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Brief communication

Lifestyle activities in mid-life contribute to cognitive reserve in late-life, independent of education, occupation, and late-life activities

Dennis Chan [a,*], Meredith Shafto [b], Rogier Kievit [b], Fiona Matthews [c], Molly Spink [b], Michael Valenzuela [d,e], Cam-CAN, Rik N. Henson [b]

[a] Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK
[b] MRC Cognition and Brain Sciences Unit, Cambridge, UK
[c] Faculty of Medical Sciences, University of Newcastle, Callaghan, Australia
[d] Brain and Mind Centre, University of Sydney, Sydney, Australia
[e] School of Medical Sciences, Sydney Medical School, University of Sydney, Sydney, Australia

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ABSTRACT

This study tested the hypothesis that mid-life intellectual, physical, and social activities contribute to cognitive reserve (CR). Two hundred five individuals (196 with magnetic resonance imaging) aged 66–88 years from the Cambridge Centre for Ageing and Neuroscience (www.cam-can.com) were studied, with cognitive ability and structural brain health measured as fluid IQ and total gray matter volume, respectively. Mid-life activities (MAs) were measured using the Lifetime of Experiences Questionnaire. Multivariable linear regression found that MAs made a unique contribution to late-life cognitive ability independent of education, occupation, and late-life activities. Crucially, MAs moderated the relationship between late-life cognitive ability and brain health, with the cognitive ability of people with higher MA less dependent on their brain structure, consistent with the concept of CR. In conclusion, MAs contribute uniquely to CR. The modifiability of these activities has implications for public health initiatives aimed at dementia prevention.

1. Introduction

1.1. Participants, materials, and analyses

The concept of cognitive reserve (CR) is used to explain why some individuals maintain cognitive ability despite impaired brain health as a consequence of aging and diseases such as Alzheimer's disease (Nilsson and Lövdén, 2018; Stern, 2012). Crucially, the CR concept encompasses the notion that late-life cognitive activity is influenced by factors occurring earlier in life. Determination of contributors to CR is therefore important for "successful" aging and prevention of dementia. While epidemiological evidence suggests that education and occupation contribute to CR (Richards and Deary, 2005), there is an increasing interest in the additional contribution of other activities undertaken in mid-life, given their potential modifiability. This interest is amplified by evidence that mid-life activities (MAs) of a social or intellectual nature are associated with higher late-life cognitive ability, after adjusting for childhood cognitive ability (Gow et al., 2017), and by a recent review concluding that low levels of physical and social activity in adulthood represent key risk factors for dementia (Livingston et al., 2017).

Rigorous definitions of CR not only predict that lifestyle factors will relate to late-life cognitive ability, but also that such factors will moderate the relationship between cognitive ability and brain structure. Specifically, the cognitive ability of individuals with high CR should be less dependent on brain structure than those with low CR, possibly as a result of compensatory functional network reorganization (Stern, 2017, see also; Nilsson and Lövdén, 2018). The present study therefore asked whether MAs contribute to CR by testing 2 hypotheses: (1) MAs contribute to late-life cognitive ability independent of early-life education, mid-life occupation, and late-life activities; and (2) MAs moderate the relationship between cognitive ability and brain structure, such that the relationship is weaker in people with who had engaged in more MAs.

* Corresponding author at: Herchel Smith Building for Brain and Mind Sciences, University of Cambridge, Robinson Way, Cambridge, CB2 0SZ, UK. Tel.: +44 1223760696.
E-mail address: dc598@cam.ac.uk (D. Chan).

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Two hundred five individuals (93 female) aged 66–88 years were selected from the Cambridge Centre for Ageing and Neuroscience (Cam-CAN, www.cam-can.com, Shafto et al., 2014) cohort (see Supplementary Materials for further description of this sample). Cognitive ability was measured using the Cattell Culture Fair test of fluid intelligence (Cattell, 1971) and lifestyle activities by the Lifetime of Experiences Questionnaire (LEQ, Valenzuela and Sachdev, 2007), modified for UK participants.

The LEQ measures a broad range of cognitively stimulating experiences and activities during 3 life phases: youth, 13–29 years; mid-life, 30–64 years; and late-life, 65 years onward. Within each phase, activities are subdivided into specific or nonspecific. Specific activities are those that are considered to be undertaken primarily within 1 particular life phase, such as education or working occupation. By contrast, nonspecific activities such as socializing and playing sports are those can be undertaken at any age, and so are applicable to any life phase. The youth specific score (YS, or education) was derived from the UK's National Career Service categories, multiplied by number of years at each category. The mid-life specific score (MS, or occupation) was based on the standard occupational classification codes from the UK Office of National Statistics, summed across 7 mid-life periods. The late-life specific score (LS, or postretirement activities) reflected social and intellectual activities such as travel or participation in volunteer organizations. The current LEQ does not cater for some "specific" activities being undertaken at other life stages (e.g., education in mid- or late-life) and so their potential contribution to CR could not be evaluated in the present study.

Scores for nonspecific activities in youth, mid-life (MA), and late-life were summed across 7 questions about social, intellectual, and physical activities. These addressed participation in (1) travel, (2) social outings, (3) playing a musical instrument, (4) artistic pastimes, (5) physical activity (mild, moderate, vigorous), (6) reading, and (7) speaking a second language. Each of the 6 resulting scores (2 types of activity, specific and nonspecific, across the 3 life phases) was scaled to a score from 0 to 10.

T1- and T2-weighted 1 mm isotropic magnetic resonance imaging scans were available for 196 participants. Brain structure was measured in terms of total gray matter volume (TGM, see Taylor et al., 2017 and Supplementary Materials). Two participants with outlying adjusted TGM values were removed. The analysis used linear regression via the "lm" function in R 3.5.0 (R Core Team, 2016) to relate Cattell scores to the 6 LEQ scores above, plus age and sex. Data and analysis scripts are available on the Open Science Framework here: https://osf.io/32gme/, which includes individual scores for the 13 LEQ questions that comprise the MA sum score.

2. Results

The covariance and correlation of Cattell, LEQ scores and age are shown in a Supplementary Table (Supplementary Materials). All LEQ scores were significantly positively correlated with each other, and with Cattell.

Multivariable regression of late-life cognitive ability on the LEQ scores, with age and sex as covariates, showed a strong overall association (adjusted $R^2 = 0.355$, F (8196) = 15.0, $p < 0.001$). In addition to the expected negative effect of age, the coefficients in Table 1 revealed a unique, positive contribution of YS (i.e., education), replicating previous studies such as Richards and Deary (2005). More interestingly, midlife nonspecific activities (MAs) also made an independent positive contribution after adjustment for all other factors. No other LEQ-based category, including the current late-life activities being performed by the individuals (reflected in both LS and late-life activities), made an independent contribution. After adjusting for age and sex, separate regression of MA on cognitive ability revealed an effect size of $R^2 = 16.0$, comparable to that for YS (education, $R^2 = 15.8\%$).

Table 1
Results of multivariable linear regression of late-life cognitive ability (Cattell) against 6 lifetime experience scores from the LEQ, plus age and sex

Variable	Coefficient	Standard error	*p*-value (df = 196)
Young specific activities	+0.465	0.128	**<0.0001**
Young nonspecific activities	+0.079	0.222	0.723
Mid-life specific activities	+0.218	0.156	0.164
Mid-life nonspecific activities	+0.989	0.229	**<0.0001**
Late-life specific activities	+0.343	0.214	0.110
Late-life nonspecific activities	−0.347	0.266	0.195
Age	−0.297	0.061	**<0.0001**
Sex	−1.00	0.781	0.201

Key: LEQ, lifetime of experiences questionnaire.
Bold values indicate a level of significance of $p < 0.05$.

To examine whether MAs contributed not just to late-life cognitive ability but also to CR, rigorously defined, we determined whether MAs moderated the relationship between late-life cognitive ability and brain structure (as indexed by TGM). We first adjusted Cattell and TGM scores for (1) education (YS score), (2) total intracranial volume to correct for interindividual differences in head size, (3) age, and (4) sex. Linear regression showed an interaction between TGM and MA in predicting Cattell (normalized interaction coefficient = −0.722, standard error = 0.331, $p = 0.030$). This moderating term was negative, meaning that the relationship between cognitive ability and brain health diminished with higher MA, as predicted by CR theory. This effect is visualized in Fig. 1, where a median split is used to divide participants into low and high MA groups: a more positive slope can be seen in the low MA group than in the high MA group.

3. Discussion

This study tested the hypothesis that lifestyle activities in midlife contribute to the CR that supports cognitive ability in late-life. Consistent with this, we found that general MAs make an

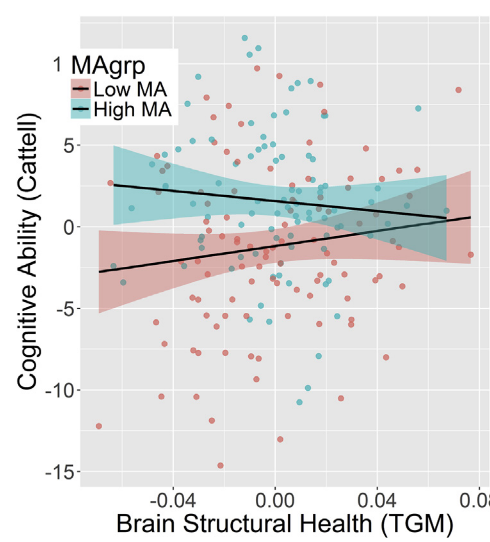

Fig. 1. There was a significant interaction between brain health (total grey matter volume, TGM) and MA in predicting cognitive health (Cattell), such that cognition in the High MA group was less dependent on brain structural health, in keeping with the concept of cognitive reserve.