LIFETIME DIET AND COGNITION

IN OLDER PEOPLE

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Abstract

Dietary intake may impact upon the trajectory of older-age cognitive change and decline via nutritional mechanisms that contribute to brain health and functioning, and to the risk of chronic diseases associated with poorer late life cognitive outcomes.

Diet is a modifiable environmental exposure. As such, it provides an avenue for intervention to promote better cognitive functioning and delay or prevent cognitive impairment and dementia that are placing an increasing burden on older individuals, their families and the health system.

The majority of studies that have investigated the nutritional determinants of healthy cognitive ageing have done so within populations older than 65, but the long-term aetiology of cognitive change extends years and even decades prior to the onset of noticeable decline. Thus, the salience of diet to an individual's cognitive ageing trajectory is likely to extend back into the life-periods prior to older age. Even the longest prospective studies do not have dietary records extending over the lifetime; therefore, determining the relationship, if any, between earlier-life diet and later-life cognitive health requires an alternate approach to gathering lifetime dietary data.

The objective of this thesis was to develop a retrospective dietary reporting instrument to measure intake from multiple life-periods, then to investigate cross-sectional and longitudinal associations between lifetime diet and cognitive performance in cognitively healthy older-adults.

Studies 1 to 3 investigated the reliability and validity of the Lifetime Diet Questionnaire (LDQ); the dietary assessment instrument developed in the context
of the thesis to measure past diet. Study 1 was a preliminary study of dietary recall using the foods and frequencies of the LDQ. The strength of associations was tested between young adults’ (n=203) recall of earlier adolescent diet, and one or more family members’ recall of the same individual’s diet over the same period. Study 2 assessed the test-retest reliability of LDQ’s five life-periods in older adults (n=51). Both measures of reliability fell within acceptable limits. In Study 1, the average association between family members recall of an individual’s past intake was 0.73, while in Study 2, the average test-retest reliability of the questionnaire across all life-periods in an older sample was 0.81. Study 3 (n=352) recruited participants from the EPOCH trial (a randomised controlled trial of Omega-3 fish oil on older-age cognitive change). The validity of long-term dietary recall was investigated by testing the associations between lifetime dietary patterns extracted from the LDQ, and the EPOCH participants’ demographic and cardiovascular health variables. Lifetime dietary patterns were related to the demographic variables of age, sex, education, income, parental background, and childhood physical activity; patterns from childhood and adulthood also predicted cardiac medication use and cholesterol level in older age.

Studies 4 and 5 used the same cohort to examine the relationships between LDQ dietary patterns and cross-sectional cognitive performance (Study 4) and 18-month cognitive change over 4 time points (Study 5). After controlling for relevant covariates and current dietary intake, all dietary patterns from the childhood period predicted baseline level of cognitive performance, and a ‘non-traditional Australian’ pattern in middle age predicted 18-month cognitive change.

These preliminary findings have implications for the relevance of diet as a lifetime determinant of older-age cognitive health.
Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Diane Hosking and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Diane Hosking

30th September 2013

Publications:


Under review:
This thesis is dedicated to my parents

Katrina and Kevin,

and children

Therese, Rachel, and John
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I would like to thank my supervisors, Dr Vanessa Danthiir, Professor Ted Nettelbeck, and Professor Carlene Wilson for the opportunity to undertake this PhD in the context of the EPOCH trial, a randomised controlled trial of Omega-3 fish oil on older-age cognitive change.

The EPOCH trial was designed by Vanessa as a collaborative project between the University of Adelaide and CSIRO Animal Food and Health Sciences. Vanessa was responsible for the implementation and analysis of the extensive cognitive test battery that formed the outcome measures for the both the trial and this thesis; her expertise and specific contribution in this regard are especially acknowledged.

I was fortunate to have had access to extensive demographic, health and lifestyle data from the project, and my thanks go to all members of the EPOCH team for their contribution; in particular, Eva Calvaresi, Chloe Mount, Donna Hughes, and Julie Syrette. A heartfelt thank you, also, to Kylie Lange for statistical advice.

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### Abbreviations

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<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AA</td>
<td>Arachidonic acid</td>
</tr>
<tr>
<td>AD</td>
<td>Alzheimer's Disease</td>
</tr>
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<td>ADNI</td>
<td>Alzheimer's Disease Neuroimaging Initiative</td>
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<tr>
<td>AIBL</td>
<td>Australian Imaging Biomarker and Lifestyle Study</td>
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<tr>
<td>ALA</td>
<td>Alpha-linolenic acid</td>
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<tr>
<td>ALSPAC</td>
<td>Avalon Longitudinal Study of Parents and Children</td>
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<td>ApoE</td>
<td>Apolipoprotein</td>
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<tr>
<td>AR1</td>
<td>First-order autoregressive covariance structure</td>
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<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>CCFFQ</td>
<td>Cancer Council Food Frequency Questionnaire</td>
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<tr>
<td>CES-D</td>
<td>Centre for Epidemiological Studies Depression scale</td>
</tr>
<tr>
<td>CFA</td>
<td>Confirmatory Factor Analysis</td>
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<tr>
<td>CHAP</td>
<td>Chicago Health and Aging Project</td>
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<tr>
<td>C-PIB</td>
<td>Carbon-labelled Pittsburgh Compound-B</td>
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<tr>
<td>DHA</td>
<td>Docosahexaenoic acid</td>
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<tr>
<td>EFA</td>
<td>Exploratory Factor Analysis</td>
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<tr>
<td>ELSA</td>
<td>English Longitudinal Study of Ageing</td>
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<tr>
<td>EM</td>
<td>Expectation Maximization</td>
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<tr>
<td>EPA</td>
<td>Eicosapentaenoic acid</td>
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<tr>
<td>EPOCH</td>
<td>Older People, Omega-3, and Cognitive Health</td>
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<tr>
<td>FFQ</td>
<td>Food Frequency Questionnaire</td>
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<tr>
<td>fMRI</td>
<td>Functional Magnetic Resonance Imaging</td>
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<td>FSR</td>
<td>Framingham Stroke Risk profile</td>
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<tr>
<td>Gc</td>
<td>Crystallised ability</td>
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<td>Gf</td>
<td>Fluid ability</td>
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<tr>
<td>HDL</td>
<td>High Density Lipoprotein</td>
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<tr>
<td>ICC</td>
<td>Intra-class correlation coefficient</td>
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<tr>
<td>IGC</td>
<td>Individual Growth Curve</td>
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<tr>
<td>kcal</td>
<td>Kilocalorie</td>
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<tr>
<td>LA</td>
<td>Linoleic acid</td>
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<tr>
<td>LBC-1921</td>
<td>The Lothian Birth Cohort of 1921</td>
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Abbreviations (continued)

LC-PUFA  Long-chain polyunsaturated fatty acid
LDL     Low Density Lipoprotein
LDQ     Lifetime Diet Questionnaire
LSADT   Longitudinal Study of Aging in Swedish Twins
MAR     Missing at Random
MCAR    Missing Completely at Random
MCI     Mild Cognitive Impairment
MeDi    The Mediterranean Diet
MMSE    Mini Mental State Examination
MRC-NHSHD The Medical Research Council National Survey of Health and Development
OLS     Ordinary Least Squares
P&P      Paper and Pencil
PET      Positron Emission Tomography
RAVLT   Rey-Auditory Verbal Learning Test
ROS     Reactive oxygen species
SATSA   Swedish Adoption Twin Study of Aging
SEM     Structural Equation Model
SLS     Seattle Longitudinal Study
UN      Unstructured covariance structure
VIF     Variance Inflation Factor
VLSA    Victoria Longitudinal Study of Aging
WHICAP  Washington Heights-Inwood Columbia Aging Project
WMH     White Matter Hypertensities
WML     White Matter Lesions
YPAS    Yale Physical Activity Scale
The objective of this thesis was to develop an assessment instrument that measured lifetime dietary intake and investigate its associations with cognitive performance in cognitively healthy older adults. The thesis presents five studies; Study 2, Study 3, and Study 4 are publications that are flanked by the unpublished results for Study 1 and Study 5.

Change and decline in cognitive abilities inevitably accompany ageing. Identifying modifiable environmental exposures that predict better cognitive functioning in older people potentially contributes to reducing the risk of decline and dementia that undermine quality of life for the rapidly increasing older proportion of the population. Dietary intake is one such exposure that potentially influences older-age cognitive status via nutritional mechanisms that support brain health and functioning, and by influencing the risk of chronic diseases that in turn predict poorer cognitive outcomes in older age.

A serious impediment to understanding the role of dietary intake in older-age cognitive health is the long-term aetiology of cognitive change; this applies regardless of whether the outcome is 'normal' age-related decline, or pathological decline and dementia. The antecedents of an individual’s cognitive ageing trajectory are the result of numerous genetic and environmental interactions that reach back across the lifetime and even prenatally (Benton, 2010b). Therefore, it is likely that any dietary impact on later life cognition is the product of a lifetime’s intake.

Due to logistic constraints, the majority of research that examines associations between diet and older-age cognitive performance has utilised a
measure of diet in later life, and at one time-point only. In the minority of studies that have assessed diet at multiple time points, the period between assessments was relatively short in comparison to the decades that comprise lifetime dietary exposure.

The current investigation between recalled lifetime diet and cognitive functioning was carried out in a sample of older adults participating in the EPOCH trial (Danthiir, Burns, Nettelbeck, Wilson, & Wittert, 2011), an 18-month randomised controlled trial of omega-3 fish oil on older-age cognitive functioning. These participants were screened for dementia and medical conditions known to impact on cognitive functioning; so decline, if any, occurring over the period of the trial would be within the context of normal ageing. It is important to emphasise that although the research for this thesis was performed in a non-clinical population, the potential findings are relevant to informing prevention strategies for pathological cognitive ageing. Indeed, the assessment of cognitive performance and cognitive change in populations without evidence of impairment is an important approach in the prevention of dementia (Sperling et al., 2011). It has been demonstrated in numerous prospective studies that those who later develop Alzheimer’s disease consistently perform more poorly on cognitive tests during the prior dementia-free period from many years earlier (Elia et al., 2000; Twamley, Ropacki, & Bondi, 2006). Thus, the identification of modifiable environmental factors (in this case past dietary intake) that predict differential cognitive outcomes offer potential pathways for prevention, or at least delay of the debilitating clinical symptoms of dementia and decline (Singh-Manoux & Kivimäki, 2010).
It will be apparent that the thesis scope is broad and crosses the boundaries of a number of research disciplines including psychology, nutrition, neuroscience, and both life-course and nutritional epidemiology. What constitutes assumed knowledge in one discipline is not necessarily well recognised in another. For the sake of clarity, an overview of the thesis structure follows and some contextual background to its content is provided.

The thesis is presented in three sections. Section A is the literature review comprising three chapters. Chapter 1 commences with an overview of cognitive ability measurement and the methodological issues inherent in determining if and when cognitive decline occurs in normally functioning adults. The chapter then draws on a broad spectrum of research to demonstrate that individual differences in the cognitive ageing trajectory are determined by genetic, environmental, and health factors that operate across the lifetime to affect later life cognitive functioning. These factors theoretically may act as moderators or mediators in any potential relationship between lifetime intake and cognition, so some explanation of their relevance to cognitive ageing is appropriate. Additionally, a number of variables representing these factors were used as covariates in subsequent analyses.

The chapter concludes with a discussion of the ‘brain reserve’ heuristic as a mechanistic explanation for cognitive ageing, and consequently promotes a life course approach to identify the determinants of healthy cognition in older age. Thus, the context is created for assessing the contribution of a lifetime’s exposure

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1 Nutritional intake is one of these factors, but it is not addressed at this point; its particular long-term relevance to cognition will be discussed in chapter two of the literature review.
to any potential environmental predictor of individual differences in older-age cognitive outcomes.

Chapter 2 focuses specifically on the nutritional aspect of the thesis. Adequate early-life nutritional intake is essential for normal brain growth and cognitive development. If nutritional deprivation impacts on the development of cognitive ability during childhood, which also predicts later-life cognitive status, then a strong rationale is evident for the need to assess diet from early-life periods when evaluating the impact of dietary intake on later-life cognition. Therefore, the first part of the chapter outlines theoretical evidence for the essential role of nutrients to early-life cognitive development. Nutrient mechanisms are also relevant to brain ageing and underpin the hypothesised role for nutritional intake as a buffer against age-related decline (Gómez-Pinilla, 2008; Uauy & Dangour, 2006). The nutritional influences on brain ageing will be discussed focusing on those nutrients that are hypothesised to have particular relevance.

The potential impact of diet on cognitive ageing has led to an explosion of studies with divergent designs, predictors, and outcomes, but with a common underlying aim of demonstrating whether what we eat can lessen the growing burden of cognitive impairment in an ageing population. The majority of such studies assess the nutritional or dietary intake of participants who have already reached older age; but the focus of this thesis is the potential impact of dietary intake from life periods prior to old age. Consequently, an overview of findings is presented from the very few studies that have examined the effect of diet from an earlier time period on older age cognition.

As stated, the objective of the thesis was to examine the potential influence of diet from across the whole life time on older-age cognition. To achieve this aim,
it was necessary to assess dietary intake from many decades earlier. Chapter 3 discusses approaches to past dietary recall and the methodological issues and limitations that need to be acknowledged and addressed.

The validity, and consequently the utility of long-term dietary recall are controversial. Section B of the thesis consists of studies one to three, presented as individual chapters that test the reliability and validity of lifetime dietary recall as assessed by the newly developed LDQ.

Study 1 used a sample of convenience from the University of Adelaide to test the inter-rater reliability of the questionnaire for the long term recall of foods using the frequency options of the LDQ. Study 2 recruited participants from the Adelaide Ageing and Cognitive Change Study and assessed test-retest reliability of lifetime dietary recall for each of the five life-periods of the questionnaire (Hosking, Danthiir, Nettelbeck, & Wilson, 2011). The questionnaire’s utility as a dietary assessment instrument was investigated in Study 3 (Hosking & Danthiir, 2013). In this study a subsample from the EPOCH trial (Danthiir, V. et al., 2011) completed the LDQ. Exploratory factor analysis extracted theoretically plausible dietary patterns for each life period. Associations were then examined between these dietary patterns and the demographic and cardiovascular health variables from the EPOCH cohort. The aim was to test whether dietary intake, as assessed by the LDQ, predicted these variables in a manner commensurate with the established relationships in the literature between diet and both demographics, and health outcomes.

Section C of the thesis consists of studies 4 and 5, together with a concluding discussion. These two studies aimed to fulfil the overarching objective of the thesis by examining whether recalled lifetime dietary intake predicted older-
age cognitive performance after controlling for relevant covariates. Study 4 (Hosking, Nettelbeck, Wilson, & Danthiir, 2013) assessed cross-sectional associations between the lifetime dietary patterns from the LDQ and the comprehensively assessed cognitive outcomes of the EPOCH trial. Study 5 tested whether lifetime dietary patterns predicted cognitive change over 18-months using the cognitive outcomes from the four time points of the trial.