART SD[a]	Other settlements	1.44 [-6.44, 9.32]	.08	<0.01	0.97 [-5.06, 7.01]	.66	0.23
	Rural	6.68 [-0.07, 13.44]			2.64 [-3.29, 8.56]		
SART Omissions[b]	Other settlements	1.09 [0.96, 1.26]	.04	<0.01	1.07 [0.97, 1.18]	.32	0.04
	Rural	1.16* [1.04, 1.30]			1.06 [0.97, 1.17]		
SART Commissions[b]	Other settlements	1.01 [0.91, 1.13]	.06	<0.01	1.01 [0.93, 1.08]	.36	0.04
	Rural	1.09 [0.99, 1.19]			1.05 [0.97, 1.13]		
Absentmindedness[c]	Other settlements	1.03 [0.72, 1.48]	.001	<0.01	1.01 [0.68, 1.47]	.002	0.08
	Rural	1.63** [1.18, 2.27]			1.63* [1.11, 2.40]		
Executive functions							
Verbal fluency[a]	Other settlements	-1.48** [-2.39, -0.56]	<.001	0.02	-1.26** [-2.12, -0.41]	.002	0.15
	Rural	-1.90*** [-2.76, -1.05]			-1.51** [-2.38, -0.62]		
CTT 2[a]	Other settlements	5.26* [0.83, 9.68]	<.001	0.01	3.58* [0.54, 6.62]	<.001	0.35
	Rural	10.17***			6.37***		

		[6.22, 14.11]			[3.44, 9.31]		
CTT Δ[a]	Other settlements	4.65** [1.92, 7.38]	<.000	0.02	3.65** [1.22, 6.07]	<.000	0.16
	Rural	8.20*** [5.78, 10.62]			5.85*** [3.47, 8.23]		
Visual reasoning[b]	Other settlements	0.94* [0.91, 0.98]	<.001	<0.01	0.96* [0.93, 0.99]	.12	0.03
	Rural	0.92*** [0.88, 0.96]			0.97 [0.94, 1.01]		

Note. N = 4,892. CI = confidence interval. P-values correspond to a Wald test of the hypothesis that estimates of cognitive performance between areas of residence were equal. Effect sizes are shown as R^2 for linear regression and pseudo-R^2 for Poisson and logistic regression. Model 2 includes all covariates. Data are weighted.

[a] Unstandardized b coefficients are shown for linear regressions.

[b] Incident Rate Ratios shown based on Poisson and Negative Binomial regressions.

[c] Odds Ratios shown based on Logistic regressions.

* p <.05, ** p <.01, *** p <.001.

† indicates statistically significant differences between the rural and "other settlements" groups.

Chapter 6 - Study Two

Population Density and Variations in Cognitive Efficiency in Older Age: Results from The Irish Longitudinal Study on Ageing.[7]

Abstract

With increasing numbers of people growing old in cities and of individuals with dementia, it is imperative to understand whether urbanisation is supportive of cognitive functioning in older age. Using data from a large sample (N = 4,699) of individuals aged 50+ participating in the first wave of The Irish Longitudinal Study on Ageing (TILDA), we tested variations in performance for global cognition, memory, processing speed, attention, and executive functions based on the population density of the area of residence, used as a measure of level of urbanisation. Multivariate regression analyses controlled for socio-demographic, health and lifestyle covariates. We found that residence in medium-high densely populated areas was significantly associated with better performance than living in areas with very low population density for immediate recall, absentmindedness, and executive functions, after controlling for covariates. Our findings identify urbanisation as a positive contributor to maintaining efficient executive functions in older age, in line with the hypothesis that urban living supports cognitive efficiency and might protect against cognitive decline.

Keywords: cognitive ageing, urbanisation, population density, executive functions.

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Introduction

With increasing numbers of older people living in cities and individuals with the dementia, "age friendly" environments, identified by good levels of accessibility, presence of green, availability of services, have emerged as a fundamental contributor to healthy and independent living in older age (World Health Organization, 2007), urging to understand the role of urbanisation in sustaining cognitive health (Buffel et al., 2012; Corburn, 2015; World Health Organization, 2007).

Epidemiological studies on geographical variations in cognitive ageing (see for a review Cassarino and Setti, 2015) indicate lower prevalence and incidence of dementia and cognitive impairment in urban rather than rural settings (Russ et al., 2012). However, the absence of a generally accepted definition of "rurality" and "urbanity" across countries urges further research utilizing alternative and more detailed measures of the place of residence to study the association between levels of urbanisation and cognitive ageing. Population density, usually defined as the number of individuals per squared unit area, is a measure of levels of urbanisation which can address this issue, as it has been associated with significant variations in health and health-related behaviour (Husted & Jorgens, 2000; Rundle et al., 2007; Russ et al., 2012; Stark, Hopkins, Gibbs, Belbin, & Hay, 2007).

The use of global indicators of cognitive health in epidemiological studies leaves unanswered the question on which specific cognitive skills are most impacted, positively or negatively, by living in an urbanised environment. Not only urban places may foster more active lifestyles, but, from an information-processing viewpoint, we recently hypothesised that urban environments can help older people

to maintain a healthier brain, acting as 'brain training,' especially for attention and executive functions (Cassarino & Setti, 2015). These crucial skills would be trained thanks to the need to deal with novelty (Robertson, 2014), multi-tasking, and the complex perceptual stimulation characteristic of city living (Cassarino & Setti, 2015). In line with this hypothesis, in a previous study (Cassarino et al., 2016) we showed that urban residents aged 50+ in Ireland performed better than rural dwellers in tasks linked to executive functions such as verbal fluency and Colour Trail Making Test, when health and lifestyle factors were controlled for.

On the other hand, experimental studies on psychological restoration (Berto, 2014; S. Kaplan, 1995) suggest that exposure to natural and green settings, as opposed to urban contexts, benefits attention, relieves from stress, and fosters copying skills, providing evidence for detrimental effects of urbanisation from a cognitive perspective (Van Den Berg, Hartig, & Staats, 2007). In addition, animal and human studies on crowding suggest that overpopulation and space restrictions are associated with reduced cognitive control (van Rompay, Galetzka, Pruyn, & Garcia, 2008; Hui & Bateson, 1991; Freedman, Klevansky, & Ehrlich, 1971) and can negatively affect spatial memory in older age (Merriman et al., 2016). Although crowding could be related to both a subjective experience and objective population density (Stokols, 1972), one might expect that living in a more or less urbanised (and complex) environment impacts cognitive functions differently, especially for older individuals with increasing functional limitations (Cassarino & Setti, 2016a). In fact, studies have shown that living in urban environments induces the individual to prioritise exploratory over focused attentional strategies, and causes higher levels of tonic arousal (Linnell et al., 2014, 2013), which, in turn, influences cognitive function.

This evidence stimulates new research to investigate variations in multiple cognitive skills in older age based on levels of urbanisation, and using measures of population density can help to clarify this association. No studies have in fact explored, to the best of our knowledge, performance for multiple cognitive skills in healthy community-dwelling older individuals in relation to population density.

In the present study, we used data from The Irish Longitudinal Study on Ageing (TILDA) and from the Irish Census 2006 to explore whether better performance in a comprehensive battery of cognitive assessments was associated with higher levels of population density, and therefore whether healthy older adults living in low densely populated areas may be at risk of insufficient stimulation provided by the lived environment.

Based on the literature discussed above, the results of our previous work on urban/rural variations in cognition (Cassarino et al., 2016), the evidence of a nonlinear trend between land-use mix and prevalence of dementia found recently (Wu et al., 2015; Wu, Prina, Jones, Matthews, & Brayne, 2016), and the recently suggested hypothesis that urban environments which are sufficiently but not overwhelmingly complex can offer an optimal level of stimulation for cognition in ageing (Cassarino & Setti, 2016a), we predicted better cognitive performance, particularly in relation to executive functions, for medium-high levels of population density, with worse performance for very low or very high levels of urbanisation.

Methods

Participants

The sample for this study included 4,698 healthy community-dwelling Irish people aged 50 and older who completed a physical and cognitive health assessment in the first wave (data collected between 2009 and 2011) of The Irish Longitudinal Study on Ageing (TILDA), a large cohort study on the health, well-being and socioeconomic circumstances of Irish older people (A. Barrett et al., 2011; Kenny et al., 2010). The health assessment is conducted every four years (Cronin et al., 2013).

Design

Cross-sectional analyses were conducted on variations in performance for a comprehensive set of cognitive skills based on population density of the area of residence, while controlling for several covariates. An anonymised released version of the dataset for the first wave of TILDA (see http://www.ucd.ie/issda/data/tilda/) was used to maintain data confidentiality. Ethical approval was obtained before data collection, and all respondents provided signed informed consent (Kenny et al., 2010); no individuals with severe cognitive impairment took part in the first wave (Whelan & Savva, 2013). Further details on the design and methodology of TILDA, as well as the comparability with other longitudinal studies are available elsewhere (Savva et al., 2013; Whelan & Savva, 2013).

Population density

Population density of the place of residence of each TILDA participant was derived from the Irish Census 2006 (Central Statistics Office, 2006) and defined as number of inhabitants per hectare (1 hectare is equivalent to 2.47 acres) averaged at the level of the electoral division. Electoral divisions were the smallest legally defined administrative areas in Ireland in 2006 with an average size of 20 km^2

(ranging from 0.04 km^2 in urban areas to 163 km^2 in rural areas). For reasons of anonymity, the variable was categorised in six groups of increasing population density adopting categories used in the Irish Census: (1) Very low population density, less than 0.5 persons per hectare (i.e., less than one person every two hectares); (2) Low population density, between 0.5 and 1 person per hectare; (3) Medium-Low population density, between 1 and 10; (4) Medium-High population density, between 10 and 25; (5) High population density, between 25 and 50; (6) Very High population density, more than 50 persons per hectare. As shown in Table 6.1, in our sample over 98% of participants in rural areas (with less than 1,500 inhabitants) lived in electoral division with less than 10 persons per hectare (very-low to medium-low population density), whereas 92% of urban participants (i.e., living in the Dublin area) were in an electoral division with 10 or more persons per hectare (medium-high to very-high population density). Participants living in other settlements (places with a population going from 1,500 to less than 200,000 inhabitants) were instead more spread across electoral divisions of varying population density, although 74% lived in areas with medium-low to high population density.

It is to note that the adopted categorisation of population density is relative to the Irish context, which has a high number of settlements with low and very low population density, and very few highly populated areas; however, whether an optimal absolute population density in terms of cognitive ageing can be determined is discussed in the Discussion section.

Table 6.1

Distribution of electoral divisions with varying population density by level of urbanisation of the place of residence

Population density group	Place of residence [a]		
	Urban (Dublin)	Other settlements	Rural
1 (x < 0.5)	< 30 (< 1.5) [b]	105 (9.60)	1,501 (68.58)
2 (0.5 <= x < 1)	0 (0)	86 (7.38)	427 (19.5)
3 (1 <= x < 10)	98 (6.82)	359 (29.03)	233 (10.39)
4 (10 <= x < 25	238 (17.45)	352 (28.81)	< 30 (< 1.0) [b]
5 (25 <= x < 50)	606 (45.17)	216 (16.99)	< 30 (< 1.0) [b]
6 (x >= 50)	336 (29.45)	88 (8.19)	0 (0)

Notes. *a* Place of residence categories were derived from Study One (see Chapter 5)
b Cells with less than 30 observations (or less than 1.5%) are shown as <30 for reasons of anonymity.

Cognitive Measures

Cognitive performance was assessed in terms of global cognition, memory, speed of processing, attention, and executive functions.

Measures of global cognition included the Montreal Cognitive Assessment Test (MoCA) (Nasreddine et al., 2005) and the Mini Mental State Examination (MMSE) (Folstein et al., 1975), this one recoded as number of errors. Memory was measured in terms of immediate and delayed recall of a list of 10 words, recall and recognition of six images in a Picture Memory Test, and success/failure in a task of prospective memory (i.e., reminding the interviewer to record the time upon occurrence of a certain event). Speed of processing was assessed through the cognitive mean reaction time (in seconds) for the Choice Reaction Time Test, and the mean completion time (seconds) for the Colour Trail Making Test Part 1 (CTT 1) (D'Elia et al., 1996). Attention was measured in terms of self-rated frequency of absentmindedness, and through the Sustained Attention to Response Task (Robertson et al., 1997) in terms of reaction time (milliseconds, SART RT), standard

deviation from the mean reaction time (a measure of variability of performance, SART SD), number of omissions (SART Omissions), and number of commissions (SART Commissions), and self-rated frequency of absentmindedness. Measures of executive functions included a verbal fluency test, a 6-items test of visual reasoning, the mean completion time (seconds) for the Colour Trail Making Test Part 2 (D'Elia et al., 1996), and the mean change in completion time from CTT 1 to CTT 2 (CTT Δ). CTT errors were not analysed due to the very low error rate (less than 10% for one error and less than 2% for two or more errors).

Covariates

Covariates included *a priori* selected measures which have been associated with cognitive performance in older age in the existing literature.

Socio-demographic data, including sex, age, educational attainment, and current social class as per Irish Census (Central Statistics Office, 2011, p. 75).

Physical and mental health was assessed in terms of body mass index (BMI), self-rated hearing or vision problems, presence of disabilities in activities of daily living (ADL) and/or instrumental activities of daily living (IADL), number of chronic conditions, use of polypharmacy, and clinical symptoms of depression measured through the Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977).

Social engagement and lifestyle included household composition (cohabiting or not), perceived frequency of loneliness as measured through CES-D, the Berkman-Syme Social Network Index (Berkman & Syme, 1979), participation in lifelong learning, engagement in physical activity as measured through the

International Physical Activity Questionnaire Short form (Craig et al., 2003) and smoking habits.

Lastly, childhood circumstances included father social class as per Irish Census (Central Statistics Office, 2011), childhood urban or rural residence, and self-rated childhood health (intended as birth to 14 years of age).

Statistical analyses

Statistical analyses were performed using Stata version 12 (StataCorp LP, Texas). Survey data analyses were conducted by applying sampling weights. These were calculated for each participant in TILDA as the inverse of the probability that an individual in the Irish older population selected at random with same age, sex and educational attainment would have completed the health assessment (Kearney et al., 2011; Kenny et al., 2010), with participants from groups less likely to participate having a higher weight. Chi-squared statistics were used to explore associations between categorical variables, Kruskal Wallis for ordinal variables, and one-way analysis of variance (ANOVA) for continuous variables. Regression models explored variations in cognitive performance across the six groups of population density: Linear regression was used for continuous variables (MoCA, CRT, CTT 1, SART RT; SART SD, fluency, CTT 2, CTT Δ), Poisson regression for count variables (MMSE errors, immediate and delayed recall, Picture recall and recognition, visual reasoning), Negative Binomial regression for count variables with over dispersion (SART Omissions and Commissions), and Logistic regression for categorical variables (prospective memory and absentmindedness).

Differences in cognitive performance between participants living in the least densely populated areas represented the reference group (Group 1 = less than 0.5

persons per hectare) and groups 2-6 of population density were explored in univariate analyses (Model 1), and in multivariate analyses including all covariates (Model 2). We conducted a Wald test of the null hypothesis that the coefficients across the groups of population density were equal. Statistical significance was indicated by a *p*-value lower than .05.

Validity checks included a re-run of the regression analyses based on quintiles of population density, and on unweighted data.

Results

Sample characteristics

Detailed descriptive data for the covariates for the total sample and based on population density are shown in the Table 6.2. In this sample (Mean age = 62.5, standard deviation = 8.7, median age = 61; 51.3% female) 35.9% of participants lived in the least populated areas (Group 1), while less than 10% (9.8) lived in the most populated areas (Group 6). Overall, the sample was healthy and socially engaged. Compared to Group 1, participants living in more densely populated areas were significantly older, slightly more educated and in a professional career (excluding Group 6); also, participants living in areas with medium to vary high population density had higher BMI, higher number of chronic conditions and use of polypharmacy, and slightly more chances of having a disability or depressive symptoms compared to the reference group, as well as slightly lower social connectedness.

Table 6.2

Participants' Characteristics by Total Sample and Population Density Group

Characteristic	Total sample (N = 4,698)	Population density group						p-value
		1 (n = 1,620, 35.9%) Ref.	2 (n = 514, 11.3%)	3 (n = 691, 14.2%)	4 (n = 613, 12.4%)	5 (n = 836, 16.4%)	6 (n = 424, 9.8%)	
Sex, n (%)								.14
Male	2,145 (48.7)	732 (49.3)	238 (49.9)	337 (51)	271 (47.1)	383 (48.6)	184 (44.2)	
Female	2,553 (51.3)	888 (50.7)	276 (50.1)	354 (49)	342 (52.9)	453 (51.4)	240 (55.8)	
Age, mean (*SD*)	65.5 (8.71)	61.8 (8.61)	62.1 (7.8)	62.1 (8.8)	62.4 (8.6)	63.3 (9.2)**	64.6 (8.6)***	.003
Education, n (%)								<.001
None/Primary	1,075 (33.6)	410 (36.3)	132 (36.2)	124 (27.2)	101 (24.5)	160 (29.8)	148 (48.1)	
Secondary	1,972 (45.8)	705 (46.3)	231 (47.2)	300 (48.8)*	280 (52.2)**	303 (42.4)	153 (35.7)**	
Third/Higher	1,651 (20.6)	505 (17.5)	151 (16.6)	267 (23.9)***	232 (23.3)***	373 (27.7)***	123 (16.2)	
Social class, n (%)								<.001
Professional	1,207 (26.3)	314 (14.5)	111 (17.3)	196 (24.2)	212 (29.8)	284 (27.4)	90 (16)	
Non manual	625 (13.1)	154 (8.8)	69 (13.4)	99 (14.6)	98 (16.1)	125 (15.6)	80 (17.6)**	
Manual	910 (23.6)	294 (21.1)	115 (25.5)	130 (23.4)**	98 (20.1)***	156 (24.7)**	117 (33.4)	
Farmers/self-employed (not specified)	621 (14.9)	332 (23.9)	80 (17.1)*	81 (12.7)***	49 (8.3)***	60 (7.2)***	19 (4.4)***	
Unemployed	1,146 (28)	452 (31.6)	119 (26.6)	152 (24.9)***	131 (25.7)***	184 (25.1)***	108 (28.5)	
BMI, mean (*SD*)	28.8 (4.9)	29.1 (4.7)	29.1 (5.1)	28.7 (4.9)	28.6 (5.1)	28.1 (4.8)***	29.3 (5.3)	<.001
Self-rated hearing, n (%)								.54
Poor/Fair	642 (15.1)	231 (16.4)	75 (15.7)	89 (13.7)	76 (13.4)	111 (13.8)	60 (15.8)	
Good/Excellent	4,056 (84.9)	1,389 (83.6)	439 (84.3)	602 (86.3)	537 (86.6)	725 (86.1)	364 (84.2)	
Self-rated vision, n (%)								.13
Poor/Fair	356 (8.9)	140 (9.8)	40 (8.9)	36 (5.6)	44 (8.6)	62 (9)	34 (10.5)	
Good/excellent	4,342 (91.1)	1,480 (90.2)	474 (91.1)	655 (94.4)	569 (91.3)	774 (91)	390 (89.5)	

No. chronic conditions, mean (*SD*)	1.9 (1.6)	1.8 (1.6)	1.8 (1.5)	1.8 (1.6)	1.9 (1.7)	2.1 (1.7)*	2.3 (1.7)***	.001
Polypharmacy, n (%)								.005
No	3,819 (79.9)	1,353 (82.5)	415 (79.2)	583 (82.8)	482 (77.6)	658 (77.7)	328 (74.3)	
Yes	879 (20.1)	267 (17.5)	99 (20.8)	108 (17.2)	131 (22.4)*	178 (22.3)*	96 (25.6)***	
Disabilities, n (%)								.003
No	4,244 (89.3)	1,487 (91.3)	468 (90.2)	617 (88.3)	537 (86.1)	762 (90.5)	373 (84.1)	
Yes	454 (10.7)	133 (8.7)	46 (9.8)	74 (11.7)	76 (13.9)**	74 (9.5)	51 (15.8)**	
Depressive symptoms, n (%)								.03
None	3,484 (73.5)	1,228 (75.8)	385 (74.6)	527 (75.3)	434 (70.1)	616 (72.4)	294 (67.5)	
Moderate	809 (17.5)	273 (16.9)	92 (17.4)	103 (15.5)	122 (20.6)	143 (17.6)	76 (19.1)	
Severe	405 (8.9)	119 (7.3)	37 (8)	61 (9.2)	57 (9.4)	77 (9.9)*	54 (13.3)**	
Cohabiting, n (%)								.02
No	865 (19)	255 (16.2)	83 (17.1)	126 (18.9)	130 (22.1)	173 (21.6)	98 (23.3)	
Yes	3,833 (81)	1,365 (83.8)	431 (82.9)	565 (81.1)	483 (77.9)	663 (78.4)	326 (76.7)	
Loneliness, (%)								.03
Rarely	3,864 (82)	1,360 (83.7)	435 (85.2)	571 (82.4)	487 (78.8)	676 (80.1)	335 (78.1)	
Some of the time	522 (11.2)	169 (10.7)	48 (8.7)	80 (11.6)	77 (13.1)	98 (12.3)	50 (11.3)	
Moderate amount/all the of time	312 (6.8)	91 (5.5)	31 (6.1)	40 (6.1)	49 (8.1)*	62 (7.5)	39 (10.6)**	
Berkman-Syme Social Network Index, n (%)								<.001
Mostly isolated	265 (6.2)	70 (4.5)	21 (4.4)	41 (6.5)	40 (7.8)	57 (8.1)	36 (8.7)	
Moderately isolated	1,145 (25.2)	329 (20.4)	126 (25.7)	178 (26.6)	157 (27.2)	210 (26.5)	145 (35.5)	
Moderately integrated	1,955 (42.1)	705 (45.1)	212 (41.6)	262 (37.7)*	248 (39.1)**	364 (43.7)**	164 (39.2)**	
Mostly integrated	1,333 (26.5)	516 (30.1)	155 (28.3)	210 (29.2)	168 (26)**	205 (21.7)***	79 (16.6)***	

Lifelong learning, n (%)								.001
No	3,962 (87.1)	1,426 (90.2)	437 (87.6)	565 (83.9)	503 (85.4)	682 (84.2)	349 (86.2)	
Yes	736 (12.97)	194 (9.8)	77 (12.4)	126 (16.1)***	110 (14.6)**	154 (15.8)***	75 (13.8)*	
Physical activity, n (%)								.01
Low/inactive	1,346 (29.7)	442 (28.2)	154 (31.2)	205 (30.8)	181 (29.8)	239 (29.9)	125 (31.9)	
Moderate	1,660 (34.5)	522 (31.6)	168 (31.5)	239 (33.4)	239 (38.8)	320 (37.4)	172 (39.8)	
Vigorous	1,692 (25.7)	656 (40.2)	192 (37.3)	247 (35.7)	193 (31.3)	277 (32.7)	127 (28.2)**	
Smoking status, n (%)								<.001
Never	2,156 (44.4)	833 (50.1)	215 (40.7)	293 (41.2)	260 (41.9)	384 (43.5)	171 (37.5)	
Current	1,814 (38.6)	571 (35.7)	211 (41.4)**	298 (43.1)***	252 (39.8)*	319 (38.2)	163 (39.1)**	
Past	728 (16.9)	216 (14.2)	88 (17.9)*	100 (15.8)	101 (18.3)**	133 (18.3)*	90 (23.4)***	
Father social class, n (%)								<.001
Professional	705 (11.7)	162 (7.7)	51 (7.7)	116 (13.8)	124 (17.2)	192 (17.9)	60 (10.8)	
Non Manual	411 (7.7)	58 (2.8)	32 (5.6)*	70 (8.7)*	81 (12.8)**	125 (14.2)***	45 (9.2)**	
Manual	2,111 (48.4)	609 (38.6)	244 (49.9)	321 (50.7)	284 (50.6)**	384 (52.9)**	269 (68.3)	
Farmer	1,136 (24.6)	643 (41.2)	148 (28.9)	129 (18.6)***	92 (13.8)***	93 (9.7)***	31 (6.1)***	
Unemployed	335 (7.6)	148 (9.6)	39 (7.8)	55 (8.1)**	32 (5.6)***	42 (5.3)***	19 (5.6)**	
Childhood residence, n (%)								<.001
Urban	1,984 (10.3)	295 (15.6)	139 (25.3)	330 (44.5)	364 (59.6)	542 (66)	314 (74.1)	
Rural	2,714 (59.7)	1,325 (84.4)	375 (74.7)***	361 (55.5)***	249 (40.4)***	294 (34)***	110 (25.9)***	
Childhood self-rated health, n (%)								.12
Poor/Fair	302 (6.7)	96 (5.9)	35 (7.3)	34 (5.5)	47 (8.5)	53 (6.4)	37 (9.4)	
Good/Excellent	4,369 (93.3)	1,524 (94.1)	479 (92.7)	657 (94.5)	566 (91.5)	783 (93.6)	387 (90.6)	

Note. SD = standard deviation; BMI = Body Mass Index. Population density groups: (1) less than 0.5 people per hectare; (2) between 0.5 and 1 person per hectare; (3) between 1 and 10; (4) between 10 and 25; (5) between 25 and 50; (6) more than 50 persons per hectare. P-values correspond to a Wald test of the hypothesis that differences between the population density group 1 (Reference) and groups 2-6 were equal to 0. Data are weighted.
* p <.05, ** p < .01 and *** p < .001

Univariate analyses of cognitive scores across the six groups of population density (Model 1, Table 6.3) showed that participants in the population density groups 3-5 (between one person per hectare and less than 50 persons per hectare) had slightly but significantly better performance than those living in the least densely populated area (Group 1 = less than 0.5 persons per hectare) for global cognition (MoCA, MMSE error), memory (immediate and delayed recall, Picture recognition), CTT 1, attention (SART SD, Omissions and Commissions, absentmindedness), and all measures of executive functions. Participants in the most populated areas (Group 6) showed better performance than the reference group at the Picture Recognition Test and in terms of reaction times at the SART (SART RT). No differences were found for prospective memory, Picture recall or Cognitive Reaction Time (CRT).

Table 6.3

Estimates of Cognitive Performance for Total Sample and by Population Density Group (Model 1, Groups 2-6 as compared to Group 1)

Cognitive measure	Total sample (*N* = 4,698)	Population density group						P-value
		1 (*n* = 1,620, 35.9%) Ref.	2 (*n* = 514, 11.3%)	3 (*n* = 691, 14.2%)	4 (*n* = 613, 12.4%)	5 (*n* = 836, 16.4%)	6 (*n* = 424, 9.8%)	
Global cognition								
MoCA, mean (*SD*)	24.7 (3.4)	24.4 (3.4)	24.3 (3.6)**	24.8 (3.2)***	25.3 (3.3)***	25.3 (3.3)***	24.8 (3.1)	<.001
MMSE errors[a], median (IQR)	1 (2-0)	1 (3-0)	1 (3-0)	1 (2-0)***	1 (2-0)***	1 (2-0)***	1 (2-0)	<.001
Memory								
Immediate recall, median (IQR)	7 (8-5.5)	6.5 (7.5-5.5)	6.5 (7.5-5.5)	7 (8-6)**	7 (8-6)***	7 (8-6)***	7 (8-5.5)	<.001
Delayed recall, median (IQR)	6 (8-4)	6 (7-4)	6 (8-4)	6 (8-5)**	6 (8-5)***	6 (8-5)***	6 (8-4)	<.001
Picture recall, median (IQR)	3 (4-3)	3 (4-3)	3 (4-3)	3 (4-3)	3 (4-3)	3 (4-3)	3 (4-3)	.55
Picture recognition, median (IQR)	6 (6-5)	6 (6-5)	6 (6-5)	6 (6-5)**	6 (6-6)***	6 (6-5)***	6 (6-5)**	<.001
Prospective memory (success), n (%)	3,846 (79.6)	1,327 (79.6)	429 (82.3)	582 (81.7)	487 (77.2)	681 (79.3)	340 (77.6)	.52
Speed of processing								
CRT[a] (ms), mean (*SD*)	520.7 (154.5)	525.3 (152.9)	522.2 (146.7)	508.2 (136.7)	517.6 (182.8)	515.3 (140.5)	532.8 (169.8)	.09
CTT 1[a] (sec), mean (*SD*)	57.7 (26.1)	59.5 (25.7)	57.1 (27.4)	53.8 (22.8)***	55.6 (26.8)*	57.6 (27.7)	60.5 (25.5)	<.001
Attention								
SART RT[a] (ms), mean (*SD*)	384.9 (100.3)	383.9 (97.3)	383.5 (99.8)	375.1 (95.6)	381.7 (102.8)	387.6 (104.1)	403.6 (104.8)*	.02
SART SD[a], mean (*SD*)	126.7 (76.4)	130.6 (75.6)	132.6 (82.7)	117.1 (67.9)***	116.9 (75.6)**	124.8 (77.3)	135.8 (78.3)	<.001
SART Omissions[a], median (IQR)	5 (11-2)	5 (12-2)	5 (13-2)	4 (10-1)**	4 (9-1)	5 (11-1)*	5 (13-2)	.004
SART Commissions [a], median (IQR)	3 (6-1)	3 (6-2)	3 (6-2)	3 (5-1)*	3 (5-1)**	3 (6-1)	3 (7-1)	.006

Absentmindedness (most/all the time), n (%)	363 (8.2)	154 (9.8)	45 (9.9)	53 (8.8)	32 (5.2)	54 (6.7)	25 (6.1)	.008
Executive functions								
Verbal fluency, mean (*SD*)	20.7 (6.8)	20.3 (6.4)	19.7 (6.4)	21.3 (6.6)*	21.1 (7.2)	22.1 (7.6)**	20.4 (6.5)	.002
CTT 2 [a] (sec), mean (*SD*)	114.9 (43.6)	121.1 (44.9)	116.1 (45.2)	109.3 (39.4)***	108.5 (43.6)***	109.3 (41.1)***	117.7 (42.2)	<.001
CTT Δ [a], mean (*SD*)	57.2 (29.2)	61.5 (30.5)	58.9 (27.7)	55.5 (27.7)***	52.9 (27.9)***	51.6 (27.6)***	57.2 (28.3)*	<.001
Visual reasoning, median (IQR)	3 (4-2)	3 (4-2)	3 (4-2)	3 (4-2)**	3 (4-2)***	3 (4-2)***	3 (4-2)	<.001

Note. MoCA = Montreal Cognitive Assessment, MMSE = Mini Mental State Examination, PIC = Picture Memory Test, CRT = Choice Reaction Time, CTT = Colour Trail Making Test, SART = Sustained Attention to Response Task, *SD* = standard deviation, IQR = interquartile range.
P-values correspond to a Wald test of the null hypothesis that the coefficients across the population density categories were equal. Data are weighted.
[a] Higher values for these measures indicate worse performance.
* p <.05, ** p < .01 and *** p < .001.

Regression Analyses

Multivariate analyses adjusted for all covariates (Model 2) are presented in Table 6.4. Estimates are shown as unstandardized b coefficients for linear regression, incident rate ratios (I.R.R.) for Poisson and Negative Binomial regression, and odds ratios (O.R.) for logistic regression. The analyses showed that these differences were maintained for immediate recall ($p < .05$), absentmindedness ($p < .01$), CTT 2 ($p < .01$) and CTT Δ ($p < .001$). Overall, after controlling for all covariates, living in areas with medium-high population density (Groups 3-5), as compared to residence in areas with very low population density (Group 1), was associated with better cognitive performance (see Figure 6.1). Specifically, when compared to Group 1, a 3% increase in performance was found in terms of immediate recall for Group 4 (I.R.R. = 1.03, $p < .05$) and Group 5 (I.R.R. = 1.03, $p < .05$). Participants in Group 4 and 6 were approximately 50% less likely to be absentminded most or all the times (Group 4: O.R. = 0.47, $p < .01$; Group 6: O.R. = 0.49, $p < .05$). In terms of executive functions, we found faster completion times at the CTT 2 for Groups 3-6 (Group 3: b = -5.49, $p < .01$; Group 4: b = -6.21, $p < .01$; Group 5, b = -6.80, $p < .001$; Group 6: b = -4.58, $p < .05$), and a smaller increase in completion time from CTT 1 to CTT 2 (CTT Δ) for Groups 4-6 (Group 4, b = -4.62, $p < .01$; Group 5 b = -6.68, $p < .001$; Group 6, b = -3.93, $p = < .05$).

Regression analyses using quintiles of population density and those with unweighted data partially confirmed these results (see Appendix 1).

Table 6.4

Regression Analyses of Cognitive Scores Based on Population Density Adjusted for all Covariates (Model 2)

		Population density (Reference: Group 1, x < 0.5)					
Cognitive measure	Estimate	Group 2 0.5 <= x < 1	Group 3 1 <= x < 10	Group 4 10 <= x < 25	Group 5 25 <= x < 50	Group 6 x >= 50	P-value (effect size)
Global cognition							
MoCA	b	-0.18	-0.04	0.23	0.29	0.34	.08
	95% CI	[-0.61; 0.24]	[-0.34; 0.26]	[-0.09; 0.54]	[-0.01; 0.59]	[-0.04; 0.72]	
MMSE errors	I.R.R.	1.04	0.97	0.91	0.89	0.90	.22
	95% CI	[0.92; 1.16]	[0.87; 1.08]	[0.79; 1.03]	[0.79; 1.01]	[0.77; 1.06]	
Memory							
Immediate recall	I.R.R.	0.98	1.02	1.03*	1.03*	1.03	.002 (0.02)
	95% CI	[0.95; 1.02]	[0.99; 1.04]	[1.01; 1.05]	[1.01; 1.05]	[0.99; 1.06]	
Delayed recall	I.R.R.	0.99	1.02	1.03	1.03	1.04	.42
	95% CI	[0.95; 1.05]	[0.97; 1.06]	[0.99; 1.07]	[0.99; 1.07]	[0.98; 1.11]	
Picture recognition	I.R.R.	1.01	1.01	1.02**	1.01	1.01*	.07
	95% CI	[0.99; 1.02]	[0.99; 1.02]	[1.01; 1.03]	[0.99; 1.02]	[1.00; 1.03]	
Speed of processing							
CTT 1[a]	b	-2.14	-3.26**	-1.58	-0.12	-0.65	.06
	95% CI	[-4.92; 0.65]	[-5.46; -1.05]	[-3.85; 0.69]	[-2.57; 2.34]	[-3.55; 2.24]	
Attention							
SART RT[a]	b	0.41	-3.48	3.74	6.51	14.95*	.16
	95% CI	[-9.58; 8.76]	[-12.92; 5.96]	[-5.67; 13.15]	[-2.89; 15.90]	[1.79; 28.10]	
SART SD[a]	b	3.57	-5.87	-6.78	0.87	0.54	.08
	95% CI	[-4.34; 11.48]	[-12.14; 0.39]	[-14.32; 0.76]	[-5.97; 7.73]	[-8.85; 9.92]	
SART Omissions[a]	I.R.R.	1.09	0.92	1.00	1.02	0.97	.29
	95% CI	[0.96; 1.24]	[0.82; 1.03]	[0.85; 1.17]	[0.92; 1.14]	[0.85; 1.09]	
SART Errors[a]	I.R.R.	1.04	0.93	0.89	1.00	0.98	.16
	95% CI	[0.94; 1.15]	[0.85; 1.02]	[0.81; 0.99]	[0.92; 1.08]	[0.88; 1.09]	
Absentmindedness	O.R.	0.99	0.91	0.47**	0.66	0.49*	.008 (0.08)
	95% CI	[0.68; 1.45]	[0.60; 1.38]	[0.30; 0.72]	[0.43; 1.02]	[0.27; 0.88]	
Executive functions							
Verbal fluency	b	-0.59	0.42	0.06	1.15*	0.41	.14
	95% CI	[-1.57; 0.39]	[-0.46; 1.30]	[-0.96; 1.08]	[0.08; 2.22]	[-0.69; 1.51]	
CTT 2[a]	b	-3.55	-5.49**	-6.21**	-6.80***	-4.58*	.005 (0.35)
	95% CI	[-7.98; 0.88]	[-9.55; -1.42]	[-9.94; -2.47]	[-10.61; -2.99]	[-8.68; 0.49]	

CTT Δ[a]	b	-1.41	-2.23	-4.62**	-6.68***	-3.93*	<.001 (0.16)
	95% CI	[-4.52; 1.69]	[-5.35; 0.88]	[-7.28; -1.95]	[-9.60; -3.76]	[-7.65; 0.22]	
Visual reasoning	I.R.R.	1.03	1.01	1.04	1.04*	1.02	.30
	95% CI	[0.98; 1.07]	[0.97; 1.05]	[0.99; 1.09]	[1.01; 1.08]	[0.97; 1.07]	

Note. CI = confidence interval, CRT = Choice Reaction Time, CTT = Colour Trail Making Test, MoCA = Montreal Cognitive Assessment, MMSE = Mini Mental State Examination, SART = Sustained Attention to Response Task. Estimates indicate differences in cognitive performance between population density groups 2-6 and group 1: Unstandardized b coefficients are shown for linear regressions, Incident Rate Ratios (I.R.R.) shown for Poisson and Negative Binomial regressions, and Odds Ratios (O.R) for Logistic regression. P-values correspond to a Wald test of the null hypothesis that the coefficients across the population density categories are equal. Effect sizes are shown as R^2 for linear variables and pseudo-R^2 for count variables. All covariates are accounted for. Data are weighted.
a Higher values for these measures indicate worse performance.
* p <.05, ** p < .01 and *** p < .001.

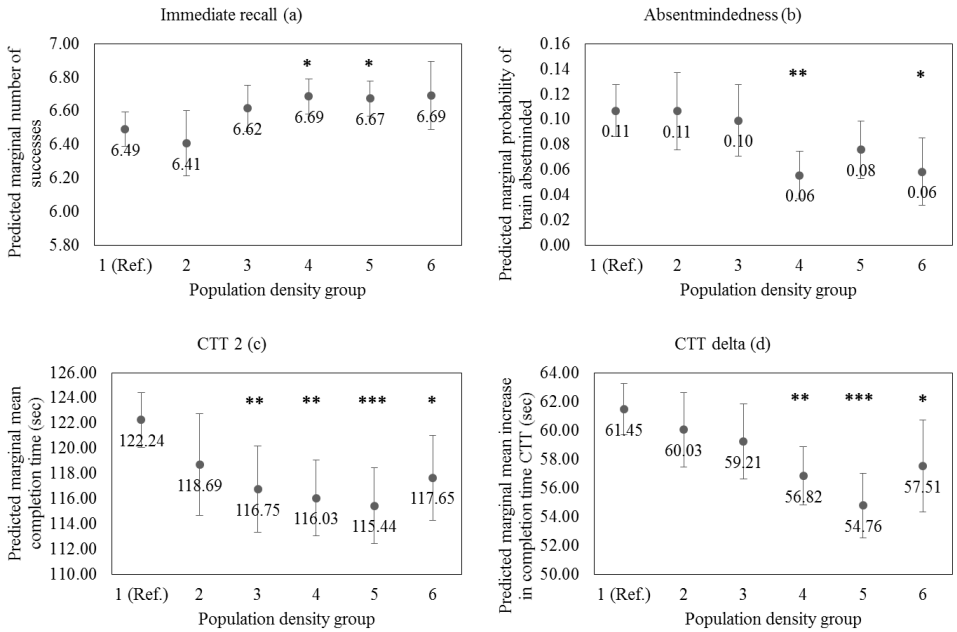


Figure 6.1

Predicted marginal cognitive performance by population density group (Groups 2-6 as compared to Group 1). Population density groups: (1) less than 0.5 people per hectare; (2) between 0.5 and 1 person per hectare; (3) between 1 and 10; (4) between 10 and 25; (5) between 25 and 50; (6) more than 50 persons per hectare. Error bars represent 95% confidence intervals. All covariates are controlled for (Model 2). Predicted marginal estimates are shown for immediate recall (a), absentmindedness (b), Colour Trail Making Test Part 2 (CTT 2, c), and Colour Trail Making Test Delta (CTT Δ, d). Significant differences in score from Group 1 are indicated at the level * p <.05, ** p < .01 and *** p < .001.

Discussion

Our data showed, in line with our hypothesis, that for a sample of healthy older individuals living in areas with medium to high population density was associated with significantly better cognitive performance than living in areas with very low population density in terms of immediate recall, absentmindedness and executive functions (CTT 2 and CTT Δ) after controlling for socio-demographic, health and lifestyle covariates. Measures of global cognition (MoCA, MMSE) and other measures of executive functions (verbal fluency and visual reasoning) followed this pattern, however the effect of population density did not reach statistical significance. Our data, considering the number of covariates controlled for, is in line with the hypothesis that living in an urban (and complex) environment *per se* trains cognitive skills involved in executive control (Cassarino & Setti, 2015), and crucial to successfully interact with the surrounding environment, in terms of processing incoming information in the short-term (immediate recall), maintaining attentional focus (low absentmindedness) and dealing with multiple sources of information and tasks at the same time (CTT 2 and CTT Δ). These skills are subject to age-related changes (Andrés et al., 2006; McAvinue et al., 2012; Setti et al., 2014) and may benefit from interacting with a stimulating environment, with implications for healthy cognitive ageing and cognitive reserve (Stern, 2009).

These results consolidate and significantly extend our previous findings on rural/urban variations in cognitive ageing (Cassarino et al., 2016) for absentmindedness and executive functions (but not immediate recall).

The results do not fully support the initial hypothesis that very high levels of population density would be associated with worse cognitive performance than

living in medium-high densely populated areas, which was based on the studies on crowding. This might be due to the fact that areas with very high population density in Ireland do not have such a level of crowding (as for example a big metropolis would have) to show detrimental cognitive effects. Nonetheless, Group 6 (most densely populated areas) showed smaller differences in performance from Group 1 than groups 4-5. As our measure of population density was captured at the level of electoral divisions rather than broad urban/rural environments, these differences indicate meso-level variations in cognitive performance (i.e., at the level of neighbourhoods or small administrative areas) within the same macro environment (both Group 5 and Group 6 corresponded to electoral divisions mainly found in urban areas). In this sense, such pattern of results develops our previous findings on urban-rural variations in performance, and are in line with a nonlinear dose-response relationship between levels of urbanisation and cognition in ageing found in previous studies (Wu et al., 2015). This result needs further exploration using a more balanced number of participants between categories of population density, as well as environmental measures at neighbourhood/community level (Wu et al., 2014).

Whether it is possible to determine an optimal level of population density to support healthy cognitive ageing in an absolute sense, or whether cultural and associated lifestyle differences may indicate that a relative measure is more appropriate remains to be established in future cross-national studies.

Other environmental factors, such as exposure to toxins or accessibility to healthy food could have contributed to our results (Cassarino & Setti, 2015). However, our analyses controlled for measures which are proxies of environmental exposure (i.e. health conditions) and healthy diet (i.e. BMI), supporting our hypothesis.

Our sample size was too limited for an analysis of the interaction between age and population density, which is a limitation of the present study. However, the use of sampling weights to maintain the representativeness of the sample, and the analyses on the unweighted data and on quintiles of population density support the validity of the present findings.

This study is, to our knowledge, the first to explore a comprehensive set of cognitive skills in older age in relation to population density, and to show, together with our previous findings (Cassarino et al., 2016), that geographical variations in different cognitive dimensions exist independently of the individual's global health and lifestyle. The observed variations indicate that the place of residence could provide the individual with a cognitive advantage or disadvantage that would need to be compensated with interventions on lifestyle (Cassarino & Setti, 2016b) or cognitive training tailored to the specific environment of residence, as shown for example in relation to the influence of neighbourhood socioeconomic status on cognitive interventions (Sisco & Marsiske, 2012).

Longitudinal studies will clarify potential causal relationships as well as the clinical relevance of our results. While the differences in the scores between participants in different population density groups were relatively small, they may indicate a disadvantage which could potentially increase over time and become of clinical importance. This cannot be elucidated by the cross-sectional data due to potential cohort effects.

In addition, a more in-depth exploration of specific physical characteristics of the proximal environment of residence (i.e., neighbourhood) such as presence of green, noise, or environmental legibility, together with an exploration of the

neurophysiological correlates of living in a more or less cognitive stimulating environment (Chen, He, & Yu, 2016; Lederbogen et al., 2011), will enrich our findings by identifying factors contributing to make an environment cognitive-friendly (Mitchell & Burton, 2006), and therefore supporting the cognitive efficiency of an increasing ageing population with multi-morbidities which could potentially be amplified by an insufficiently stimulating environment.

Chapter 7 - Study Three

Travel Time to Gateways and Cognitive Health in The Irish Longitudinal Study on Ageing.[8]

Abstract

Accessibility to urban environments can affect health in older age, but the impact on cognitive health in ageing remains unclear. We explored variations in several cognitive skills (global cognition, memory, attention, executive functions) for 4,888 healthy people aged 50+ in Ireland based on travel time to urban environments, defined as "gateways", while controlling for health and lifestyle covariates. Interactions with driving status were tested. Despite the overall healthy sample, participants living farther from gateways showed a small but significant decrease in performance for global cognition, delayed recall, attentional accuracy and executive functions. Driving status did not affect these results.

Keywords: Aging, cognitive health, travel time, urban, driving.

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Introduction

Interest is constantly growing in identifying protective factors for cognitive health in older age (World Health Organization, 2012, 2015), especially in relation to environmental resources that can help to prevent physical and cognitive decline with ageing (Corburn, 2015; Giles-Corti et al., 2016; World Health Organization, 2007). Exploring variations in cognitive functioning in healthy older populations based on accessibility to urban, and more resourced, environments can inform strategies to support successful ageing and help healthcare and planning policies to offer environmental and preventive interventions for healthy ageing in the places where they are most needed.

Geographical variations in dementia and cognitive impairment have been reported worldwide (Cassarino & Setti, 2015; Russ et al., 2012), with a general trend indicating better cognitive ageing for older populations living in urban rather than rural places. Recently, we identified urban/rural variations in specific cognitive skills, including executive functions, global cognitive functioning and memory in Ireland (Cassarino et al., 2016). Further research in the UK has identified a nonlinear association between cognitive impairment/dementia and opportunities offered by the environment measured in terms of land-use mix (Wu et al., 2015; Wu, Prina, et al., 2016). One possibility is that urban environments, as well as environments with higher land-use mix, would provide more cognitive stimulation and afford higher opportunities to avail of environmental resources for healthy ageing (Cassarino and Setti, 2015; Wu et al., 2015, 2016). In the present paper we tested the hypothesis that living in a place at shorter travel distance from gateways, i.e. urban environments, would be associated with better cognitive health. This could be due to living in a stimulating and busier environment as well as to the possibility of availing of

resources. In order to distinguish these two aspects, which can however co-exist, we explored potential moderating effects of individual-level factors including social engagement and lifestyle as well as sex, age, educational attainment and health.

In addition, we explored whether driving status moderated variations in cognition based on travel time to gateways, given the evidence that being or not a driver, as well as changes in driving status, can affect health outcomes and mobility in older age (Anstey, Windsor, Luszcz, & Andrews, 2006; Dickerson et al., 2007; Edwards, Lunsman, Perkins, Rebok, & Roth, 2009; Paez, Mercado, Farber, Morency, & Roorda, 2010).

In order to test these hypotheses, we employed Geographic Information Systems (GIS) to explore variations in a comprehensive set of cognitive skills in a nationally representative sample of community-dwelling individuals aged 50 and older in Ireland, based on accessibility (i.e., travel time by car) to gateways, defined in the Irish National Spatial Strategy 2002 – 2020 as environments offering service infrastructure and stimulating activities (corresponding to urban areas with 100,000 or more inhabitants, see Method section for further detail). Evidence exists of geographical inequalities in terms of accessibility to health or leisure resources that can impact health and behavioural outcomes in older age (Buor, 2002; Horner, Duncan, Wood, Valdez-Torres, & Stansbury, 2015; Jørgensen, Torp-Pedersen, Gislason, Andersson, & Holm, 2015; Sungyop Kim, 2011; Koller et al., 2010; Nordbakke & Schwanen, 2015; Paez et al., 2010). Thus, exploring travel distance or time to urban environments, while considering individual-level factors, can help to better understand the role of the lived environment for cognitive ageing (Raknes, Morken, & Hunskår, 2014; Zielinski, Borgquist, & Halling, 2013).

Methods

Participants

The sample for this study included 4,888 healthy community-dwelling Irish people aged 50 and older who completed a physical and cognitive health assessment in the first wave (2009 - 2011) of The Irish Longitudinal Study on Ageing (TILDA). TILDA is a large cohort study on the health, well-being and socioeconomic circumstances of Irish older people conducted every two years (Barrett et al., 2011; Kenny et al., 2010), with a comprehensive physical and cognitive assessment completed every four years (Cronin et al., 2013).

Design

Cross-sectional analyses were conducted on variations in performance for a comprehensive set of cognitive skills based on the time needed to travel to the nearest gateway from the participants' place of residence (see "Travel time to nearest gateway" section for a detailed description of this measure), while controlling for several covariates. An anonymised released version of the dataset for the first wave (see http://www.ucd.ie/issda/data/tilda/) was used in order to maintain confidentiality and protection of anonymity. Ethical approval was obtained at the beginning of the data collection, and all respondents provided signed informed consent before participation (Kenny et al., 2010); no individuals with severe cognitive impairment took part in the data collection (Whelan & Savva, 2013).

Travel Time to Nearest Gateway

The explanatory variable for this study was the average drive time (in minutes) needed to travel to the nearest gateway from the participants' place of residence captured at the level of Small Areas units through Geographic Information

Systems (GIS) by the All-Island Research Observatory (AIRO), Maynooth University, Ireland. Small Areas are the most detailed spatial statistical units available for the Republic of Ireland (introduced by the Irish Central Statistics Office in 2011), corresponding to areas comprised of 80-100 households and with an average size of 3.5km^2. Gateways are defined by the Irish National Spatial Strategy 2002 – 2020 (http://nss.ie/pdfs/Completea.pdf, p.40) as urban settlements (100,000 or more inhabitants) with a wide range of service infrastructure, including transport, education and health facilities, and therefore with enhanced environmental quality and more opportunities for accessibility and participation than other settlements. Drive times were based on average drive-time speeds.

This measure was merged with the first wave of TILDA in order to provide each participant with an averaged measure of accessibility to key urban centres from their Small Area of residence (travel time from the centre of the Small Area to closest access point to a gateway). To comply with data confidentiality, the variable was censored at 99.75%.

Cognitive Measures

Measures of cognitive performance included global cognition, memory, speed of processing, attention, and executive functions collected in TILDA (Kenny et al., 2010).

Global cognition was measured as mean score (0 to 30) at the Montreal Cognitive Assessment Test (Nasreddine et al., 2005), and mean number of errors (0 to 30) at the Mini Mental State Examination (Folstein et al., 1975). Measures of memory included immediate and delayed recall of a list of 10 words based on the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery

(Morris et al., 1989), recall and recognition of six images in a Picture Memory Test taken from the Cambridge Mental Disorders of the Elderly Examination, or CAMDEX, (Roth et al., 1986), and success/failure in a task of prospective memory (i.e., reminding the interviewer to record the time upon occurrence of a certain event). Speed of processing was measured in terms of mean cognitive reaction time (in seconds) at the Choice Reaction Time Test, and completion time (seconds) for the Colour Trail Making Test Part 1 (D'Elia et al., 1996). Attention was measured as self-rated frequency of being absentminded (never/sometimes vs, most/all the time), and through the Sustained Attention to Response Task (Robertson et al., 1997) in terms of reaction time (milliseconds, SART RT), standard deviation from the mean reaction time (a measure of variability of performance, SART SD), number of commission errors (SART Commissions, 0 to 23), and number of omissions (SART Omissions, 0 to 142). Measures of executive functions included a verbal fluency (animal naming) test (Lezak, 2004), a 6-items test of visual reasoning taken from the CAMDEX, mean completion time (seconds) for the Colour Trail Making Test 2 (D'Elia et al., 1996), and mean change in completion time from CTT 1 to CTT 2 (CTT Δ), this last considered a measure of executive functions adjusted for biases due to differences in visuo-motor functioning (Ble et al., 2005). CTT errors were not analysed due to the very low error rate (less than 10% for one error and less than 2% for two or more errors).

Covariates

Covariates included *a priori* selected measures which have been associated with cognitive performance in older age in the existing literature, and may be subject to geographical variations.

Socio-demographic covariates included sex, age, educational attainment (none/primary, secondary, third/higher), and current social class (Professional/managerial, non-manual, manual, farmer or self-employed not specified, unemployed) as per Irish Census (Central Statistics Office, 2011, p. 75). We grouped farmers and self-employed not specified together as these groups had very few observations.

Physical and mental health included body mass index (BMI, kg/cm^2), self-rated hearing and vision (poor/fair vs. good/excellent), presence of disabilities (coded as yes or no) in activities of daily living (ADL) and/or instrumental activities of daily living (IADL), use of polypharmacy (more than five medications), clinical symptoms of depression (none/mild, moderate, severe) measured through the Center for Epidemiologic Studies Depression Scale (CES-D, (Radloff, 1977) and number of chronic conditions. This last variable was a composite measure informing on the presence of one or more among the following: high blood pressure or hypertension, angina, heart attack, congestive heart failure, diabetes or high blood sugar, stroke, mini-stroke or transient ischemic attack (TIA), high cholesterol, heart murmur, abnormal heart rhythm, other heart trouble, chronic lung disease, asthma, arthritis, osteoporosis, cancer or malignant tumour, Parkinson's disease, emotional/nervous/psychiatric problem, alcohol or substance abuse, stomach ulcers, varicose ulcers, cirrhosis or serious liver damage.

Social engagement and lifestyle included: household composition (cohabiting or not); perceived frequency of loneliness (rarely or never, some of the time, most of/all the time) measured through the CES-D (Radloff, 1977); the Berkman-Syme Social Network Index indicating whether the person is mostly isolated, moderately isolated, moderately integrated or mostly integrated in social terms (Berkman &

Syme, 1979); participation in lifelong learning in the past 12 months (any courses or any other education and training); level of engagement in physical activity on a weekly basis (none/low, moderate, vigorous) as measured through the International Physical Activity Questionnaire Short form (Craig et al., 2003), and smoking habits (never, past, or current smoker);

Lastly, we controlled for childhood circumstances, including father social class as per Irish Census (Central Statistics Office, 2011), childhood urban or rural residence, and self-rated childhood health (poor/fair vs good/excellent, up to 14 years of age).

Statistical analyses

Statistical analyses were performed using Stata version 12 (StataCorp LP, Texas). Survey data analyses were conducted by applying sampling weights. These were calculated for each participant in TILDA as the inverse of the probability that an individual in the older population of Ireland selected at random with same age, sex and educational attainment would have completed the health assessment (Kearney et al., 2011; Kenny et al., 2010; Whelan & Savva, 2013), with participants from groups less likely to participate having a higher weight. Further details on the design and methodology of TILDA, as well as the comparability with other longitudinal studies are available elsewhere (Savva et al., 2013; Whelan & Savva, 2013). Associations between travel time to gateways and cognitive measures or covariates were explored in bivariate analyses using Spearman correlation for continuous or ordinal variables, and logistic and multinomial logistic regression for categorical variables. Regression models were used to analyse variations in cognitive performance based on travel time to the nearest gateway in univariate analyses

(Model 1), and in multivariate analyses including all covariates (Model 2). Based on the psychometric characteristics of the cognitive measures (analyses not shown), linear regression was used for continuous variables (MoCA, CTT 1, SART RT, SART SD, fluency, CTT 2, CTT Δ), poisson regression for count variables (MMSE errors, immediate and delayed recall, Picture recall and recognition, visual reasoning), negative binomial regression for count variables with over-dispersion (SART Commissions and Omissions), and logistic regression for categorical variables (prospective memory and absentmindedness).

A Wald test of the null hypothesis that differences between the regression coefficients based on travel time to gateways was conducted. Statistical significance was indicated by a *p*-value lower than .05.

Variations in cognitive performance were also explored based on interactions between travel time to gateways and driving status (driving or not) to control for potential moderating effects, as well as interactions with individual-level covariates (sex, age, educational attainment, health, loneliness, social engagement, and lifestyle).

As validity checks, we conducted nonparametric regression analyses on continuous variables, and ran the regression analyses for all the cognitive measures on the unweighted data.

Results

Sample characteristics

In the study sample (Mean age 62.45, standard deviation = 8.70; 51.29% female) the average travel time to the nearest gateway was 32.28 minutes (standard

deviation = 21.67), while the median travel time was 28 minutes (interquartile range = 46-14), going from a minimum of 3 minutes to a maximum of 119 minutes. The distribution of the variable was right-skewed (skewness = 1.03).

Participants' characteristics, as well as the bivariate associations with travel time to the nearest gateway, are shown in Table 7.1. The sample was overall young-older, healthy, and socially and physically engaged. Some small variations emerged with increasing travel time to gateways: Participants living farther from gateways were slightly younger, less educated (mainly primary or secondary level), working mainly as farmers or self-employed, or unemployed, more likely to report some form of disability or chronic conditions, but slightly more socially integrated, more likely to cohabit and more physically active, as well as more likely to drive. Measures of cognition showed significant, although very small, correlations with the explanatory variable in terms of global cognition (MoCA, MMSE), memory (immediate and delayed recall, Picture recognition), accuracy in the SART (SD, omissions and commissions), and all measures of executive functions, with a general pattern of worse performance for participants living at longer distances from gateways. No significant associations were found with speed of processing, Picture recall, prospective memory, reaction times in the SART, or absentmindedness (see Table 7.1).

Table 7.1

Sample Characteristics and Association with Travel Time to Gateways

Characteristic	Total sample	Association with travel time to gateways	P-value
	n (%)	Mean (*SD*)	
Sex			.55
Male	2,233 (48.71)	32.45 (20.87)	
Female	2,655 (51.29)	32.14 (22.24)	
Education			<.001
None/Primary	1,104 (33.21)	32.59 (18.15)	
Secondary	2,058 (46.07)	33.28 (20.86)	
Third/Higher	1,726 (20.72)	29.64 (26.24)*	
Social class			<.001
Professional	1,259 (20.37)	28.92 (22.84)	
Non manual	650 (13.14)	29.19 (21.33)*	
Manual	937 (22.47)	31.17 (20.22)	
Farmers/self-employed (not specified)	649 (15.02)	38.52 (20.56)***	
Unemployed	1,193 (28)	33.24 (20.70)***	
Self-rated hearing			.74
Poor/Fair	664 (14.91)	32.03 (20.01)	
Good/Excellent	4,224 (85.09)	32.35 (21.86)	
Self-rated vision			.03
Poor/Fair	383 (9.11)	34.98 (22.28)	
Good/Excellent	4,505 (90.89)	32.02 (21.45)*	
Polypharmacy			.09
No	3,984 (80.21)	32.62 (21.78)	
Yes	904 (19.79)	30.99 (20.74)	
Disabilities			.03
No	4,423 (89.46)	32.58 (21.83)	
Yes	465 (10.54)	29.88 (19.37)*	
Depressive symptoms			.03
None	3,636 (73.72)	32.69 (21.87)	
Moderate	836 (17.46)	32.11 (21.52)	
Severe	416 (8.82)	29.39 (18.99)*	
Cohabiting			.23
No	896 (18.92)	31.32 (21.45)	

Yes	3,992 (81.08)	32.52 (21.60)	
Loneliness			<.001
Rarely	4,032 (82.23)	32.84 (21.90)	
Some of the time	539 (11.14)	31.51 (20.62)	
Moderate/all the time	317 (6.63)	26.91 (18.31)***	
Berkman-Syme Social Network Index			.003
Mostly isolated	273 (6.11)	29.51 (21.15)	
Moderately isolated	1,189 (25.15)	30.44 (21.23)	
Moderately integrated	2,034 (42.03)	33.43 (21.87)*	
Mostly integrated	1,392 (26.72)	32.90 (21.32)*	
Participation in lifelong learning			.004
No	4,128 (87.09)	32.71 (21.44)	
Yes	760 (12.91)	29.52 (21.99)**	
Driving status			<.001
Non-driver	1,047 (24.17)	28.25 (20.49)	
Driver	3,841 (75.83)	33.58 (21.75)***	
Physical activity			.02
Low/inactive	1,403 (29.77)	31.08 (20.47)	
Moderate	1,737 (34.64)	31.58 (22.34)	
Vigorous	1,748 (35.59)	34.01 (21.68)**	
Smoking habits			.07
Never	2,232 (44.18)	33.19 (22.21)	
Past	1,894 (38.8)	31.19 (20.92)*	
Current	762 (17.02)	32.49 (21.29)	
Father social class			<.001
Professional	737 (11.77)	29.04 (23.17)	
Non Manual	431 (7.76)	23.92 (20.01)***	
Manual	2,193 (48.36)	29.98 (20.17)	
Farmer	1,173 (24.45)	39.13 (20.67)***	
Unemployed	354 (7.66)	38.58 (24.18)***	
Childhood residence			<.001
Urban	2,050 (40.09)	24.51 (19.34)	

Rural	2,838 (59.91)	37.51 (21.37)***	
Childhood self-rated health			.16
Poor/Fair	310 (6.67)	30.58 (20.07)	
Good/Excellent	4,578 (93.33)	32.42 (21.69)	
Prospective memory			.44
Fail	889 (19.35)	31.83 (19.47)	
Success	3,999 (80.65)	32.42 (22.13)	
Absentmindedness			.13
Never/sometimes	4,510 (91.99)	32.15 (21.72)	
Most/all the time	378 (8.01)	33.91 (19.96)	

	Mean (*SD*)	Correlation	
Age	62.45 (8.70)	-0.05	<.001
BMI	28.81 (4.974)	0.04	.002
No. chronic conditions	1.94 (1.63)	-0.03	.02
MoCA	24.75 (3.36)	-0.11	<.001
MMSE errors [a], median (IQR)	1 (2-0)	0.07	<.001
Immediate recall, median (IQR)	7 (8-5.5)	-0.07	<.001
Delayed recall, median (IQR)	6 (8-4)	-0.08	<.001
Picture recall, median (IQR)	3 (4-3)	-0.01	.57
Picture recognition, median (IQR)	6 (6-5)	-0.05	<.001
CRT (sec) [a]	520.39 (154.03)	0.02	.19
CTT 1 (sec) [a]	57.75 (26.14)	0.01	.56
SART RT (ms) [a]	384.11 (100.19)	-0.01	.45
SART SD [a]	126.47 (76.47)	0.04	.006
SART Omissions [a], median (IQR)	5 (11-2)	0.03	.02
SART Commissions [a], median (IQR)	3 (6-1)	0.05	<.001
Verbal fluency	20.68 (6.76)	-0.08	<.001
CTT 2 (sec) [a]	114.91 (43.58)	0.05	<.001
CTT Δ [a]	57.16 (29.11)	0.07	<.001
Visual reasoning, median (IQR)	3 (4-2)	-0.05	<.001

Note. MoCA = Montreal Cognitive Assessment, MMSE = Mini Mental State Examination, PIC = Picture Memory Test, CRT = Choice Reaction Time, CTT = Colour Trail Making Test, SART = Sustained Attention to Response Task, *SD* = standard deviation, IQR = interquartile range. Correlation coefficients are presented as Spearman rho. P-values indicate for continuous and count variables the statistical significance of correlations with travel time to gateways and for categorical variables the statistical significance of differences between groups of participants based on travel time to gateways. Data are weighted. Specific between-groups differences in travel time are indicated as * $p < .05$, ** $p < .01$, *** $p < .001$

[a] Higher values indicate worse cognitive performance.

Regression analyses

The results of regression models are presented in Table 7.2 for cognitive measures which showed a significant association with travel time to gateways in the bivariate analyses (therefore excluding Picture recall, prospective memory, speed of processing, SART RT and absentmindedness, see Table 7.1). Univariate regression analyses (Model 1) indicated significantly poorer, although very small in terms of score, cognitive performance for participants who resided at a longer distance from gateways in all cognitive measures. These results were maintained in multivariate analyses controlling for all covariates (Model 2) for global cognition, immediate and delayed recall, the standard deviation of reaction times in the SART (SART SD) and errors of commission (SART commissions), verbal fluency and CTT Δ.

Nonparametric analyses on continuous variables confirmed the results of Model 2 for MoCA, fluency and CTT Δ, but not for SART SD. In addition, analyses on unweighted data confirmed the results of Model 2 for all measures except immediate recall. Therefore, measures of global cognition (MoCA, MMSE errors), delayed recall, SART errors of commission, fluency and CTT Δ showed the most consistent pattern.

No significant interactions between travel time to gateways and driving status, or between travel time and age, were found for any of the cognitive measures (data not shown). We found a potential moderating effect of sex for CTT 2, indicating a slightly lower decrease in performance for female rather than male participants with increasing travel time to gateways (b = -0.11, p =.047, 95% CI = -0.20, -0.001; Wald test: $F(1, 625) = 3.95$, p = .04).

Educational attainment also moderated the variations in performance for several cognitive measures, showing higher scores (although with very small effects) for participants with secondary or third/higher educational level, as compared to participants with none/primary education, for longer travel time to gateways. Significant interactions were found for MoCA [secondary: b = 0.02, p = .009, 95% CI = 0.003, 0.03; third/higher: b = 0.02, p = .031, 95% CI = 0.001, 0.03; Wald test: $F(2, 624) = 3.50$, p = .03], immediate recall [secondary: I.R.R. = 1.001, p = .033, 95% CI = 1.0001, 1.001; third/higher: I.R.R: = 1.001, p = .001, 95% CI = 1.0004, 1.002; Wald test: $F(2, 624) = 4.57$, p = .01], CTT 1 [secondary: b = -0.14, p = .004, 95% CI = -0.24, -0.04; third/higher: b = -0.11, p = .026, 95% CI = -0.21, -0.01; Wald test: $F(2, 624) = 4.12$, p = .02], SART omissions [secondary: I.R.R. = 0.996 p = .033, 95% CI = 0.992, 0.999; third/higher: I.R.R: = 0.994, p = .011, 95% CI = 0.991, 0.998; Wald test: $F(2, 624) = 3.91$, p = .02], CTT 2 [secondary: b = -0.25, p = .002, 95% CI = -0.41, -0.09; third/higher: b = -0.26, p = .002, 95% CI = -0.42, -0.09; Wald test: $F(2, 624) = 5.31$, p = .005], CTT Δ [secondary: b = -0.11, p = .048, 95% CI = -0.22, -0.001; third/higher: b = -0.15, p = .01, 95% CI = -0.26, -0.04; Wald test: $F(2, 624) = 3.39$, p = .034], and visual reasoning [secondary: I.R.R. = 1.002 p = .006, 95% CI = 1.001, 1.004; third/higher: I.R.R: = 1.002, p = .003, 95% CI = 1.001, 1.004; Wald test: $F(2, 624) = 4.61$, p = .01].

No moderating effects of health, social or lifestyle covariates were found.

Table 7.2

Estimates of Cognitive Performance by Travel Time to Gateways in Univariate (Model 1) and Multivariate Analyses (Model 2)

Cognitive measure	Model 1			Model 2		
	Estimates [95% CI]	*P* - value	R^2	Estimates [95% CI]	*P* - value	R^2
Global cognition						
MoCA	-0.02 [-0.02, -0.01]	<.001	0.02	-0.01 [-0.01, 0.005]	<.001	0.23
MMSE errors [a,b]	1.01 [1.002, 1.006]	<.001	<0.01	1.002 [1.001, 1.004]	.007	0.12
Memory						
Immediate recall[a,b]	0.99 [0.99, 0.99]	<.001	<0.01	0.99 [0.99, 0.99]	.009	0.02
Delayed recall[a,b]	0.99 [0.99, 0.99]	<.001	<0.01	0.99 [0.99, 0.99]	.02	0.04
Picture recognition [b]	0.99 [0.99, 0.99]	.001	<0.01	0.99 [0.99, 0.99]	.054	<0.01
Attention						
SART SD [a]	0.16 [0.04, 0.29]	.01	<0.01	0.12 [.01, 0.24]	.03	0.21
SART Omissions [a,b]	1.002 [1.001, 1.005]	.01	<0.01	1.001 [0.99, 1.002]	.31	0.04
SART Commissions [a,b]	1.002 [1.001, 1.003]	.02	<0.01	1.001 [1.0002, 1.002]	.04	0.04
Executive functions						
Verbal fluency	-0.03 [-0.04, -0.01]	<.001	<0.01	-0.02 [-0.04, -0.01]	.004	0.15
CTT 2[a]	0.12 [0.04, 0.19]	.003	<0.01	0.04 [-0.08, 0.11]	.21	0.33
CTT Δ[a]	0.10 [0.05, 0.15]	<.001	0.01	0.05 [0.01, 0.09]	.02	0.15
Visual reasoning [b]	-0.99 [0.99, 0.99]	.004	<0.01	0.99 [0.99, 1.001]	.26	0.03

Note. CI = confidence interval, MoCA = Montreal Cognitive Assessment, MMSE = Mini Mental State Examination, PIC = Picture Memory Test, CRT = Choice Reaction Time, CTT = Colour Trail Making Test, SART = Sustained Attention to Response Task. Estimates correspond to unstandardized b coefficients for continuous variables and incidence rate ratios for count variables. P-values correspond to the Wald test of the null hypothesis that the effect of travel time to gateways on cognitive performance is equal to 0. Data are weighted.

[a] Higher values correspond to worse performance

[b] Estimates correspond to incident rate ratios for count variables

Discussion

The results of our analyses indicate significant variations in cognitive performance based on travel time to the nearest gateway, with lower scores in terms of global cognition, delayed recall, accuracy in attention, and some measures of executive functions for participants living farther from urban environments, in line with our initial hypothesis. These variations are small in terms of score, therefore we do not claim them to be clinically relevant. Nonetheless they support the proposal that the environment may influence cognition in itself, independently from individual factors such as lifestyle. Specifically, here we investigated travel time to gateways as indicator of whether the participants' lived environment was more or less isolated, assuming that a more isolated environment offers less opportunities for cognitive stimulation (Cassarino & Setti, 2015).

These results develop the findings of previous studies which indicated a cognitive advantage, mainly related to executive functions, for participants living in urban rather than rural areas (Cassarino et al., 2016). We suggested in that study that such cognitive advantage might depend on the higher levels of complexity and stimulation provided by an urbanised environment, which can "train" the brain to respond more effectively to environmental demands. Here we explored such association through a continuous measure of distance from the participants' area of residence to urban environments, to see whether a higher accessibility to a stimulating and resourced place would be associated with a cognitive advantage. After controlling for a comprehensive set of covariates, we confirmed a significant although pattern of worse performance with increasing travel time to gateways for executive functions, in line with the previously found urban/rural differences, but also found variations in cognitive measures which had not emerged before (e.g.,

SART).These variations were of a very small magnitude, mostly due to the healthy and relatively young sample included in the analyses.

Overall, our findings are in line with the evidence of worse health and behavioural outcomes for older individuals with limited accessibility to urban environments, which offer potentially more resources and services than rural places. However, the focus of previous studies using similar measures of accessibility mainly on patient populations (Jørgensen et al., 2015; Koller et al., 2010) or on general health status in ageing (Raknes et al., 2014; Zielinski et al., 2013), and the lack of studies which, to our knowledge, have looked at travel time to services/activities and cognitive functioning in healthy older samples, limits the comparisons of our results to previous findings. Participants living farther away from gateways were less educated, more farmers, they were more engaged in vigorous physical activity and they had good social engagement. This profile is to be expected for participants living in mostly rural areas in Ireland. The relatively high level of social engagement and physical activity can contribute in accounting for the small absolute effects of distance to gateways on cognition, as these are well-known protective factors for cognitive ageing. Nonetheless a small, but significant, contribution of the environment itself was found here.

The results did not appear to be affected by the participants' driving status, as we found no significant interactions, contrary to significant associations between driving status and healthy ageing found in previous studies (Anstey et al., 2006; Dickerson et al., 2007). However, the vast majority of our participants (approximately 75%) were drivers, which is a necessity when living in rural areas in Ireland, and this, together with their healthy status, is the likely cause of the absence of significant interactions.

Although we found no significant moderating effects of age, future studies comparing drivers and non-drivers of different age groups might highlight significant associations with cognitive health based on accessibility to services and activities.

Having a higher educational attainment was found to moderate the association between travel time to gateways and cognition, although once again with small effects, for some of the measures, including variables which had not shown significant variations based on travel time in Model 2 (i.e., CTT 1, SART omissions, CTT 2, and visual reasoning). Given the well-established protective role of education (both in childhood and later in life) for healthy cognitive ageing (Robertson, 2014; Stern, 2009) and the low level of participation of our participants in lifelong learning (12.9%), this result highlights the importance of interventions promoting the engagement in intellectual activities tailored to the profile of the place of residence.

We did not have access to the travel habits of our participants, thus our data do not provide information either on the direction of travelling or on the frequency of visits to gateways. It has been argued that with increasing age, people tend to use more their local places and become therefore more susceptible to their proximal environments (Glass & Balfour, 2003; Oswald & Wahl, 2005); however, the relatively young age and good health of our sample, the fact that most of them drive, and the clustering of services and amenities in urban centres in Ireland, suggest that our participants might have multiple reasons (work, health, leisure) to travel towards gateways rather than the contrary. In addition, data on work commuting provided by the Irish Census 2011(see http://www.cso.ie/en/media/csoie/census/documents/census2011profile10/Profile_10_Full_Document.pdf, pp. 19-20) shows a larger net inflow than outflow in cities such as Dublin or Cork (included in the list of gateways for Ireland); as

approximately 39% of our sample was employed, one might expect that would be likely to travel to gateways frequently. Despite the limitation of not knowing whether our participants actually used urban centres, it is intuitive to think, and it has been shown in the existing literature, that individuals who have better accessibility (i.e., who live closer) to stimulating and resourced environments are more likely to use them and benefit from them either in terms of health or lifestyle (Buor, 2002; Nordbakke & Schwanen, 2015). Our study was intended as a first observation of variations in cognitive health associated with accessibility to urban places which could become significant with time as participants grow older and are more prone to functional limitations and chronic conditions. These might in fact impact negatively on individuals' mobility and ability to access service infrastructure or stimulating activities. Longitudinal studies integrating information on travel behaviour will further the understanding of these cross-sectional results and their potential clinical relevance. Having the opportunity to highlight changes over time in cognitive functioning in healthy older adults could have strong implications for preventive interventions to promote cognitive health and ageing in place.

In addition, using GIS data on environmental resources for cognitive health at the level of the neighbourhood or local community (e.g., accessibility to usable green areas, network connectivity, walkability) will allow for a more in-depth analysis of environmental correlates of healthy cognitive ageing, as found for example in recent studies on dementia/cognitive impairment in relation to land-use mix (Wu et al., 2015; Wu, Prina, et al., 2016).

This line of research considering geographical variations in multiple cognitive skills in ageing can have potential implications for the planning of services

and interventions to contrast cognitive chronic conditions tailored to the specific cognitive profile of the area of residence.

Chapter 8 - Study Four

Cognitive Changes over Time Based on Place of Residence: Longitudinal Analyses of The Irish Longitudinal Study on Ageing[9]

Abstract

Objectives - Recent cross-sectional studies on geographical variations in cognitive functioning in older age indicate an advantage in terms of executive functions for individuals living in urban rather than rural places. The present study explored whether changes in cognitive performance over two years were associated with the level of urbanisation of place of residence.

Methods – Data on 3,766 healthy community-dwelling individuals (Mean age = 62.35, *SD* = 9.93) who took part in the first and second wave of The Irish Longitudinal Study on Ageing (TILDA) was used to analyse whether residence in urban places (over 200,000 inhabitants), rural places (less than 1,500 inhabitants) or other settlements (1,500 to 200,000 inhabitants) at baseline (first wave) was associated with significant changes in global cognition, memory and verbal fluency at two-year follow-up of time, while controlling for socio-demographic, health and lifestyle covariates.

Results – Our data indicate no significant effects of place of residence on changes in cognition over two years when controlling for covariates, but highlighted potential effects of practice.

[9] This chapter is planned for submission to a peer-reviewed journal. Authors: Cassarino M., Kenny R.A., & Setti A.

Conclusions – Our results suggest that for this relatively young and healthy sample of older adults the small change in cognitive function registered cannot be ascribed to place of residence. More broadly, assessing cognitive functioning over a short interval time in a healthy older sample might be no cost-effective considering the impact of practice effects on the variables measured.

Introduction

Identifying protective factors to contrast cognitive decline over time is a global priority given the growing number of older individuals with dementia and cognitive impairment worldwide (World Health Organization, 2012). In recent years, research has explored the role of lifestyle and environmental influences for healthy cognitive ageing, indicating elements such as the engagement in social, physical and intellectual activities as beneficial to cognitive reserve over the lifespan and to maintaining cognitive efficiency late in life (Hertzog et al., 2008; Stern, 2012; Zhu et al., 2017). Although animal studies have shown that living in an enriched and stimulating environment causes positive physical changes to the brain which promote healthy cognitive ageing (Arendash et al., 2004; Berardi et al., 2007; Rosenzweig et al., 1962), it is an open question whether the lived environment plays a role in maintaining such cognitive efficiency in humans as well. Given increasing levels of urbanisation worldwide (World Health Organization, 2007), a first step to address that question is to consider the potential impact of urbanisation on cognitive ageing by looking at whether more or less urbanised environments broadly support better cognitive functioning with increasing age (what we defined as macro level of analysis in the model proposed in Chapter 3). In our framework exploring the impact of the physical lived environment on cognitive processing (Cassarino & Setti, 2015), we suggested that urban living may benefit cognitive health in older age more than rural residence because exposing individuals to more enriched and complex environments, in line with models of cognitive reserve highlighting the role of environmental novelty in preventing cognitive decline - novelty which characterises urban more than rural places (Robertson, 2014). This suggestion was based on epidemiological studies which have shown variations in the prevalence and

incidence of dementia and cognitive impairment associated with urban vs. rural residence or with land-use mix where urban residence appears to be a protective factor (Gavrila et al., 2009; Russ et al., 2012; Wu et al., 2015; Wu, Prina, et al., 2016). Similarly, in our previous cross-sectional study (Cassarino et al., 2016) we showed that executive functions - high level cognitive skills involved in multi-tasking, problem solving and reasoning which enable us to process and interact with complex information - were more efficient in urban than rural areas for a large sample of healthy individuals aged 50 and older. This evidence is important because it identifies an advantage or disadvantage simply in living in a certain place, when taking into account individual social and lifestyle circumstances, which are clearly determinant factors (Abbott et al., 2004; Albert et al., 1995; Baker et al., 2010; Stern, 2012; Stine-Morrow et al., 2008; Zunzunegui, Alvarado, Ser, & Otero, 2003).

However, while cross-sectional studies provide important observational data on the associations between characteristics of the environment of residence and cognitive functioning in older adults, longitudinal studies are needed to clarify potential causal pathways linking urbanisation to changes in cognitive functioning over time and to understand which kinds of environments are more supportive of cognitive health in older age. Extensive evidence exists of cognitive changes over time dictated for instance by the neighbourhood socioeconomic status (Aneshensel et al., 2011; see for a review Cassarino & Setti, 2015; Sheffield & Peek, 2009), but to what extent living in an urban rather than rural environment is associated with cognitive changes over time remains unclear. The availability of data on older people's cognitive performance collected over a two-year interval (first and second waves) in The Irish Longitudinal Study on Ageing (TILDA, Kearney et al., 2011; Kenny et al., 2010) gives the opportunity to investigate the association between place

of residence and cognitive ageing, and it enables to clarify whether environmental effects on cognitive scores can be observed in the short-term (after two years from the baseline assessment). Although one might expect little changes over such a short period of time, recent studies on the TILDA sample have in fact shown that psychological factors affected a small decline in fluency between the two waves (Robertson, King-Kallimanis, & Kenny, 2016). As our previous cross-sectional study (Cassarino et al., 2016) showed a cognitive advantage in verbal fluency, together with other measures of executive functions and global cognition, for TILDA participants living in highly urbanised rather than rural places or other (less urbanised) settlements, the present study aimed to explore whether such advantage would be maintained also longitudinally. Although our cross-sectional analyses had not shown clear urban-rural differences in relation to memory, we checked whether TILDA participants would show changes in performance between the two waves for this cognitive dimension (measured as immediate and delayed recall, and prospective memory) and tested whether place of residence could explain such changes. Our previous study had also looked at other cognitive measures including speed of processing and attention, but as these were not assessed in the second wave of TILDA, longitudinal analyses on them could not be performed.

Therefore, we explored changes in the global cognitive functioning, memory, and executive functions of TILDA participants occurred over a two-year period of time, and whether such changes were associated with the level of urbanisation of the place of residence. For this purpose, we compared residence in urban places (defined in the Irish Census as settlements with over 200,000 inhabitants), rural areas (having less than 1,500 inhabitants), or other settlements (with a population ranging from 1,500 to 200,000 inhabitants). Assuming urban environments as more complex and

more stimulating places than rural areas, we formulated the hypothesis that older urban dwellers would show less cognitive decline over time than those living in rural areas because the complex perceptual and cognitive stimulation presented by a city would train the brain to function more efficiently and age slower (Cassarino & Setti, 2015, 2016a).

Methods

Participants

Data for this study was derived from a sample of 3,677 healthy community-dwelling Irish people aged 50 and older participating in the second wave of The Irish Longitudinal Study on Ageing (TILDA), a large cohort study on the health, well-being and socioeconomic circumstances of Irish older people conducted every two years (Barrett et al., 2011; Kenny et al., 2010), with a comprehensive physical assessment completed every four years (Cronin et al., 2013). In terms of cognitive measures, a comprehensive battery including the main aspects of cognition is tested every four years, while only some measures of cognitive functioning are assessed at each wave, i.e., every two years (see Cognitive measures section for details). The sample for the present study included participants who completed both a computer-assisted personal interview (CAPI) and a physical and health assessment at wave one (W1, January 2009 – July 2011), and the CAPI at wave two (W2, April 2012 – January 2013), and for whom information on the geographical location of the place of residence had been collected at W1. The overall response rate at W2 was 86% (W1: N = 8,175; W2: N = 6,995). Data from any respondents who were new at W2, those who had passed away between the waves and data from proxy interviews (due

to a physical or cognitive impairment of the respondent) were removed (N = 408) to protect anonymity. Further information on the methodology employed in the two Waves is available elsewhere (http://tilda.tcd.ie/assets/pdf/Wave2-Key-Findings-Report.pdf).

Previous longitudinal studies on cognition for W1 and W2 of TILDA (Robertson, King-Kallimanis, & Kenny, 2016) have shown that participants not included in W2 had statistically significant poorer cognitive functioning, for which reason attrition weights were applied to the present study (see the "Statistical Analyses" section below for details).

Design

Longitudinal analyses were conducted on changes in performance for a set of cognitive skills over a two-year timeframe based on residence in either urban, rural or other areas at W1, while controlling for several covariates. Anonymised publicly released versions of the datasets for W1 and W2 (see http://www.ucd.ie/issda/data/tilda/) were used in order to maintain confidentiality and protection of anonymity. Ethical approval was obtained at the beginning of the data collection, and all respondents provided signed informed consent before participation (Kenny et al., 2010); no individuals with severe cognitive impairment took part in the data collection at baseline (Whelan & Savva, 2013).

Place of residence

The independent variable for this study was the geographical location of residence of the respondent at the time of the interview at W1 as assessed by the interviewer according to three categories: (a) Urban places; (b) Other settlements; (c) Rural areas. Based on the Irish Census 2011 (www.cso.ie), the "Urban" category

refers to the Dublin area, which is the only urban settlement with more than 200,000 inhabitants in the Republic of Ireland, while the category “Other settlements” include five Cities, five Boroughs, and 75 Towns with a population ranging from 1,500 to less than 200,000 inhabitants; lastly, rural areas are settlements with a population of less than 1,500 inhabitants.

Cognitive Measures

Measures of cognitive performance collected both at W1 and W2 (Kenny et al., 2010) included: the mean number of errors (0 to 30) at the Mini Mental State Examination (Folstein et al., 1975) as a measure of global cognitive functioning; memory measured through immediate and delayed recall of a list of 10 words based on the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) battery (Morris et al., 1989), and success/failure in a task of prospective memory (i.e., reminding the interviewer to record the time upon occurrence of a certain event); a verbal fluency (animal naming) test (Lezak, 2004) as a measure of executive functions.

For the purposes of the present study we considered cognitive performance at W2, as well as changes in cognitive performance between the two waves derived as cognitive score at W2 minus cognitive score at W1 for continuous and count variables (ΔMMSE errors, Δ Immediate recall, Δ Delayed recall, Δ Fluency) and as a categorical measure for prospective memory (1 "Stable successful" 2 "Stable not successful" 3 "Improvement" 4 "Decline").

These types of recoding were based on previous longitudinal studies on cognition (Robertson et al., 2016; Zunzunegui et al., 2003).

Covariates

Covariates included *a priori* selected measures (and changes in some of these measures between the two waves) which have been associated with cognitive performance in older age in the existing literature, and may be associated with geographical variations. The recoding of some variables was based on the methodology of previous longitudinal studies on cognition for the TILDA sample (Robertson et al., 2016).

Socio-demographic covariates included sex, age, educational attainment (none/primary, secondary, third/higher), and social class (Professional/managerial, non-manual, manual, farmer or self-employed not specified, unemployed) as per Irish Census (Central Statistics Office, 2011, p. 75) at W1 (baseline). The categories of the variable social class "farmers" and "self-employed not specified" were originally separated but we decided to group them together because each had very few observations. We also included changes in employment status between the two waves (1 "Employed at W1 and W2", 2 "Unemployed at W1 and W2", 3 "Newly employed in W2", 4 "Employed in W1 but not in W2"). Note that unemployed participants included both retired and individuals not working for other reasons (e.g. in training, working in the home, sick or invalid).

Physical and mental health included body mass index (BMI, kg/cm2), changes in BMI (Δ BMI, BMI W2 – BMI W1), self-rated hearing and vision (0 "poor/fair", 1 "good/excellent") at W1 and changes between the two waves (1 "Stable Good/Excellent", 2 "Stable Poor/Fair", 3 "Improvement", 4 "Decline"), presence of disabilities (0 "Presence of disabilities", 1 "No disabilities") in activities of daily living (ADL) and/or instrumental activities of daily living (IADL) and changes between the two waves (1 "No disabilities W1 and W2", 2 "Stable level of

disabilities", 3 "Reduced disabilities", 34 "Increased disabilities"), use of polypharmacy (using more than five medications, 0 "No", 1 "Yes") at W1 and changes between the two waves (1 "No polypharmacy W1 and W2", 2 "Polypharmacy W1 and W2", 3 "Increase in number of medications", 4 "Decrease"), clinical symptoms of depression (0 "None/mild", 1 "Moderate", 2 "Severe") at W1 measured through the Center for Epidemiologic Studies Depression Scale (CES-D, (Radloff, 1977) and changes between the two waves (0 "None/Mild both waves", 1 "Stable level of symptoms in both Waves", 2 "Reduced severity W1 to W2", 3 "Increased severity W1 to W2"), and number of chronic conditions at W1 (note that no data on chronic conditions was available in the public release of W2, impeding the calculation of changes in the number of chronic conditions between the two waves). This last variable was a composite measure informing on the presence of one or more among the following: high blood pressure or hypertension, angina, heart attack, congestive heart failure, diabetes or high blood sugar, stroke, mini-stroke or transient ischemic attack (TIA), high cholesterol, heart murmur, abnormal heart rhythm, other heart trouble, chronic lung disease, asthma, arthritis, osteoporosis, cancer or malignant tumour, Parkinson's disease, emotional/nervous/psychiatric problem, alcohol or substance abuse, stomach ulcers, varicose ulcers, cirrhosis or serious liver damage.

Cognitive scores at W1 were used as a covariate as well.

Social engagement and lifestyle included the presence of at least two close ties (friends and/or relatives) at W1 and changes between the two waves (0 "Stable less than two close ties, 2 "Stable more than two close ties" 3 "Increase W1 to W2", 4 "Decrease W1 to W2"), perceived frequency of loneliness (rarely or never, some

of the time, most of/all the time) measured through the CES-D (Radloff, 1977) at W1 and changes between the two waves (0 "Rarely/never W1&W2" 1 "Stable level loneliness W1&W2" 2 "Reduced loneliness W1 to W2" 3 "Increased loneliness W1 to W2"), frequency of engagement in exercise or sport (0 “Never”, 1 “Yearly/monthly”, 2 “Weekly”, 3 “Daily”) and changes between the two waves (1 “Never/yearly/monthly both Waves”, 2 “Stable weekly/daily both Waves”, 3 “Increased frequency W1 to W2”, 4 “Decreased frequency W1 to W2”).

Lastly, we controlled for childhood circumstances, including father social class (professional/managerial, non-manual, manual, farmer, unemployed) as per Irish Census (Central Statistics Office, 2011), childhood urban or rural residence, and self-rated childhood health (poor/fair vs good/excellent, up to 14 years of age).

Statistical analyses

Statistical analyses were performed using Stata version 12 (StataCorp LP). Survey data analyses were conducted by applying sampling weights. These were calculated for each participant in TILDA as the inverse of the probability that an individual in the older population of Ireland selected at random with same age, sex and educational attainment would have completed the health assessment at W1 (Kearney et al., 2011; Kenny et al., 2010; Whelan & Savva, 2013), with participants from groups less likely to participate having a higher weight. Further details on the design and methodology of TILDA, as well as the comparability with other longitudinal studies are available elsewhere (Savva et al., 2013; Whelan & Savva, 2013). Sampling weights at W1 were multiplied by the attrition weights. Attrition weights were calculated as the inverse of the probability that a respondent took part in W2 given their participation in the health assessment W1 and their likelihood or returning to W2. A logistic regression was employed to predict the participants’

likelihood of returning to W2 based on their age, sex, education, marital status, employment status, health (including presence of disabilities, use of medications, self-rated health, depression, smoking habits) and geographical location collected at baseline (W1). The attrition weights were made available by the TILDA statistics team.

Descriptive statistics were used to explore changes in performance between the two waves and to compare differences in cognitive performance at W2 between participants living in urban places, other settlements, or rural areas. Paired-samples t-test was used for linear variables, Wilcoxon Signed-Rank test for ordinal variables, and chi-square test for categorical measures.

Regression analyses explored the association between place of residence at baseline (W1) and cognitive performance in univariate analyses (Model 1), and in multivariate analyses including all covariates (Model 2).

In order to check the effects of place of residence on cognitive scores at W2 while controlling for cognitive scores at W1, we conducted Poisson regression for MMSE errors, immediate and delayed recall, linear regression for verbal fluency, and modified Poisson regression with robust error variance for prospective memory.

In order to check for effects on changes in performance between the two Waves, we used linear regression for continuous measures (ΔMMSE errors, Δ Immediate recall, Δ Delayed recall, Δ Fluency) and ordered logistic regression for categorical variables of change (Δ Prospective memory).

We conducted a Wald test of the null hypothesis that differences between the regression coefficients based on place of residence were equal to 0. Statistical significance was indicated by a *p*-value lower than .05.

Results

Sample characteristics at W1 and changes between the two waves

In this sample (*N* = 3,677, mean age at W1 = 62.35, *SD* = 9.93; median age = 62, IQR = 70 - 55; 48.9% female) 26.9% lived in urban places, 29.1% in other settlements, and 43.9% in rural areas at W1.

Participants' characteristics and comparisons between the three groups of residence are shown in Table 8.1. The sample was overall healthy and socially engaged at W1 and significant changes between the two waves were noted only for BMI (slight decrease from W1 to W2, $t(3,676) = 38.16$, $p < .000$). The performance in the cognitive assessments of interest showed some small but significant changes between the two waves, with an improvement for MMSE (smaller number of errors in W2 than W1, $Z = 9.28$, $p < .000$), immediate recall (higher number of recalled words in W2 than W1, $Z = -6.43$, $p < .000$) and prospective memory (68% of those who had failed the task at W1 succeeded at W2 while approximately 87% of those who had been successful at W1 were also successful at W2, $\chi^2(1) = 302.68$, $p < .000$), a decrement in verbal fluency (lower average of named animals, $t(3,676) = 16.37$, $p < .000$), while stable performance was noted in terms of delayed recall ($Z = -0.38$, $p = .71$). Therefore, overall, performance decreased only for verbal fluency, while improvements were found for MMSE and immediate recall, and no change for delayed recall or prospective memory .

The three groups of residence did not differ at W1 in mean age, or in the proportion of female participants, but the urban group was slightly more educated and more likely to work in a professional/managerial position, as noted in previous cross-sectional analyses on a similar sample (see Chapter 5). Rural participants were more likely than the other two groups to have lived in a rural place from birth to the age of 14, and to have had a father working as a farmer or unemployed. The rural group had slightly higher BMI than the other two groups at W1, but showed a stronger decrease between the two waves compared to the urban or "other settlements" groups. On the other hand, rural participants reported lower frequency of exercise than the other two groups at W1, and these differences did not change between the two waves. Significant differences between the three groups of residence in terms of changes in cognitive performance across the two-year period emerged for MMSE errors (the urban group maintained a stable performance while the other two groups showed a slight improvement) and immediate recall (the "other settlements" group maintained a stable performance while the rural group showed an improvement, and no differences were noted with the urban group). No differences emerged for delayed recall, prospective memory or fluency.

Table 8.1

Participants' characteristics by Total Sample and Comparing Places of Residence

Measure	Total Sample	Place of residence			*P*-value
		Urban N = 983 (26.9%)	Other settlements N = 1,010 (29.1%)	Rural N = 1,684 (43.9%)	
Female (W1), n (%)	1,992 (48.91)	537 (52.35)	550 (48.61)	905 (47.02)	.05
Age at W1, mean (*SD*)	62.4 (9.93)	62.53 (9.89)	62.94 (9.51)	63.52 (10.23)	.63
Educational attainment (W1), n (%)					<.001
None/primary	793 (36.83)	206 (38.72)	185 (30.69)	402 (39.73)	
Secondary	1.526 (48.7)	339 (42.79)**	464 (55.11)	723 (48.07)	
Third/Higher	1,358 (14.47)	438 (18.5)	361 (14.2)**	559 (12.19)	
Social class (W1), n (%)					<.000
Professional/Managerial	1,047 (18.53)	356 (24.2)	302 (19.01)	389 (14.74)	
Non manual	514 (13.56)	157 (16.66)	166 (16.42)	191 (9.76)	
Manual	742 (25.49)	190 (27.01)	207 (27.24)	345 (23.39)*	
Farmer/self-employed	481 (14.07)	74 (7.22)	92 (8.25)	315 (22.12)***	
Unemployed	893 (28.36)	206 (24.92)	243 (29.07)*	444 (29.98)***	
Changes in employment status W1 to W2, n (%)					.02
Employed at W1 and W2	1,149 (28.85)	307 (29.69)	284 (25.07)	558 (30.84)	
Unemployed at W1 and W2	2,068 (59.5)	564 (60.42)	610 (62.91)	894 (56.67)	
Newly employed in W2	141 (3.76)	29 (2.58)	29 (3.11)	83 (4.91)*	
Employed in W1 but not in W2	319 (7.89)	83 (7.31)	87 (8.92)	149 (7.58)	
BMI (W1), mean (*SD*)	28.76 (5.22)	28.31 (5.15)	28.66 (5.08)	29.11 (5.32)**	.007
Changes in BMI W1 to W2, mean (*SD*)	-1.40 (2.28)	-1.21 (2.21)	-1.38 (2.28)	-1.55 (2.31)**	.002
Number of chronic conditions (W1), mean (*SD*)	1.91 (1.68)	2.06 (1.79)	1.88 (1.56)	1.84 (1.69)	.06
Self-rated good/excellent hearing (W1), n (%)	3,169 (83.97)	856 (84.39)	866 (85.77)	1,447 (82.53)	.21
Changes in hearing W1 to W2, n (%)					.57
Stable Good/Excellent	2,930 (76.13)	809 (77.90)	790 (77.27)	1,331 (74.29)	

Stable Poor/Fair	9.49 (306)	78 (9.56)	89 (8.19)	139 (10.31)	
Improvement	9.54 (202)	49 (6.05)	55 (6.03)	98 (7.17)	
Decline	7.84 (239)	47 (6.49)	76 (8.51)	116 (8.24)	
Self-rated good/excellent vision (W1), n (%)	3,410 (90.64)	917 (91.15)	937 (91.63)	1,556 (89.68)	.45
Changes in vision W1 to W2, n (%)					.14
Stable Good/Excellent	3,158 (82.43)	848 (80.65)	867 (83.47)	1,443 (82.84)	
Stable Poor/Fair	105 (3.98)	27 (4.64)	32 (3.71)	46 (3.76)	
Improvement	162 (5.38)	39 (4.21)	41 (4.67)	82 (6.56)	
Decline	252 (8.21)	69 (10.7)	70 (8.15)	113 (8.45)	
Absence of disabilities (W1), n (%)	3,346 (89.78)	890 (88.82)	911 (89.05)	1,545 (90.86)	.37
Changes in disabilities W1 to W2, n (%)					.45
No disabilities W1 and W2	3,205 (84.36)	847 (83.43)	868 (82.93)	1,490 (85.87)	
Stable level of disabilities	66 (2.85)	26 (4.13)	20 (2.81)	20 (2.11)	
Reduced disabilities	251 (6.87)	63 (6.35)	71 (7.14)	117 (7.02)	
Increased disabilities”	155 (5.92)	47 (6.09)	51 (7.13)	57 (5.01)	
Use of polypharmacy (W1), n (%)	693 (21.08)	195 (21.53)	195 (20.36)	303 (21.29)	.87
Changes in polypharmacy W1 to W2, n (%)					.88
No polypharmacy W1 and W2	2,603 (67.94)	678 (67.38)	704 (67.56)	1,221 (68.53)	
Polypharmacy W1 and W2	571 (17.8)	166 (19.05)	163 (17.67)	242 (17.13)	
Increase in number of medications	381 (10.98)	110 (11.09)	111 (12.08)	160 (10.18)	
Decrease in number of medications	122 (3.27)	29 (2.48)	32 (2.68)	61 (4.15)	
Symptoms of depression (W1), n (%)					.11
None/Mild	2,765 (73.60)	723 (70.78)	752 (73.42)	1,290 (75.44)	
Moderate	618 (17.51)	181 (20.35)	162 (16.03)	275 (16.74)	
Severe	294 (8.89)	79 (8.87)	96 (10.54)	119 (7.82)	
Changes in depressive symptoms W1 to W2, n (%)					.13

None/Mild both Waves	2,410 (63.37)	614 (59.22)	652 (63.02)	1,144 (66.15)	
Stable level of symptoms in both Waves	294 (8.96)	92 (10.75)	82 (8.79)	120 (7.97)	
Reduced severity W1 to W2	537 (15.04)	141 (14.88)	153 (15.29)	243 (14.98)	
Increased severity W1 to W2	436 (12.62)	136 (15.15)	123 (12.90)	177 (10.89)	
Number of close ties (W1), mean (*SD*)	3,642 (98.72)	972 (98.39)	1,002 (98.84)	1,668 (98.84)	.73
Changes in number of close ties W1 to W2, n (%)					.12
Stable number of ties	3,576 (96.82)	969 (97.95)	977 (96.01)	1,630 (96.67)	
Increase	27 (0.99)	7 (1.07)	6 (0.79)	14 (1.08)	
Decrease	74 (2.18)	7 (0.97)	27 (3.19)	40 (2.25)	
Perceived frequency of loneliness (W1), n (%)					.07
Rarely or never	3,078 (82.83)	813 (81.98)	830 (81.42)	1,435 (84.28)	
Some of the time	379 (11.08)	103 (10.16)	118 (13.23)	158 (10.22)	
Most of/all the time	220 (6.09)	67 (7.86)	62 (5.35)	91 (5.51)	
Changes in perceived frequency of loneliness W1 to W2, n (%)					.40
Rarely/never W1&W2	2,744 (73.39)	715 (72.97)	732 (70.98)	1,297 (75.25)	
Stable level loneliness W1&W2	133 (3.76)	38 (4.00)	47 (4.76)	48 (2.97)	
Reduced loneliness W1 to W2	410 (11.60)	113 (11.76)	117 (11.74)	180 (11.40)	
Increased loneliness W1 to W2	390 (11.24)	117 (11.27)	114 (12.51)	159 (10.38)	
Frequency of engagement in physical activity (W1), n (%)					<.001
Never	750 (27.23)	168 (23.60)	197 (25.84)	385 (30.38)	
Yearly/monthly	695 (18.37)	167 (17.42)	165 (15.49)	363 (20.85)	
Weekly	1,242 (29.94)	374 (32.33)	367 (33.41)	501 (26.17)**	
Daily	990 (24.47)	274 (26.65)	281 (25.26)	435 (22.60)*	
Changes in frequency of engagement in physical activity W1 to W2, n (%)					<.000
Stable rare	792 (26.41)	194 (24.84)	201 (25.14)	397 (28.21)	
Stable frequent	1,214 (28.64)	378 (33.69)	359 (32.14)	477 (23.24)**	

Increased frequency	804 (21.86)	187 (18.54)	227 (22.24)	390 (23.65)	
Reduced frequency	867 (23.09)	224 (22.93)	223 (20.49)	420 (24.9)	
Father social class					<.000
Professional/Managerial	588 (11.24)	224 (15.22)	175 (12.18)	189 (8.18)	
Non manual	340 (7.85)	141 (12.66)	112 (9.47)	87 (3.82)*	
Manual	1,640 (50.55)	480 (59.43)	493 (55.37)	667 (41.92)	
Farmer	869 (23.52)	94 (7.32)	176 (17.01)***	599 (37.74)***	
Unemployed	240 (6.85)	44 (5.37)	54 (5.96)	142 (8.34)***	
Rural childhood, n (%)	2,097 (57.74)	288 (26.71)	482 (48.23)***	1,327 (83.04)***	<.000
Self-rated good/excellent childhood health, n (%)	3,462 (93.62)	926 (93.87)	950 (92.88)	1,586 (93.96)	.68
Cognitive measures					
MMSE errors (W1), median (IQR)	1 (2-0)	1 (2-0)	1 (2-0)**	1 (3-0)***	<.000
MMSE errors (W2), median (IQR)	1 (2-0)	1 (2-0)	1 (2-0)	1 (2-0)	.08
Δ MMSE errors, mean (*SD*)	-0.28 (1.98)	0.01 (2.08)	-0.37 (1.78)**	-0.41 (2.04)**	.002
Immediate recall (W1), median (IQR)	6.5 (7.5-5.5)	7 (8-5.5)	7 (8-6)	6.5 (7.5-5.5)***	<.000
Immediate recall (W2), median (IQR)	7 (8-6)	7 (8-6)	7 (8-6)	6.5 (8-5.5)*	.03
Δ Immediate recall, mean (*SD*)	0.18 (1.47)	0.17 (1.35)	0.05 (1.39)	0.28 (1.59)†	.004
Delayed recall (W1), median (IQR)	6 (8-4)	6 (8-5)	6 (8-5)	6 (7-4)***	<.000
Delayed recall (W2), median (IQR)	6 (8-4)	6 (8-4)	6 (8-5)	6 (8-4)**	.008
Δ Delayed recall, mean (*SD*)	0.02 (2.34)	0.03 (2.26)	-0.12 (2.23)	0.11 (2.45)	.25
Prospective memory (W1), success, n (%)	3,047 (79.19)	804 (79.32)	847 (79.32)	1,396 (79.02)	.99
Prospective memory (W2), success, n (%)	3,139 (82.15)	854 (83.61)	888 (85.41)	1,397 (79.09)†	.01
Δ Prospective memory, n (%)					.07
Stable successful	2,708 (68.65)	723 (69.34)	765 (70.13)	1,220 (67.24)	
Stable not successful	199 (7.32)	48 (6.42)	40 (5.39)	111 (9.14)	
Improvement	431 (13.50)	131 (14.27)	123 (15.29)	177 (11.84)	
Decline	339 (10.54)	81 (9.97)	82 (9.19)	176 (11.78)	

Fluency (W1), mean (*SD*)	20.31 (6.81)	21.48 (7.26)	20.24 (6.31)*	19.64 (6.73)***	.01
Fluency (W2), mean (*SD*)	18.87 (5.89)	19.67 (5.89)	18.66 (5.56)**	18.51 (6.06)**	.007
Δ Fluency, mean (*SD*)	-1.44 (6.21)	-1.81 (6.76)	-1.57 (5.63)	-1.13 (6.21)	.25

Note. N = 3,766. All measures of change for continuous variables (delta measures) were calculated as score at W2 minus score at W1. *P*-values correspond to a Wald test of the hypothesis that differences in estimates between the urban group (reference) and the other two groups of place of residence were equal to 0. Data are weighted.
* p <.05, ** p <.01, *** p <.001
† indicates statistically significant differences (p <. 05) between the "other settlements" and rural group.

Regression analyses

Regression analyses of the association between place of residence at W1 and cognitive performance at W2 (see Table 8.2) indicated significant differences for immediate and delayed recall, prospective memory and verbal fluency, but not for MMSE, in univariate models. However, the small effects disappeared when controlling for covariates. When looking at the association between place of residence and changes in cognition between the two waves (see Table 8.3), significant differences were noted for MMSE errors and immediate recall in univariate analyses, but none of the models was significant in multivariate analyses. It is also worth noting that the change is positive as over the two years period there is no significant cognitive decline registered in the majority of the sample.

Table 8.2

Estimates of Cognitive Scores at W2 for Current Residence at W1 ("Other settlements" and "Rural" as compared to "Urban") in Model 1 (univariate analysis) and Model 2 (all Covariates accounted for).

Cognitive measure	Current residence (Ref: Urban)	Model 1			Model 2		
		Estimate [95% CI]	*p*-value	R^2	Estimate [95% CI]	*p*-value	R^2
MMSE errors[a]	Other settlements	1.03 [0.83, 1.28]	.08	<0.01	1.01 [0.86, 1.18]	.89	0.03
	Rural	1.18* [1.03, 1.38]			1.04 [0.89, 1.21]		
Immediate recall[a]	Other settlements	0.99 [0.96, 1.02]	.03	<0.01	0.99 [0.97, 1.02]	.85	<0.01
	Rural	0.96* [0.94, 0.99]			0.99 [0.97, 1.02]		
Delayed recall[a]	Other settlements	0.99 [0.94, 1.05]	.008	<0.01	0.99 [0.95, 1.03]	0.91	<0.01
	Rural	0.93** [0.88, 0.98]			0.99 [0.96, 1.04]		
Prospective memory[a]	Other settlements	1.02 [0.97, 1.07]	.003	N.a.	1.01 [0.96, 1.06]	.08	N.a.
	Rural	0.94* [0.89, 0.99]			0.96 [0.91, 1.01]		
Verbal fluency[b]	Other settlements	-1.01** [-1.74, -0.28]	.002	<0.01	-0.34 [-0.95, 0.27]	.07	0.35
	Rural	-1.16** [-1.85, -0.47]			0.30 [-0.34, 0.95]		

Note. N = 3,677. CI = confidence interval. N.a. = Not available. *P*-values correspond to a Wald test of the hypothesis that estimates of cognitive performance across the three group of residence were equal. Effect sizes are shown as R^2 for continuous variables (fluency) and pseudo-R^2 for count variables. Model 2 includes all covariates and controlled for cognitive performance at W1. Data are weighted.

[a] Incident Rate Ratios shown based on Poisson regressions.

[b] Unstandardized b coefficients are shown for linear regressions.

* p <.05, ** p <.01, *** p <.001.

Table 8.3

Estimates of Continuous Changes in Cognitive Scores for Current Residence at W1 ("Other settlements" and "Rural" as compared to "Urban") in Model 1 (univariate analysis) and Model 2 (all Covariates accounted for).

		Model 1			Model 2		
Cognitive measure	Current residence (Ref: Urban)	Estimate [95% CI]	*p*-value	R^2	Estimate [95% CI]	*p*-value	R^2
Δ MMSE errors[a]	Other settlements	-0.38** [-0.65, -0.11]	.002	<0.01	-0.13 [-0.33, 0.07]	.44	0.37
	Rural	-0.41** [-0.65, -0.17]			-0.08 [-0.27, 0.12]		
Δ Immediate recall[a]	Other settlements	-0.12 [-0.29, 0.04]	.02	<0.01	-0.08 [-0.22, 0.06]	.39	0.32
	Rural	0.11 [-0.06, 0.27]			0.007 [-0.13, 0.15]		
Δ Delayed recall[a]	Other settlements	-0.15 [-0.44, 0.14]	.25	<0.01	-0.05 [-0.31, 0.21]	.92	0.25
	Rural	0.07 [-0.21, 0.35]			-0.02 [-0.28, 0.23]		
Δ Prospective memory[b]	Other settlements	1.02 [0.81, 1.31]	.54	N.a.	0.98 [0.77, 1.25]	.21	N.a.
	Rural	0.91 [0.73, 1.15]			0.82 [0.64, 1.05]		
Δ Verbal fluency[a]	Other settlements	0.23 [-0.69, 1.16]	.25	<0.01	0.36 [-0.57, 1.29]	.02	0.02
	Rural	0.67 [-0.21, 1.56]			1.13* [0.19, 2.07]		

Note. N = 3,677. CI = confidence interval. N.a. = Not available. *P*-values correspond to a Wald test of the hypothesis that estimates of cognitive performance across the three group of residence were equal. Model 2 includes all covariates and controlled for cognitive performance at W1. Data are weighted.

[a] Unstandardized b coefficients are shown for linear regressions.

[b] Odds Ratios are shown for ordinal logistic regression.

* p <.05, ** p <.01, *** p <.001.

Discussion

Our data indicated that the cognitive performance of our sample of healthy older individuals did not show decline over two years, rather, some level of improvement. Residence in urban places, rural areas or other settlements at baseline was not associated with significant changes in cognitive performance over the two-year period when controlling for socio-demographic, health and lifestyle factors. Considering the differences in performance between places of residence cross-sectionally at W2, the overall improvement in MMSE and immediate recall (practice effect) caused the three groups to have more similar scores, reducing therefore the differences emerged at W1. Our sample had not shown differences in prospective memory or delayed recall at W1, and this patterns was maintained at W2. The sample showed instead a decline in verbal fluency between the two waves, a task of executive functions for which higher scores had been recorded for urban rather than rural participants at W1. The decline in performance occurred across the three groups of residence, but although urban participants were better than those in the other two groups of residence in univariate analyses, these differences disappeared when controlling for covariates. In sum, we feel that the effects of practice and decline are intermixed and therefore the pattern of results are of difficult interpretation at W2.

The improvements in some cognitive measures might be due either to practice effects or reduced anxiety. Data collected in the third wave of TILDA will clarify whether practice or reduced anxiety caused the observed improvements. The overall improvements do not enable us to rule out whether individual-level factors could play a bigger role than place of residence for changes in cognitive performance

in the short-term, as shown in other studies (Feeney, O'Leary, & Kenny, 2016; Robertson et al., 2016), or whether the broad categorisation of the level of urbanisation of the place of residence might have limited the emergence of differences between participants.

The lack of environmental effects on the small decline observed for verbal fluency might be due to the short period of time between the two waves. Given the small effect size of place of residence, one might in fact expect that individual level factors could play a more important role on short-term changes.

For this reason, exploring cognitive skills which are tested solely in the health assessment every four year, and which cover cognitive dimensions not tested in this study (e.g., speed of processing, attention) might be more informative of changes in cognitive health with ageing. In addition, future studies using more in-depth measures of environmental influences on cognition at the level of the neighbourhood (e.g., presence of usable green areas, streets connectivity) could be more suitable to address our initial hypothesis that urban environments would be more supportive of healthy cognitive ageing than rural areas.

Understanding the impact of urbanisation on cognitive ageing is an important and timely area of research given the growing size of cities and number of older individuals worldwide (World Health Organization, 2007), and using measures of the built environment at the level of the neighbourhood and accounting for their changes over time could clarify this association with important implications both for urban planning and for cognitive interventions tailored to the environment of residence.

The present study, while showing no significant associations between urban-rural living and cognitive performance, highlighted potential issues linked with testing cognition in a healthy older population over short periods of time, whereas considering longer intervals could be more cost-effective and informative.

Chapter 9 - Study Five

Physical Activity Moderates Urban-Rural Variations in Cognitive Health: Results from The Irish Longitudinal Study on Ageing.[10]

Abstract

Objectives - Research suggests that older adults living in urban environments have better cognitive health than rural dwellers. However, engaging in physical activity, a well-established modifiable protective influence on cognition, could moderate these geographical variations, with implications for lifestyle interventions tailored to the place of residence.

Methods - The present study analysed variations in global cognitive functioning (Montreal Cognitive Assessment, MoCA) based on the interaction between place of residence (urban, other settlements, or rural) and level of physical activity (International Physical Activity Questionnaire, IPAQ) for a nationally representative sample of 5,654 healthy Irish adults aged 50+, controlling for several covariates.

Results - We found that, while rural participants showed overall worse cognitive performance than urban dwellers, rural participants engaging in vigorous physical activity had MoCA scores similar to the urban group ($b = 0.88$, $p < .01$).

[10] Preliminary findings of these analyses were presented as Marica Cassarino, & Annalisa Setti (2016). Physical Activity Modulates Geographical Variations in Cognitive Ageing: Results from The Irish Longitudinal Study on Ageing [Poster Presentation]. I*rish Gerontological Society 64th Annual and Scientific Meeting "Developing Cultures of Excellence in Ageing and Exploring the Needs of Marginalised Groups*", Killarney, Ireland, 30-SEP-16 – 01-OCT-16.

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Conclusions – The results are in line with the hypothesis of a moderating effect of lifestyle factors on geographical variations in cognitive health in older age. Suggestions for future studies on environmental and lifestyle factors for cognitive ageing are discussed.

Keywords: physical activity; aging; urban-rural; global cognition.

Introduction

Epidemiological studies on geographical variations in dementia and cognitive impairment suggest an advantage for populations living in urban rather than rural environments (Contador et al., 2015; Nakamura et al., 2016; Nunes et al., 2010; Russ et al., 2012). With respect to healthy older populations, a recent cross-sectional study on a community-dwelling sample in Ireland (Cassarino et al., 2016) found a significant association between urban living and better performance in global cognition, measured through the Montreal Cognitive Assessment (MoCA), after controlling for a number of confounding factors. In addition, a recent study in the United Kingdom highlighted a non-linear relationship between land-use mix and the risk of cognitive impairment and dementia (Wu et al., 2015), suggesting that geographical variations in cognitive ageing might be associated with the level of stimulation provided by the lived environment, for example through the presence of services and facilities (Cassarino & Setti, 2016a; Clarke et al., 2012).

Urban environments can offer a wider range of opportunities for cognitive stimulation than rural areas, both in terms of the direct stimulation derived from living in a perceptually complex environment (Linnell et al., 2014), and in terms of opportunities for active lifestyles which promote cognitive reserve (de Frias & Dixon, 2014; Robertson, 2013; Stern, 2012). This evidence stimulates to explore which individual and environmental factors are associated with the cognitive advantage of city living. Considering opportunities for physical activity, a well-established protective factor for cognitive health in older age (Erickson, Gildengers, & Butters, 2013; Kelly et al., 2014; Ratey & Loehr, 2011b), research indicates that individual-level characteristics interact with environmental factors to determine whether older people are more or less physically active (Bauman et al., 2012; J. A.

Carlson et al., 2012; Plotnikoff, Mayhew, Birkett, Loucaides, & Fodor, 2004; Van Dyck et al., 2011), and there is growing evidence that the design of the environment of residence can influence an active lifestyle (Kerr et al., 2012; Saelens, Sallis, & Frank, 2003; Van Cauwenberg et al., 2011; Wu, Jones, et al., 2016). Some studies suggest urban-rural differences in physical activity levels (Arnadottir et al., 2009; Morgan et al., 2000) which can be associated with physical affordances or barriers in the environment of residence (Cleland et al., 2015; Wilcox et al., 2000).

Understanding in which places people are more physically active and at the same time more cognitively fit can inform on the association between cognitive health and mobility afforded by the place of residence. In turn, modifiable lifestyle factors such as physical activity could be capitalized upon in order to compensate for urban-rural differences in cognitive ageing. However, very few studies have attempted to link cognitive performance in older age to levels of engagement in physical activity specifically analysing the role of place (Bergland, Jarnlo, & Laake, 2013; Watts, Ferdous, Moore, & Burns, 2015).

The present study aimed to explore this link by assessing whether the urban-rural variations in the global cognitive functioning of an older sample highlighted in a previous study (Cassarino et al., 2016) were moderated by the level of engagement in physical activity. Based on our previous findings that healthy community-dwelling older individuals living in urban areas showed better cognitive functioning than those in rural areas, we hypothesised that levels of physical activity would moderate cognitive performance especially for rural dwellers, who most needed cognitively stimulating activities.

In addition, as the engagement in active lifestyles can change with individual-level factors such as age, gender, health status or social engagement (Carlson et al., 2012; Plotnikoff et al., 2004), we explored whether the association between global cognition, physical activity and place of residence changed based on these factors.

Methods

Participants

The present study used data from a sample of 5,654 healthy community-dwelling Irish individuals aged 50 and older (Mean age = 63.5, *SD* = 9.2; 51.5% female) who completed a comprehensive physical and cognitive health assessment in the First Wave (2009 – 2011) of The Irish Longitudinal Study on Ageing (TILDA, (A. Barrett et al., 2011; Kenny et al., 2010). TILDA is a national cohort study which explores the health, well-being and socioeconomic circumstances of the Irish older population, with the health assessment taking place every four years. The sample for the study was selected from the original sample of 5,898 participants who completed the health assessment, excluding 244 participants with missing data for either the outcome measure, explanatory measures, or covariates.

Design

Cross-sectional analyses of variations in scores at the Montreal Cognitive Assessment (MoCA) were conducted based on interactions between place of residence (Urban, other settlements or rural areas in Ireland) and the level of engagement in physical activity (low/inactive, moderate, or high), while controlling for sociodemographic, health, and lifestyle covariates. An anonymised released version of the dataset for the First Wave (see http://www.ucd.ie/issda/data/tilda/) was

used in order to maintain confidentiality and data protection. Ethical approval was obtained at the beginning of the data collection, and all respondents provided signed informed consent before participation (Kenny et al., 2010); no individuals with severe cognitive impairment were included in the First Wave (Whelan & Savva, 2013).

Sampling weights were calculated for each participant in TILDA as the inverse of the probability that an individual in the older population of Ireland selected at random with same age, sex and educational attainment would have completed the health assessment (Kearney et al., 2011; Kenny et al., 2010; Whelan & Savva, 2013), with participants from groups less likely to participate having a higher weight. Further details on the design and methodology of TILDA, as well as the comparability with other longitudinal studies are available elsewhere (Savva et al., 2013; Whelan & Savva, 2013).

Explanatory measures

The independent variables for this study were the current place of residence and level of physical activity.

Place of residence was operationalised as the geographical location of residence of the respondent at the time of the interview as assessed by the interviewer according to three categories: (a) Urban places; (b) Other settlements; (c) Rural areas. Based on the Irish Census 2011 (www.cso.ie), the "Urban" category referred to the Dublin area, the only urban settlement with more than 200,000 inhabitants in the Republic of Ireland, whereas the category "Other settlements" included five Cities, five Boroughs, and 75 Towns with a population ranging from 1,500 to less than 200,000 inhabitants; lastly, rural areas were settlements with a population of less than 1,500.

The level of physical activity was measured through the International Physical Activity Questionnaire (IPAQ) short form (Craig et al., 2003). The IPAQ short form is a standardised measure consisting of eight items which estimate the habitual time spent performing physical activities (moderate to vigorous) and inactivity (time spent sitting). This variable was operationalised into three categories according to the following scoring protocol (https://sites.google.com/site/theipaq/scoring-protocol): (1) Low/inactive, for those not meeting the criteria for categories 2 or 3; (2) Moderate, engaging in either three or more days a week of vigorous activity of at least 20 minutes per day, or five or more days a week of moderate-intensity activity or walking of at least 30 minutes per day, or five or more days a week of any combination of walking, moderate-intensity or vigorous-intensity activities achieving at least 600 MET-minutes per week; (3) High, including vigorous-intensity activity on at least three days a week and accumulating at least 1,500 MET-minutes per week, or seven or more days of any combination of walking, moderate or vigorous-intensity activities achieving at least 3,000 MET-minutes per week. MET-minutes are a measure of the volume of activity can be computed by weighting different types of activity by their energy requirements (e.g., walking has a weight of 3.3, whereas cycling has a weight of 6.0). METs are multiples of the resting metabolic rate and a MET-minute is computed by multiplying the MET score of an activity by the minutes performed. The IPAQ shows fair criterion validity and test-retest reliability (Craig et al., 2003; Tomioka, Iwamoto, Saeki, & Okamoto, 2011; Wolin, Heil, Askew, Matthews, & Bennett, 2008).

Outcome measure

The outcome variable for the study was global cognition measured as the average score at the Montreal Cognitive Assessment, or MoCA (Nasreddine et al., 2005). The MoCA provides a score of global cognitive function going from 0 (cognitive impairment) to 30 (healthy cognitive status), and it is a widely used screening tool for mild cognitive impairment in clinical settings (Coen, Robertson, Kenny, & King-Kallimanis, 2016; Dong et al., 2010; Nasreddine et al., 2005). The analyses were conducted on MoCA only rather than other measures included in the previous chapters as we felt it was more adequate to explore the potential effects of lifestyle on a measure of global cognition sensitive to mild cognitive impairment based on the existing literature on behavioural and cognitive health (Andel et al., 2008; Baker et al., 2010). In addition, interactions between place of residence and the engagement in physical activity conducted in Study One (Chapter 5) had shown significant results for MoCA only..

Covariates

We selected *a priori* covariates which can be associated with geographical variations in cognitive performance as well as the engagement in physical activity, including socio-demographic data, physical and mental health, social engagement and lifestyle, childhood circumstances.

Socio-demographic data included sex, age, educational attainment (none/some primary, primary, intermediate/junior/group certificate or equivalent, leaving certificate or equivalent, diploma/certificate, primary degree, postgraduate/higher degree), and current social class as per Irish Census

(professional/managerial, non-manual, manual, farmers, self-employed (not specified), unemployed).

Physical and mental health was assessed in terms of body mass index (BMI, kg/cm2), self-rated hearing (poor/fair, good/excellent), self-rated vision (poor/fair, good/excellent), presence of disabilities in activities of daily living (ADL) and/or instrumental activities of daily living (IADL), use of polypharmacy (more than five medications), clinical symptoms of depression (none, moderate, severe) measured through the Center for Epidemiologic Studies Depression Scale (CES-D, (Radloff, 1977), and number of chronic conditions. Number of chronic conditions was a composite variable informing on the presence of one or more among the following: high blood pressure or hypertension, angina, heart attack, congestive heart failure, diabetes or high blood sugar, stroke, mini-stroke or transient ischemic attack (TIA), high cholesterol, heart murmur, abnormal heart rhythm, other heart trouble, chronic lung disease, asthma, arthritis, osteoporosis, cancer or malignant tumour, Parkinson's disease, emotional/nervous/psychiatric problem, alcohol or substance abuse, stomach ulcers, varicose ulcers, cirrhosis or serious liver damage.

Measures of social engagement and lifestyle included household composition (cohabiting or not), perceived frequency of loneliness (never/rarely, some of the time, moderate amount of time, all the time) as measured through the CES-D (Radloff, 1977), social connectedness (mostly isolated, moderately isolated, moderately integrated, mostly integrated) measured through the Berkman-Syme Social Network Index (Berkman & Syme, 1979), participation in lifelong learning, and smoking habits (never, past, current).

Lastly, childhood circumstances included father social class as per Irish Census (Central Statistics Office, 2011), childhood (intended as birth to 14 years of age) urban or rural residence, and self-rated childhood health (poor/fair vs. good/excellent).

Statistical Analyses

Statistical analyses were performed using Stata version 12 (StataCorp LP, Texas). Survey data analyses were conducted by applying sampling weights as described in the Design section (Barrett et al., 2011). Chi-square statistics were used to explore associations between categorical variables. Linear regression models were used to explore variations in MoCA scores associated with the interaction between place of residence and level of physical activity, in univariate analyses (Model 1), and in multivariate analyses controlling for all covariates (Model 2). In the regression models, urban participants with low/no engagement in physical activity represented the reference group to which all other groups were compared in terms of cognitive scores. Post-estimation analyses were conducted using the adjusted Wald test of linear hypotheses.

As validity check of our analyses, we conducted Poisson regression analyses considering the MoCA scores as a count variable, in order to check for nonparametric associations. In addition, we re-ran the linear regression analyses without applying sampling weights. Lastly, we conducted the regression analyses including only one independent variable at a time (place of residence, level of physical activity).

We conducted a Wald test of the hypothesis that interaction effects for place of residence and level of engagement in physical activity were equal to 0. Statistical

significance was indicated by a p-value lower than .05. R^2 was used as measure of effect size.

Results

Descriptive Data

In our sample (N = 5,654), 1,462 (24.5%) participants lived in an urban area, 1,543 (27.1%) in other settlements, and 2,649 (48.5%) in rural areas. In terms of physical activity, 1,679 (31.3%) individuals reported low or no engagement in some form of physical activity, 1,999 (34.4%) engaged in moderate physical activity, and 1,976 (34.3%) had high level of engagement in physical activity.

Chi-square statistics indicated small but significant differences in the level of engagement in physical activity between the three areas of residence, $\chi 2(4, N = 5{,}654) = 39.8$, $p = .0003$, Cramer's V = 0.06, with 37% of rural participants engaging in vigorous physical activity, whereas 39.5% of urban participants and 36.1% of people living in other settlements reported moderate levels (see Table 9.1).

Table 9.1

Level of Engagement in Physical Activity by Place of Residence, n (%)

	Place of residence		
IPAQ level	Urban	Other settlements	Rural
Inactive/Low	408 (29.47)	463 (31.4)	474 (31)
Moderate	580 (39.53)	566 (36.12)	514 (32.48)
Vigorous	474 (31)	853 (30.75)	988 (37.06)

Notes. IPAQ = International Physical Activity Questionnaire short form

The average MoCA score for the sample was 24.16 (SD = 3.99). This is a relatively low score for healthy older adults compared to other countries, and the reasons are likely due to cultural differences, as discussed elsewhere (Savva et al.,

2013). In terms of differences in mean MoCA scores between the three areas of residence, urban participants (M = 25.11, SD = 3.50) had significantly better performance than those living either in other settlements (M = 24.18, SD = 3.91, p =.000), or those in rural areas (M = 23.68, SD = 4.01, p = .000). Place of residence explained about 2% of variance in the MoCA scores, R^2 = 0.21, F(2, 620) = 34.15, p = .000. Considering global cognition based on the level of engagement in physical activity, participants with low or no engagement (M = 23.35, SD = 4.45) scored lower than either those reporting a moderate level of engagement (M = 24.27, SD = 3.88, p = .000) or those with high level of engagement (M = 24.81, SD = 3.44, p = .000). Physical activity explained about 2% of variance in the MoCA scores, R^2 = 0.22, F(2, 620) = 44.34, p = .000.

Sample characteristics are shown in Table 9.2 and Table 9.3. Looking at the covariates in relation to place of residence (see Table 9.2), rural living, when compared to urban dwelling, was significantly associated with slightly lower educational attainment (fewer individuals with primary or higher degree) and belonging to a manual, farmer or self-employed (not specified) social class. Rural participants had slightly higher BMI, but fewer chronic conditions than urban dwellers; moreover, they were more likely to cohabit and reported more integrated social networks, although less likely to take part in lifelong learning. Lastly, the rural group was also more likely than the urban group to have lived in a rural place before the age of 14, and to have had a father working either as manual or farmer, or being unemployed.

Table 9.2

Estimates of Socio-demographic, Health and Lifestyle Characteristics for Total Sample and Place of Residence

Characteristic	Total sample (N = 5,654)	Urban (n = 1,462)	Other settlements (n = 1,543)	Rural (n = 2.649)	*P*-value (Effect size)
MoCA, mean (*SD*)	24.16 (3.91)	25.11 (3.52)	24.18 (3.91)***	23.68 (4.01)***	<.000 (0.02)
Female, n (%)	3,059 (51.53)	803 (53.24)	835 (51.86)	1,421 (50.49)	.13
Age, mean (*SD*)	63.47 (9.05)	63.72 (9.25)	63.52 (9.02)	63.32 (8.95)	.69
Education, n (%)					<.000 (0.09)
None/Some primary	164 (4.21)	48 (4.98)	39 (3.72)	77 (4.09)	
Primary	1,295 (33.39)	308 (31.48)	325 (30.79)	662 (35.81)	
Intermediate/ junior/group certificate or equivalent	1,337 (25.01)	260 (19.79)	384 (26.5)	693 (26.81)	
Leaving certificate or equivalent	994 (18.65)	253 (19.09)	299 (20.76)*	442 (17.24)	
Diploma/ Certificate	968 (9.56)	253 (10.48)	277 (9.87)	438 (8.92)*	
Primary degree	538 (5.47)	203 (8.37)	124 (4.77)**	211 (4.40)***	
Postgraduate (Higher degree)	358 (3.71)	137 (5.80)	95 (3.58)*	126 (2.72)***	
Current social class, n (%)					<.000 (0.21)
Professional/ma nagerial	1,394 (19.25)	468 (25.59)	400 (21.01)	526 (14.99)	
Non manual	717 (12.27)	228 (15.53)	231 (15.09)	258 (9.01)	
Manual	1,145 (24.73)	295 (26.53)	325 (26.05)	525 (23.05)**	
Farmers	323 (7.48)	1 (0.09)	13 (1.06)**	309 (14.92)***	
Self-employed (not specified)	425 (7.52)	99 (6.77)	122 (7.57)	204 (7.89)***	
Unemployed	1,417 (28.74)	327 (25.49)	389 (29.22)*	701 (30.14)***	
BMI, mean (*SD*)	28.81 (4.89)	28.36 (4.87)	28.69 (5.04)	29.11 (4.80)***	<.001 (<0.01)

No. chronic conditions, mean (*SD*)	2.01 (1.67)	2.15 (1.76)	2.02 (1.67)	1.92 (1.63)**	.005 (<0.01)
Self-rated hearing, good/excellent, n (%)	4,848 (84.12)	1,272 (88.68)	1,321 (85.05)	2,255 (82.82)	.09
Self-rated vision, good/excellent, n (%)	5,145 (89.34)	1,345 (90.33)	1,400 (89.24)	2,400 (88.90)	.52
Polypharmacy, n (%)	1,156 (22.43)	313 (23.55)	340 (23.69)	503 (21.16)	.15
Disabilities, n (%)					.03 (0.04)
None	5,030 (87.41)	1,294 (86.83)	1,354 (86.03)	2.382 (88.47)	
IADL	156 (3.4)	48 (4.29)	49 (3.93)	59 (2.67)*	
ADL	282 (5.23)	83 (5.97)	84 (5.86)	115 (4.49)	
ADL + IADL	186 (3.96	37 (2.91)	56 (4.17)	93 (4.37)	
Depressive symptoms, n (%)					.048 (0.03)
None	4,157 (72.7)	1,054 (70.55)	1,119 (71.57)	1,984 (74.44)	
Moderate	991 (17.89)	276 (19.79)	261 (17.44)	454 (17.18)*	
Severe	506 (9.39)	132 (9.65)	163 (10.99)	211 (8.38)	
Cohabiting, n (%)	4,537 (79.11)	1,157 (78.46)	1,172 (74.21)*	2,208 (82.18)*	<.000 (0.08)
Loneliness, n (%)					.04 (0.03)
Rarely	4,609 (80.8)	1,190 (80.26)	1,217 (78.05)	2,202 (82.61)	
Some of the time	648 (11.87)	161 (11.42)	201 (13.34)	286 (11.27)	
Moderate amount of time	289 (5.19)	81 (5.78)	92 (6.08)	116 (4.39)	
All the time	108 (2.14)	30 (2.53)	33 (2.53)	45 (1.72)	
Social Network Index, n (%)					<.000 (0.09)
Mostly isolated	349 (6.82)	119 (9.06)	110 (8.43)	120 (4.79)	
Moderately isolated	1,432 (26.51)	416 (30.44)	433 (29.17)	583 (23.03)***	
Moderately integrated	2,320 (41.38)	593 (40.22)	608 (39.08)	1,119 (43.24)***	
Mostly integrated	1,553 (25.29)	334 (20.27)	392 (23.31)	827 (28.93)**	

Lifelong learning, yes, n (%)	820 (11.83)	290 (16.35)	219 (11.86)**	311 (9.53)***	<.000 (0.08)
Smoking status, n (%)					<.001 (0.06)
Never	2,537 (43.46)	620 (39.85)	654 (41.33)	1,263 (46.47)	
Past	2,223 (39.47)	598 (41.07)	606 (38.74)	1,019 (39.06)*	
Current	894 (17.07)	244 (19.07)	283 (19.93)	367 (14.46)***	
Father social class, n (%)					<.000 (0.25)
Professional	777 (10.47)	289 (15.4)	229 (11.59)	259 (7.35)	
Non Manual	462 (7.03)	192 (11.98)	155 (8.94)	115 (3.47)**	
Manual	2,436 (46.05)	705 (54.48)	734 (51.96)	997 (38.49)**	
Farmer	1,354 (24.91)	136 (8.25)	261 (16.28)***	957 (38.14)***	
Unemployed	399 (7.47)	65 (4.85)	95 (6.49)**	239 (9.34)***	
Unknown	226 (4.06)	75 (5.04)	69 (4.73)	82 (3.20)	
Childhood rural residence, n (%)	3,324 (61.11)	438 (29.56)	752 (49.81)***	2,134 (83.34)***	<.000 (0.48)
Childhood self-rated health, good/excellent, n (%)	5,289 (93.11)	1,369 (93.24)	1,429 (91.61)	2,491 (93.88)	.06

Note. *SD* = standard deviation; MoCA = Montreal Cognitive Assessment; BMI = Body Mass Index; ADL = activities of daily living; IADL = instrumental activities of daily living. *P*-values correspond to a Wald test of the hypothesis that estimates across places of residence were equal. Effect sizes are expressed as R^2 for continuous variables while Cramer's V for categorical variables. Percentages are shown by place of residence. Data are weighted. Significant differences between Other settlements and Urban or Rural and Urban are indicated at the level * p <.05, ** p < .01 and *** p < .001.

The scores at the IPAQ (see Table 9.3 for details) indicated higher engagement in physical activity for younger participants, for men, for more educated participants and for those belonging to a higher social class. In terms of health, as expectable, engagement in moderate to vigorous exercise as compared to low or no physical activity was associated with having less disabilities, fewer chronic conditions, lower BMI, and more positively self-rated hearing and vision. In addition, participants who reported high level of physical activity were also more socially engaged than those with low or no exercise.

Table 9.3

Estimates of Socio-demographic, Health and Lifestyle Characteristics for Levels of Engagement in Physical Activity (IPAQ)

Characteristic	IPAQ level			*P*-value (Effect size)
	Low/inactive (n = 1,679)	Moderate (n = 1,999)	High (n = 1,976)	
MoCA, mean (*SD*)	23.35 (4.24)	24.26 (3.88)***	24.80 (3.44)***	<.000 (0.02)
Female, n (%)	1,035 (60.2)	1,164 (55.27)**	860 (39.88)***	<.000 (0.18)
Age, mean (*SD*)	65.62 (9.46)	63.52 (9.02)***	61.47 (8.16)***	<.000 (0.03)
Education, n (%)				<.000 (0.07)
None/Some primary	68 (5.86)	53 (3.82)	43 (3.09)	
Primary	425 (36.68)	449 (33.29)	421 (30.51)*	
Intermediate/junior/group certificate or equivalent	416 (24.58)	442 (23.73)	479 (26.68)*	
Leaving certificate or equivalent	306 (18.15)	347 (18.8)	341 (18.94)*	
Diploma/Certificate	245 (7.51)	355 (10.03)**	368 (10.96)***	
Primary degree	136 (4.37)	220 (6.44)***	182 (5.51)**	
Postgraduate(Higher degree)	83 (2.84)	133 (3.98)*	142 (4.30)**	
Current social class, n (%)				<.000 (0.14)
Professional/managerial	398 (18.52)	538 (21.18)	458 (17.96)	
Non manual	210 (11.8)	292 (14.27)	215 (10.68)	
Manual	330 (24.49)	384 (23.75)	431 (25.93)	
Farmers	49 (4.24)	75 (5.04)	199 (12.85)***	
Self-employed (not specified)	90 (5.25)	137 (6.83)	198 (10.26)***	
Unemployed	510 (35.69)	505 (28.93)**	402 (22.32)***	
BMI, mean (*SD*)	29.76 (5.44)	28.38 (4.64)***	28.39 (4.42)***	<.000 (0.02)
No. chronic conditions, mean (*SD*)	2.47 (1.79)	1.99 (1.64)***	1.59 (1.45)***	<.000 (0.04)
Self-rated hearing, good/excellent, n (%)	1,400 (81.08)	1,741 (85.84)**	1,707 (85.18)**	<.001 (0.06)
Self-rated vision, good/excellent, n (%)	1,474 (84.79)	1,845 (91.33)***	1,826 (91.5)***	<.000 (0.10)
Polypharmacy, n (%)	500 (32.6)	394 (21.85)***	262 (13.74)***	<.000 (0.19)
Disabilities				<.000 (0.17)
None	1,349 (77.71)	1,819 (89.7)	1,862 (93.95)	
IADL	75 (5.6)	56 (3.46)**	25 (1.35)***	
ADL	121 (7.41)	87 (4.75)***	74 (3.71)***	
ADL + IADL	134 (9.27)	37 (2.08)***	15 (0.98)***	
Depressive symptoms, n (%)				<.000 (0.11)

None	1,098 (63.97)	1,495 (74.57)	1,564 (78.83)	
Moderate	359 (21.94)	342 (17.17)***	290 (14.91)***	
Severe	222 (14.09)	162 (8.25)***	122 (6.26)***	
Cohabiting, n (%)	1,291 (75.11)	1,607 (79.39)**	1,639 (82.49)***	<.000 (0.07)
Loneliness, n (%)				<.000 (0.08)
Rarely	1,290 (75.28)	1,629 (81.21)	1,690 (85.43)	
Some of the time	228 (14.18)	235 (12.21)*	185 (9.42)***	
Moderate amount of time	113 (7.12)	93 (4.37)**	83 (4.26)***	
All the time	48 (3.42)	42 (2.22)*	18 (0.89)***	
Social Network Index, n (%)				<.000 (0.09)
Mostly isolated	143 (9.52)	108 (5.74)	98 (5.44)	
Moderately isolated	485 (30.84)	501 (25.87)*	446 (23.19)	
Moderately integrated	657 (39.06)	847 (43.39)***	816 (41.48)***	
Mostly integrated	394 (20.58)	543 (24.99)***	616 (29.89)***	
Lifelong learning, yes, n (%)	200 (9.34)	293 (11.88)*	327 (14.05)***	<.000 (0.06)
Smoking status, n (%)				.41
Never	740 (43.53)	912 (43.92)	885 (42.84)	
Past	647 (38.11)	799 (40.19)	777 (39.99)	
Current	292 (18.35)	288 (15.9)	314 (17.08)	
Father social class, n (%)				.28
Professional	209 (9.41)	304 (11.61)	264 (10.29)	
Non Manual	143 (7.27)	150 (6.69)	169 (7.16)	
Manual	737 (46.78)	874 (46.82)	825 (44.6)	
Farmer	388 (24.33)	449 (23.16)	517 (27.2)	
Unemployed	130 (7.83)	146 (7.67)	123 (6.93)	
Unknown	72 (4.38)	76 (4.03)	78 (3.82)	
Childhood rural residence, n (%)	995 (61.62)	1,121 (57.68)	1,208 (64.08)	.003 (0.06)
Childhood self-rated health, good/excellent, n (%)	1,569 (92.67)	1,861 (92.79)	1,859 (93.82)	.37

Note. IPAQ = International Physical Activity Questionnaire; SD = standard deviation; MoCA = Montreal Cognitive Assessment; BMI = Body Mass Index; ADL = activities of daily living; IADL = instrumental activities of daily living. *P*-values correspond to a Wald test of the hypothesis that estimates across places of residence were equal. Effect sizes are expressed as R^2 for continuous variables while Cramer's V for categorical variables. Percentages are shown by IPAQ level. Data are weighted.
Significant differences between Moderate and Low/inactive levels or High and Low/inactive are indicated at the level * p <.05, ** p < .01 and *** p < .001.

Regression Analyses

The results of linear regression analyses on MoCA scores based on place of residence and IPAQ score (see Table 9.4) showed a significant interaction for participants living in rural areas with high level of engagement in physical activity both in the unadjusted model (Model 1) and after controlling for all covariates (Model 2). Specifically, after controlling for confounders, while place of residence showed a main effect with urban participants having higher MoCA scores (estimated marginal M = 24.62, standard error = 0.10) than rural dwellers (b = -0.99, p = .000), we found similar scores for physically active rural participants (estimated marginal M = 24.52, standard error = 0.19), who showed significantly better cognitive performance than those not engaging in physical activity (b = 0.88, p = .003, see Figure 9.1). The Adjusted Wald test indicated a significant unique contribution of the interaction to the final model $F(1, 621) = 8.98$, p = .003. Analyses using Poisson regression and unweighted linear regression analyses confirmed these results both for the unadjusted and adjusted model (data not shown).

No interactions were found for participants in the "other settlements" group. This group showed slightly lower cognitive scores than the urban group, however the differences did not reach statistical significance.

We found no significant interactions with sex, age, health or social engagement. Significant interactions with educational attainment were found for participants living in the "other settlements" group, with individuals with high levels of physical activity but low or no education showing worse scores than those with higher educational attainment (data not shown). The small number of observations in each subgroup, however, makes this result difficult to interpret.

Table 9.4

Estimates of MoCA scores based on interactions between place of residence and level of engagement in physical activity

Predictors	Model 1 b (95% CI)	Model 2 b (95% CI)
Residence (Ref: Urban)		
Other settlements	-0.99** (-1.65 - -0.33)	-0.48 (-1.01 – 0.04)
Rural areas	-1.86*** (-2.46 - -1.26)	-0.99*** (-1.48 - -0.51)
IPAQ (Ref: Low/inactive)		
Moderate	0.63* (0.11 – 1.15)	-0.04 (-0.51 – 0.43)
High	1.01*** (0.47 – 1.54)	-0.02 (-0.46 – 0.42)
Residence/IPAQ (Ref: Urban/inactive)		
Other settlements/Moderate	0.01 (-0.79 – 0.80)	-0.16 (-0.84 – 0.53)
Other settlements/High	0.24 (-0.54 – 1.01)	-0.02 (-0.67 – 0.63)
Rural/Moderate	0.41 (-0.26 – 1.09)	0.29 (-0.32 – 0.91)
Rural/High	0.81* (0.11 – 1.50)	0.88** (0.31 – 1.46)
R^2	0.05	0.32

Notes. N = 5,654. CI = Confidence Interval. IPAQ = International Physical Activity Questionnaire – short form. Estimates indicate differences in MoCA scores from the reference category (Urban residents with low or no engagement in physical activity). Model 2 includes all demographic, health, social, lifestyle, and childhood covariates. Data are weighted.
* p <.05, ** p <.01, *** p <.001.

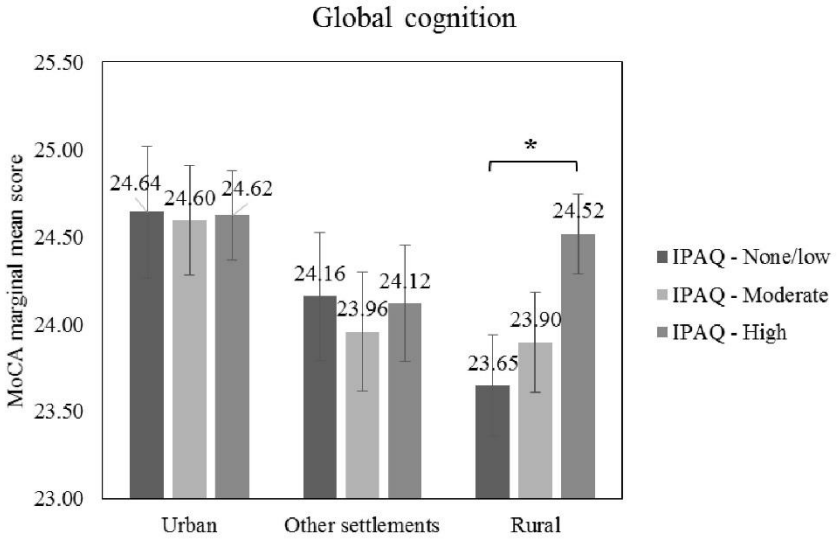


Figure 9.1

Estimated marginal mean MoCA scores for interactions between place of residence (urban, other settlements, rural) and level of engagement in physical activity (None/low, moderate, high) measured through the IPAQ short form. Model adjusted for all covariates. Error bars represent 95% confidence intervals.

Discussion

The data showed that the global cognitive functioning of a sample of over 5,000 healthy community-dwelling individuals aged 50 and older varied significantly, although moderately, based on the geographical location of residence and the level of engagement in physical activity. Overall, urban individuals in our sample were more physically active and more cognitively fit in terms of global cognition than rural dwellers. However, rural dwellers who were physically active had slightly higher MoCA scores than those with low or no engagement in physical activity, showing no differences in cognitive performance with the urban group, when individual-level covariates were accounted for. The association between cognitive function, physical activity and place of residence was independent of other individual-level factors such as age, gender, health status or social engagement, contrary to the results of other studies (Plotnikoff et al., 2004; Van Dyck et al., 2011). We also analysed differences in cognitive performance between the urban and the "other settlements" groups, but found no significant results after controlling for confounders.

Our results extend previous findings on urban-rural differences in cognitive performance for a similar sample of healthy older individuals (Cassarino et al., 2016), and are in line with the hypothesis that modifiable lifestyle factors can compensate for geographical variations in cognitive functioning in older age.

Although the cross-sectional nature of the study does not allow to draw conclusions on causality, our findings offer an observational insight on the interaction between lifestyle and environmental factors for cognitive ageing which deserves further investigation in a longitudinal perspective. In fact, the association

found could inform strategies to implement interventions for active and healthy ageing tailored to the place of residence.

The small variations in cognitive performance based on place of residence and physical activity are expected given the healthy and relatively young sample, but future longitudinal investigations could highlight differences in cognitive ageing trajectories based on environmental and lifestyle factors that might be of clinical significance, and further inform health-care interventions.

Further studies should also investigate specific environmental opportunities and barriers to being physically active in urban or rural environments which may impact cognitive health, for example by exploring whether older people living in different places are more or less likely to engage in specific types of physical activity, either leisure-oriented or transportation-oriented, and by considering perceived as well as objective environmental correlates of physical activity – information unfortunately not available for this sample. While in fact one might expect rural places to offer fewer opportunities for active lifestyles, other studies (Arnadottir et al., 2009) have found that older people engaged in specific types of physical activity (leisure- vs. transportation-oriented) depending on urban or rural residence. Importantly, future research should investigate specific environmental factors, such as neighbourhood physical characteristics (e.g., green, level of accessibility), which can support healthy cognitive ageing through cognitive stimulation or by fostering physical activity.

Chapter 10 - Discussion

Taken together, the results (see Appendix 2 for a summary) confirm the hypothesis that different places of residence are associated with different efficiency in cognitive performance. Specifically, we hypothesised that executive functions (operationalised in TILDA as verbal fluency, Coloured Trail Making Test Part 2 and Δ measure, and visual reasoning) and attention (measured in TILDA in terms of sustained attention through the SART and in terms of self-reported absentmindedness) would be the most sensitive to be modified by environmental stimulation. By looking at a sample of healthy community-dwelling people aged 50 and older in Ireland we found significant cross-sectional associations between varying levels of urbanisation of the place of residence and variations in cognitive performance mainly in relation to executive functions (variations found in studies One to Three), as expected, and in terms of absentmindedness (although not in all three cross-sectional studies). No clear variations were found instead in relation to the SART. In addition, variations were noted in terms of global cognition, immediate recall, but less consistent across studies. The variations showed a general pattern of better performance for participants living in more urbanised places, when controlling for socio-demographic, health and lifestyle covariates. No clear or significant patterns of variations were noted for the remaining measures of memory (delayed recall, Picture recall or recognition, prospective memory), speed of processing, or visual reasoning.

Specifically, in terms of executive functions, we found higher scores in verbal fluency and a smaller increase in completion time from Part 1 to Part 2 of the Coloured Trail Making Test (CTT Δ) for urban rather than rural participants or participants living in other settlements (Study One). Analyses carried using travel

time to urban environments as a measure of place of residence (Study Three) confirmed these results, indicating small improvements in performance for participants living closer to cities. Analyses on population density (Study Two) confirmed the results on CTT Δ, with better performance for participants living in medium-highly populated areas, but not on verbal fluency, and also indicated faster responses at the CTT 2 for participants living in more densely populated areas. These results are in line with our initial hypothesis that urban environments may be more stimulating in adult age for high-level cognitive skills involved in processing complex perceptual stimulation coming from the multiple sources present in the surrounding environment (e.g. busy roads, multiple people, noise). Interestingly, the data on population density indicated that participants living in medium-highly densely populated areas had the best level of performance in terms of executive functions, whereas participants in areas with the highest level of population density showed smaller differences from those living in areas with very low density.

A similar nonlinear pattern was found for immediate recall in both Study One and Study Two: In study One we noted that participants in the "other settlements" group, corresponding to areas of residence with intermediate levels of urbanisation, had better performance than participants living in rural or urban places; in Study Two, participants living in medium-high (but not the highest) densely populated areas were slightly more likely than those living in rural places (very low population density) to have high scores in this task.

No clear variations were noted for delayed recall, in line with the differentiation between short-term verbal processing in the phonological loop (immediate recall) and the integration of long-term information happening in the

episodic buffer which is required in delayed recall suggested by Baddeley and Wilson (2002). This finding may indicate that immediate memory is more stimulated in urban environments, while there is no positive effect on long-term memory, as this is plausibly not directly 'trained' by the sensory stimulation in urban environments that needs to be processed online (e.g. position of other pedestrians, noise of incoming cars) but not retained in long-term memory.

The similarities in the pattern of results between immediate recall and executive functions could be due to the fact that immediate recall is a measure of short-term processing of verbal information, a component of working memory which requires executive control (Baddeley & Wilson, 2002; Duff, Schoenberg, Scott, & Adams, 2005). Neuropsychological studies, however, indicate contrasting evidence on the link between executive functions and short-term verbal and visual memory (Duff et al., 2005; Logie, Cocchini, Delia Sala, & Baddeley, 2004; MacPherson, Sala, Logie, & Wilcock, 2007; Quinette et al., 2003).

To summarise the data on the Coloured Trail Making Test (CTT 2 and CTT Δ), verbal fluency and immediate memory indicate that urban living (and living in more densely populated places) is associated with better cognitive performance. Specifically the data suggest a non-linear pattern which is in line with existing studies indicating a nonlinear relationship between urban land-mix use and prevalence and incidence of dementia and cognitive impairment (Wu et al., 2015; Wu, Prina, et al., 2016), also in line with our hypothesis that increased urbanisation is beneficial for cognitive functioning up to a certain point over which the level of environmental stimulation would become over-loading and therefore detrimental in cognitive terms. This could be associated with an optimal level of complexity presented by the physical environment, i.e., a level of perceptual stimulation which

stimulates cognition without being too challenging (see Chapter 3). This interpretation of the results is however limited by the fact that we did not find significant nonlinear associations between travel time to urban environments (tested by using quadratic terms) and either executive functions or immediate recall in Study Three, while a positive association between shorter distance from urban places and better performance was confirmed for these measures.

In terms of visual memory (Picture memory test), no significant differences based on level of urbanisation were found in the recall task. As this task required a delayed recall of visual information, the absence of variations is in line with that of delayed verbal recall. Small differences in the visual recognition task were noted in Study One, with urban participants showing better performance than the other two groups. However, these variations did not reach significance in the other two studies. The fact that the Picture memory task used in TILDA had only six pictures might have caused it to be an easy task to complete, as for example the participants' recognition performance showed a ceiling effect, and as a consequence can have affected the absence of significant results.

Better performance in terms of global cognitive functioning (MoCA and MMSE) was noted for increased levels of urbanisation both when comparing the urban, rural and "other settlements" groups, and when exploring variations based on travel time from the participant's area of residence to urban places (although of a very small magnitude). These results are in line with the epidemiological literature on geographical variations in dementia and cognitive impairment based on urban vs. rural residence (Bae et al., 2015; Klich-Rączka et al., 2014; Russ et al., 2012), and suggest a general status of better cognitive health in more urbanised areas. We

hypothesised in Study One that the variations emerged for the tests of global cognition could be due to their executive functions components, based on fact that the MoCA has more tasks than the MMSE testing executive functions (Dong et al., 2010; Zadikoff et al., 2008) and that we found stronger differences between areas of residence for MoCA than MMSE (half a score difference between the urban group and the other two for MoCA against approximately a quarter of a score for MMSE). However, previous studies have indicated limitations both in relation to the reliability of the MoCA and the MMSE (Feeney, Savva, et al., 2016) and in relation to identifying a clear cognitive domain structure in the MoCA (Coen et al., 2016), which, together with the absence of the participants' scores in the subtests of each assessment batter, limit clear conclusions on a potential link between MoCA and executive functions in this sample. In addition, we did not find significant variations in these tests based on the level of population density of the area of residence, which limits our conclusions of a possible dose-response effect of characteristics of the built environment on cognition, as found in other studies (Wu et al., 2015; Wu, Prina, et al., 2016).

We found a significant moderating effect of engaging in physical activity on geographical variations in MoCA scores, as described in Study Five: While participants in the urban group showed overall higher engagement in physical activity and higher MoCA scores than the rural group, we noted that physically active rural participants had no different performance from the urban group. Such interaction was not found for MMSE scores, possibly due to the smaller differences between groups of place of residence emerged in the regression models and also to a higher sensitivity of the MoCA (Dong et al., 2010; Nasreddine et al., 2005; Zadikoff et al., 2008). Nonetheless, this result suggests that lifestyle factors play an important

role for general global health status in adult age, as well-established by the literature on cognitive reserve and the association between active lifestyles and better cognitive ageing (Fratiglioni et al., 2004; Küster et al., 2016).

Absentmindedness, a measure of the ability to sustained attention in spite of distractors, and a key skill to successfully carry daily activities in a complex and busy environment, was the only measure of attention which showed significant variations based on urban vs. rural residence and on population density. Similarly to measures of executive functions, we found that participants in urban environments reported a significant lower risk of being absentminded most or all the times than participants in the rural or "other settlements" groups. This pattern was confirmed in the analyses on population density, although significant differences between participants in the least populated areas and the other groups of population density in terms of risk of being absentminded were noted for the Medium-High group (10 to 25 persons per hectare) and Very High group (more than 50 persons per hectare) groups, but not for the intermediate group with High population density (25 to 50 persons per hectare), which does not fully support our hypothesis of an optimal level of complexity for cognition for medium-high levels of urbanisation. It is also worth noting that what is considered high population density for Ireland may be relatively low in comparison with highly urbanised environments worldwide.

No clear patterns of variations emerged in the SART, which has been associated with self-reported measures of attention in previous studies (Robertson et al., 1997). Despite slower responses were noted in the SART for urban participants when compared to the other groups in Study One, this result was however not replicated in either Study Two or Three, and no clear patterns in terms of accuracy

emerged in any study. Assuming the place of residence as a form of long-term exposure to a certain level of urbanisation, the absence of significant results for the SART is in contrast with the existing literature on cognitive restoration which suggests better attentional performance for exposure to natural rather than urban scenes (Berman et al., 2008; Berto, 2005; Gamble et al., 2014). The restorative effects of exposure to natural scenes suggested in the attention restoration theory (ART; Kaplan & Kaplan, 1989; Kaplan, 1995) have been shown mainly in young populations, with very few studies indicating effects in the same direction for older groups (Gamble et al., 2014; Ottosson & Grahn, 2006). While our data does not support these studies, it is instead in line with the recent finding of no restorative effects on the SART of exposure to natural scenes in a healthy sample of individuals aged 60 and older (Cassarino, Tuohy, & Setti, In revision), although a moderating effect of place of residence (urban vs. rural) emerged with rural participants exposed to urban scenes showing faster and less accurate (more impulsive) responses in the task. Whether familiarity with a certain type of environment affects attentional processes remains however to be established. Cross-national studies, for example, have found more defocused attentional strategies in highly urbanised environments (operationalised as more cluttered and complex) when compared to groups living in remote rural areas (Caparos et al., 2012; de Fockert et al., 2011; Linnell et al., 2013), and studies using eye-tracking report more exploratory rather than focused scanning strategies used when viewing urban vs. natural scenes varying in complexity and clutter (Wu et al., 2014). The differences in results with our studies may lie in the older age of our population which can imply a longer residence in a more or less complex environment and therefore a stronger adaptation to the level of

environmental stimulation. Despite our analyses controlled for age, information on the duration of residence would have better supported this type of interpretation.

No variations emerged in terms of speed of processing (Choice Reaction Time Test, Coloured Trail Making Test Part 1). This result is not in line with the hypothesis of a common resource (i.e., cognitive speed) subtending cognitive processing in older age suggested by Salthouse in relation to the CRT (Salthouse, 2004; Salthouse, Hancock, Meinz, & Hambrick, 1996), and by Setti et al. in relation to the CTT (Setti, Loughman, Savva, & Kenny, 2015). Rather, the data seems to suggest that geographical variations in cognitive performance are more likely to appear in a healthy older population for high-level and more complex cognitive skills such as executive functions rather than low-level perceptual processing. One might argue that issues with speed of processing should be more evident in an ageing population which is more at risk of functional decline for example in terms of hearing or vision, but we found no modification effects of age for measures of speed of processing. The correlation between these measures and the performance at the SART (see Table 4.3), and the lack of significant variations in either types of performance, poses the question on whether considering the place of residence at the macro scale of the level of urbanisation is insufficient to highlight environmental effects on attentional processes, and deserves further investigation using measures at the level of the neighbourhood or proximal environment of residence.

In Study One we explored potential moderating effects of childhood place of residence (urban vs. rural) on the association between current place of residence and cognitive performance, to account for potential effects of migration (see p.142 and p.155). Initial analyses (p.142) had indicated that living in an urban environment as a

child (birth to 14 years of age) compensated for the cognitive disadvantage of living in a rural place as an adult in terms of MoCA, verbal fluency and the Coloured Trail Making Test Part 2 (CTT 2), when controlling for all covariates, suggesting lifespan associations between the level of urbanisation of the place of residence and executive functions. However, validity checks using analyses on a larger sample obtained by using current social class rather than income as a measure of socio-economic status in our models (see p.155) confirmed a significant interaction for CTT 2, but not for MoCA or verbal fluency, and indicated potential moderating effects of urban childhood residence for current rural dwellers in terms of delayed recall and CTT Δ. Analyses of interactions between current and past residence were also conducted in the study on population density (Study Two) but they did not show a clear pattern (data not included), likely due to the small number of observations in some of the categories (e.g., only 110 participants had lived in a rural environment as children and were currently residing in areas with very high population density). Similarly, analyses of the interaction between childhood residence and travel time to gateways (Study Three) did not show significant effects (data not included) which was expected given the very small magnitude of the estimates in the regression analyses on the main effects of travel time.

These results, together with the absence of a measure of childhood cognitive performance, as discussed in Study One (see Discussion p. 146), do not allow for clear conclusions on the role of childhood residence. Nonetheless, variations in cognitive functioning based on characteristics of the place of residence in a lifespan perspective deserve further investigation to clarify potential long-term environmental effects as well as causal pathways (e.g., whether cognitive status causes migration as suggested in some studies, or vice versa).

Longitudinal analyses of changes in cognitive performance over a two-period interval based on residence in urban areas, rural places or "other settlements" did not show significant results for any of the measures of interest (MMSE errors, immediate and delayed recall, prospective memory, or fluency). As discussed previously, the short period of time between the two waves of interest, as well as learning effects that emerged for some of the measures, can explain the lack of significant changes, while comparing the cognitive scores over four year intervals (the lag of time between each health assessment in TILDA) might provide more informative results and reduce effects of practice.

Taken together, our findings are in line with our framework (Chapter 2) as well as models and studies discussed in the literature review which suggest that cognitive processing in adult age can benefit from exposure to higher levels of environmental stimulation or environmental enrichment, in this project operationalised as level of urbanisation (Berlyne, 1970; Diamond, 2001; Lawton & Nahemow, 1973; Linnell et al., 2014, 2013; Rapoport & Hawkes, 1970). We found variations mainly in executive functions which, given the young-old and healthy sample, suggest that high-level complex cognitive skills are more susceptible to the level of environmental stimulation than others when individuals are still healthy and independent. However, our findings do not fully support our initial hypothesis of a nonlinear association between levels of environmental stimulation and cognitive performance, and whether this depends on the fact that the most urbanised areas in Ireland (i.e., Dublin) do not reach levels of complexity presented by bigger metropolises remains to be established by future studies. In addition, as discussed above, our results are not in line with attention restoration theory (Kaplan, 1995) which suggests variations in attention based exposure to urban or natural settings.

Considering our model on environmental complexity and cognition (Chapter 3), the slightly different results of our three cross-sectional studies (i.e., variations in some cognitive measures emerged in Study Two or Three had not been shown in Study One) which tested the macro and meso levels of analysis support the idea that the investigation of environmental correlates of cognitive performance should encompass multiple geographical scales. However, additional measures of complexity at the meso and micro level are needed to fully understand which level of environmental stimulation is optimal for cognitive processing in adult age.

Strengths and limitations

The present project had the advantage of using a large nationally representative sample of individuals and of adopting sampling weights to reduce potential selection biases. While large sample size can increase the risk of incurring in false positive results, we proposed multiple operationalisations of urbanisation to support our initial model, including broad urban/rural categories, levels of population density, and a continuous measure of travel time to gateways which we used as a proxy of accessibility to urban environments, and identified a consistent pattern of better performance in executive functions for groups living in more urbanised environments. Although the measures of place of residence were all related to the level of urbanisation, they offered an exploration of the place of residence at different geographical scales. Firstly, by using broad urban/rural categories in Study One, we investigated the macro level of analysis proposed in our model (see Chapter 3) and tested broad urban/rural variations in multiple cognitive skills for a healthy adult population to advance the knowledge about geographical variations in dementia and cognitive impairment shown in the epidemiological literature. Study Two and Study Three used measures of level of urbanisation at the scale of the local

area of residence (electoral division and Small Area unit respectively), testing therefore the meso level of analysis proposed in our model. Considering population density, local areas with high population density are often more resourced and more stimulating than those less densely populated; however, increased levels of population density mean also higher levels of crowding, which has been associated with negative cognitive outcomes (as discussed in Chapter 6). Therefore by comparing local areas of residence ($20km^2$ in size on average) with varying levels of population density (see Table 6.1 for a distribution of electoral divisions with varying population density across urban and rural places) Study Two aimed at testing our hypothesis of a nonlinear association between the level of environmental complexity (operationalised as increasing levels of crowding/resources) and cognitive performance across multiple domains. Lastly, by using travel time to gateways (i.e., urban centres) as a GIS measure of accessibility to more complex environments from the proximal area of residence captured at the level of Small Areas, in Study Three we tested the hypothesis that the distance from a complex environment, rather than the fact of living in a more or less urbanised environment, could affect patterns of variations in cognitive performance.

By exploring multiple measures of cognitive performance across several domains, our studies offered a thorough investigation of the potential impact of urbanisation on cognitive skills in older age which few or no studies have done so far, and which highlighted specific associations between the place of residence and executive functions that deserve further investigation. In addition, thanks to the diverse range of assessments conducted in TILDA, our regression models accounted for a comprehensive set of individual-level covariates and showed that, even after

controlling for confounders, the level of urbanisation of the place of residence had small but significant associations with variations in cognitive performance.

Limitations specific to each study have been described in the Discussion sections of each study presented in this thesis. Our models indicated small effect sizes for measures of place of residence, but these are nonetheless informative because they show that geographical variations in specific cognitive skills can emerge even in a healthy sample of middle-aged and older adults, and could be exacerbated with age to the point of reaching clinical significance. In this sense, our data is to be considered as a first step in the investigation of the impact that urbanisation can have on the potential progression into cognitive chronic conditions.

As discussed in Study One (Chapter 5), the absence of a measure of cognitive performance in childhood limits our ability to rule out the possibility that IQ might have dictated migration patterns towards urban places. However, our analyses of interactions between current and childhood place of residence found different results for specific cognitive domains (executive functions vs. memory) after controlling for socioeconomic covariates (e.g., education) strongly associated with IQ, which supports the idea that the lived environment could impact specific cognitive functions.

Our sample had a higher number of participants in rural rather than urban areas. These differences depend mainly on the higher proportion of rural rather than urban settlements in the specific setting of the study (Ireland), and while the unbalanced number of observations in the categories of our predictor variables might have affected our results, the use of sampling weights enhanced the representativeness of the sample.

The cross-sectional design of the majority of the studies carried in the project does not allow to make conclusions on causality in relation to our results, but it offers an observational insight of geographical variations in cognitive health which could progress into clustered conditions and have clinical relevance, and therefore deserve further investigation, especially in a longitudinal fashion.

Lastly, in accordance with our hypothesis executive functions were significantly associated with place of residence even when correcting for multiple comparisons (conducted for each study separately through Holm method, corrected p = .0001). However, the results on cognitive measures other than executive functions need to be interpreted with caution because nonsignificant after correcting for multiple comparisons

Despite the highlighted limitations, this project contributed to the current knowledge on "age-friendly" environments (World Health Organization, 2007) from a cognitive perspective by indicating that an urban environment may be more supportive than rural areas of high-level cognitive skills such as executive functions, and by showing that geographical variations in these skills can appear relatively early in adult age.

Future directions

The project can be considered as a first step in the investigation of factors that make an environment age-friendly from a cognitive perspective, and our studies showed that macro and meso level geographical variations in specific cognitive skills exist in a healthy adult population, with an interesting pattern of better performance in terms of executive functions for increasing levels of urbanisations. However, these findings need to be developed experimentally at a smaller scale by using specific

operationalisations of complexity which include physical characteristics of neighbourhoods and perceptual features of environmental scenes, in order to test our hypothesis of a nonlinear association between environmental complexity and cognitive health in older age. Specifically, employing more detailed environmental measures at the neighbourhood level, such as presence of green, noise, or street legibility, together with low-level features causing higher or lower perceptual load, will help to test our model more comprehensively and to identify the specific environmental factors supporting better executive functions in adult age. In addition, adopting Bayesian statistics will help to build adequate models of the individual's on-line interaction with the environment.

Qualitative methodologies, including walking interviews and focus groups, will be used to capture individuals' subjective experiences of the impact of the built environment on cognitive and perceptual processing. The findings of qualitative investigations will be integrated with those of the experimental testing adopting a mixed-methods approach in order to have an account of objective and subjective dimensions of environmental complexity. In addition, neurophysiology techniques (e.g., electroencephalography) used both in a laboratory setting and in outdoor ecological settings will provide a better understanding of whether specific neurophysiological responses are associated with interacting with more or less complex environments.

This interdisciplinary approach will provide a comprehensive investigation of factors that make the lived environment more or less cognitive-friendly.

Importantly, longitudinal investigations following the evolution of the observed variations in cognition with increasing age will enable to highlight the

mechanisms through which the built environment can affect cognitive ageing, as well as clarify whether living in a more or less complex environment can cause clinically relevant differences in cognitive functioning.

As practice implications specifically for Ireland, the project calls for lifestyle and cognitive interventions aimed at older people especially in rural areas, in order to compensate for a cognitive disadvantage which is now small but can potentially increase with age. On a more general level, the project and its future developments aim to inform more ecological forms of cognitive interventions using the environment as a source of training. Ultimately, we hope to inform urban design on environmental resources that can be optimised to promote cognitive health in ageing.

Conclusions

The thesis, through an in-depth analysis of the literature provides a theoretical framework for the study of the association between environmental stimulation of cognitive abilities and cognitive ageing, and presents novel empirical evidence to support part of the model (macro and meso scales). The studies conducted as part of this doctoral project indicate a significant positive association between urbanisation and high-level cognitive skills involved in the executive control of our actions, in multi-tasking and dealing with complex information coming from the environment, when controlling for health, lifestyle and other individual-level potential confounders. This association appears to be in line with the hypothesis that living in a complex urban environment can train cognitive skills that are important to deal with the multiple tasks and distractors faced on a daily basis, and to successfully navigate the environment, with implications, for example, for mobility (Donoghue et al., 2012; Donoghue, Dooley, & Kenny, 2016; Merriman,

Whyatt, Setti, Craig, & Newell, 2015; Setti et al., 2011) and for designing healthcare and cognitive interventions tailored to the specific environment of residence (Sisco & Marsiske, 2012). Exploring the impact of urban environments on cognitive skills can contribute to better understand what factors make an environment not only "age-friendly", but also "cognitive-friendly" (Mitchell & Burton, 2006), an issue of growing importance given the demographic changes happening worldwide (World Health Organization, 2007).

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Appendix 1

Results of regression analyses conducted on quintiles of population density and on unweighted data as validity checks for Study Two (Chapter 6)

Regression analyses based on quintiles of population density for the same sample used in the analyses run on the categorical measure of population density confirmed the results on immediate recall, CTT 2 and CTT Δ. Specifically, after controlling for all covariates, participants in areas with medium-high quintiles of population density showed better performance than those living in areas with the lowest quintile of population density for immediate recall (4^{th} quintile: I.R.R. = 1.04, $p < .01$; 5^{th} quintile: I.R.R. = 1.03, $p < .05$), CTT 2 (3^{rd} quintile: b = -4.10, $p < .05$; 4^{th} quintile: b = -5.24, $p < .05$; 5^{th} quintile: b = -4.31, $p < .05$) and CTT Δ (4^{th} quintile: b = -4.35, $p < .01$; 5^{th} quintile: b = -5.20, $p < .01$). No significant effects emerged for absentmindedness.

Regression analyses on the unweighted data for the same sample confirmed the variations in CTT 2 (Group 3: b = -5.49, p = .003; Group 4 = -6.21, p = .002; Group 5 = -6.81, p < .000: Group 6: b = -4.58, p = .04) and CTT Δ (Group 4: b = -4.09, p = .002; Group 5: b = -5.96, p < .000; Group 6: b = -3.48, p = .03), and showed significant differences between the group living in the lowest densely populated area and groups in medium-high populated areas for absentmindedness (Group 4: O.R. = 0.49, p = .001; Group 5: O.R. = 0.64, p = .02; Group 6: O.R. = 0.51, p = .006), while no significant differences where noted for immediate recall.

Appendix 2

Summary of results on geographical variations in cognitive performance

Appendix Table 1

Cognitive Measures with Significant Geographical Variations (indicate by X) across the Studies Conducted

Study	Cognitive measure																	
	MoCA	MMSE	Immediate recall	Delayed recall	Picture recall	Picture recognition	Prospective memory	CRT	CTT 1	SART RT	SART SD	SART Omissions	SART Commissions	Absentmindedness	Fluency	CTT 2	CTT Δ	Visual reasoning
One (Urban-rural)	X	X	X			X				X				X	X		X	
One (larger sample)	X	X	X			X				X					X	X	X	
Two (Population density			X											X		X	X	
Three (Travel time)	X	X		X									X		X		X	
Four (Longitudinal)																		
Five (Residence*IPAQ)	X																	

Note. MoCA = Montreal Cognitive Assessment, MMSE = Mini Mental State Examination, CRT = Choice Reaction Time Test, CTT 1 = Coloured Trail Making Test Part 1, SART = Sustained Attention to Reaction Task (RT = reaction times in seconds; SD = standard deviation from mean reaction times), CTT 2 = Coloured Trail Making Test Part 2, CTT Δ = Coloured Trail Making Test Part 2 minus Part 1.