Psychiatry Research: Neuroimaging 247 (2016) 65–70

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Review article

Cerebral correlates of cognitive reserve

Lawrence J Whalley [a,b,*], Roger T Staff [a,c], Helen C Fox [a], Alison D Murray [a]

[a] Aberdeen Biomedical Imaging Centre, College of Life Sciences and Medicine, University of Aberdeen, Aberdeen AB25 2ZD, UK
[b] Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK
[c] NHS Grampian, Foresterhill, Aberdeen, UK

ARTICLE INFO

Article history:
Received 9 October 2015
Accepted 13 October 2015
Available online 19 October 2015

Keywords:
Cognitive reserve
Childhood IQ
White matter hyperintensities
Functional MRI
Cortical complexity
Structural equation model
Cognitive aging
Alzheimer's disease

ABSTRACT

Cognitive reserve is a hypothetical concept introduced to explain discrepancies between severity of clinical dementia syndromes and the extent of dementia pathology. We examined cognitive reserve in a research programme that followed up a non-clinical sample born in 1921 or 1936 and IQ-tested age 11 years in 1932 or 1947. Structural MRI exams were acquired in about 50% of the sample from whom a subsample were recruited into an additional fMRI study. Here, we summarise findings from seven inter-related studies. These support an understanding of cognitive reserve as a balance between positive life course activity-driven experiences and the negative effects of brain pathologies including cerebrovascular disease and total and regional brain volume loss. Hypothesised structural equation models illustrate the relative causal effects of these positive and negative contributions. Cognitive reserve is considered in the context of choice of interventions to prevent dementia and the opposing effects of cerebrovascular disease and Alzheimer like brain appearances.

Contents

1. Introduction . . . 65
1.1. Cerebral correlates . . . 66
1.2. Cognitive reserve . . . 66
2. Methods . . . 66
2.1. The Aberdeen birth cohort studies . . . 66
3. The studies . . . 66
3.1. Cognitive reserve and brain volume . . . 66
3.2. Intelligence, cognitive reserve and brain aging . . . 66
3.3. An fMRI study of successful cognitive aging . . . 67
3.4. Cortical complexity and cognitive aging . . . 67
3.5. Childhood socioeconomic status influences adult hippocampal size . . . 67
3.6. Is there a balance between cognitive reserve, cerebrovascular disease and Alzheimer's disease? . . . 69
3.7. Do childhood socioeconomic circumstances influence the occurrence of brain hyperintensities? . . . 69
4. Comment . . . 69
Acknowledgements . . . 70
References . . . 70

1. Introduction

Population trends in age structure accelerated rapidly throughout the 20th century. As numbers of old people increased, so concerns grew that diseases associated with aging would increase in prevalence and potentially jeopardise health care provisions for the elderly. Dementia is a major cause of disability and death affecting about 5% of all those over age 65 years and about 20% of those aged 85 years or more. Although recent reports of falling prevalence of dementia give rise to cautious optimism that

* Corresponding author at: Aberdeen Biomedical Imaging Centre, College of Life Sciences and Medicine, University of Aberdeen, Aberdeen AB25 2ZD, UK.
E-mail address: l.j.whalley@abdn.ac.uk (L. Whalley).

http://dx.doi.org/10.1016/j.pscychresns.2015.10.012
0925-4927/

dementia may prove somewhat less of a burden on health services, effective dementia prevention strategies remain a major priority in the 21st century.

Disappointed by the results of recent trials of anti-amyloid therapies in Alzheimer's disease (AD), alternative approaches to dementia prevention are now widely discussed. Attention has turned to possible explanations of decreased AD prevalence detected in surveys in Sweden (Qiu et al., 2013) and England (Matthews et al., 2013) and comparable data from Holland and the US. From these reports, two broad themes emerged. The **first** concerns comparisons between recent reduced dementia prevalence and established downward trends in heart-disease and stroke (McGovern et al., 1996; Soros et al., 2012). The **second**, draws on reports of the benefits for cognitive aging and possible dementia protection that can be linked to lifestyles that are cognitively demanding, socially engaged and physically active (Angevaren et al., 2008; Fratiglioni and Qiu, 2011; Barnes et al., 2013).

In this review, we describe our approach to the concept of cognitive reserve. Our aim is to make tractable the investigation of cognitive reserve with the intention of identifying those components that could enhance its protective or compensatory potential and inform the design of studies to prevent or delay dementia onset.

1.1. Cerebral correlates

The cerebral cortex is a complex layered and much folded bilateral structure that makes up the cerebral hemispheres. Age-related changes in the cerebral cortex are multi-factorial and affect neurones and glia, the cerebral vasculature and the white matter tracts. In life, these changes are detectable using advanced brain imaging techniques that accurately measure brain structures, vascular pathologies (including small vessel disease) and regional brain metabolic differences. Our studies on cognitive reserve have largely relied on structural magnetic resonance imaging (MRI) and, to a much lesser extent, functional MRI (fMRI) to reveal differences in blood oxygen level detection (BOLD) responses in comparisons between experimental conditions.

1.2. Cognitive reserve

Quantification of cognitive reserve depends upon the precise measurement of cognitive performance. A wide range of cognitive domains makes up overall cognitive function and shares common variance (a general factor 'g') that explains the extent to which domains are inter-correlated. In our studies we have selected a small number of standardised cognitive tests that capture verbal learning (auditory verbal learning test, AVLT) and spatial ability (Block Design, BD); non-verbal reasoning, Raven's Standardised Progressive Matrices (RPM); mental speed (Digit Symbol, DS) and verbal fluency (Guilford's Uses of Common Objects). Baseline childhood IQ was taken from historical records of testing of children using the Moray House Test (Deary et al., 2009). Age-related cognitive change was estimated from the difference between observed current cognitive performance in late adulthood and cognitive performance predicted from Moray House Test scores converted to standard IQ-type scores (mean 100, standard deviation 15). It was hypothesised that cognitive reserve would be a major positive influence on individual differences between observed current cognitive performance and expected performance predicted by childhood IQ. Negative influences include age-related brain pathology (brain atrophy and brain lesion load thought to be of cerebrovascular origin).

2. Methods

2.1. The Aberdeen birth cohort studies

Since 1998, we have followed up local community residents who at age about 11 years were at school in Aberdeen and sat a group-administered IQ-type test. Full details are given elsewhere (Whalley et al., 2011). Briefly, the Aberdeen birth cohort studies were started in 1998 when Scottish Mental survey archives of the Scottish Council for Research in Education were re-discovered and permissions obtained to follow-up survivors born in 1921 or 1936 and then aged about 77 or 64 years and who had entered (or were about to enter) the age of greatest risk for Alzheimer's disease (AD). Sources of attrition from the study, exposures to childhood adversity, nutritional, genetic and life style factors of possible relevance to extent of age-related cognitive decline and the timing of onset of dementia are given elsewhere (Whalley et al. 2011). By 2014, the feasibility of following up more than 75% of Scottish Mental Survey survivors living in the Aberdeen area without dementia was well-established, dementia ascertainment to age about 88 years was completed in the 1921 birth cohort and was underway in the 1936 born cohort (by then aged about 78 years). Structural MRI exams were introduced in 2001 and, by 2008, about 50% of the total sample of 791 participants has undergone at least one MRI. These databases are available to other bone fide research groups wishing to test specific hypotheses that may either replicate their own findings or make best use of the data collected in the Aberdeen studies (contact a.d.murray@abdn.ac.uk).

3. The studies

3.1. Cognitive reserve and brain volume

In our first investigation into the concept of cognitive reserve, we explored the possibility that reserve was influenced by head size (as a proxy for lifetime maximum brain size), duration of education, and occupational attainment in 92 volunteers born in 1921 and whose childhood IQ age 11 years was available. We performed neuropsychological tests of verbal memory, spatial ability, non-verbal abstract reasoning, verbal fluency and mental speed at age about 79 years and within 3 months conducted MRI exams. The fraction of total intracranial volume occupied by brain at age 79 years was used as a measure of brain shrinkage (atrophy) and density of white matter hyperintensities as a measure of cerebrovascular disease (burden). The results showed that education and occupational attainment but not total intracranial volume (a proxy for maximum brain size) contribute in this preliminary study to retention of cognitive performance from age 11 to 79 years (Staff et al., 2004). Because we had baseline childhood IQ scores, we could adjust age 79 cognitive test scores for baseline and use general linear modelling of covariance to test cognitive reserve hypotheses. Separate models were tested for verbal memory and non-verbal reasoning. The simplest model of cerebral reserve is that it is a **passive** property that protects the individual from age-related cognitive decline. This line of reasoning implies that a person with a larger brain is capable of withstanding a greater degree of age-related pathology and would decline less than a person with a smaller brain. An **active** model of cognitive reserve can be tested in a similar way after adding education as a likely contributor to verbal memory but not to non-verbal reasoning. These models of active and passive reserve were first suggested by Stern (2002).

3.2. Intelligence, cognitive reserve and brain aging

In a later analysis, using the same MRI data, and after accounting for childhood IQ, we explored relationships between specific cognitive domains, the general factor ('g') that explained variance shared between test and brain volumes. We hypothesised that brain aging would be correlated with non-uniform reductions in brain volumes and that these would be associated with scores on specific cognitive tests (Staff et al., 2006). As predicted, we found links between specific cognitive tests and brain volumes. An