Testing the cerebral reserve hypothesis in a unique cohort of elderly people

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Synopsis

The cerebral reserve hypothesis proposes that the contribution of a given amount of brain pathology to intellectual decline is modified by the extent of 'cerebral reserve'. Theoretical mediators of such reserve are larger brain size and higher intellectual attainment. This study uses childhood intelligence at age 11, MR imaging and intelligence at age 79 to test the reserve hypothesis and whether this is implemented by passive (brain reserve) or active (cognitive reserve) models. The results show that head size is independent of cognitive decline whereas those with greater levels of educational and occupational attainment decline less.

Introduction

Systematic surveys suggest no direct relationship between the extent of brain pathology and the severity of clinical manifestation of such damage (1). There are individual differences in the retention of intellectual ability in the presence of cerebral pathology sufficient to account for cognitive decline. The concept of 'cerebral reserve' was introduced to explain these individual differences. The distinction between passive and active models of 'cerebral reserve' was introduced in a recent review (2). The passive model proposes that larger brain size is protective as there are a greater number of neurons and/or synapses that can be damaged before a clinical threshold is reached. The active model proposes that the brain actively compensates for damage either by having cognitive strategies that are resistant to damage or by recruiting new neuronal networks. If the passive model is true, one would expect that, other factors being equal, those with bigger brains would demonstrate less cognitive decline for a given amount of brain pathology than those with smaller brains. If the active model is true, one would expect that those with greater levels of intellectual attainment to show less cognitive decline. These models are tested in a unique cohort of elderly subjects for whom we have prior measures of intellectual ability.

Methods

Subjects The Aberdeen 1921 Birth Cohort is a sub-sample of survivors of the Scottish Mental Survey of 1932 (3). This survey measured the intelligence of all 11 year old children attending school in Scotland on 1st June 1932 using the Moray House Test (MHT), a valid test of verbal reasoning, numerical and spatial abilities. 59 survivors have undergone repeat MHT are part of a longitudinal study of brain MRI and cognitive ageing. Number of years of education and occupational complexity on a scale of 1-9 (with 9 being the most complex) were recorded for each subject as proxies of active (cognitive) reserve.

MRI Subjects underwent brain MRI on a 1T Siemens Impact (Erlangen, Germany) using a T1W volumetric sequence (TR 11.4ms, TE 4.4ms, FA 15°, TA 6m 7s), that was used to calculate brain volume measures, and T2W sequence (TR 4000ms, TE 96ms, TA 1m 53s), that was used for scoring of white matter lesions.

Image analysis T1W volumetric data was analysed using SPM 99 (Wellcome Department of Cognitive Neurology, London, UK) and segmented into grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF) after correction for field non-uniformity. The total intracranial volume (TICV) was calculated as the sum of the GM, WM and CSF. The brain fraction (BF) was calculated as the ratio of GM and WM to the TICV. This ratio has previously been used to estimate whole brain shrinkage (4). TICV is used as a proxy for brain size before the onset of neuropathology, thus passive (brain) reserve. BF is a measure of atrophy. White matter lesions on T2W images were scored using a semiquantitative rating scale (5) by 3 observers yielding a score from 0-3. The mean score was entered into the analysis and taken as a second indicator of brain damage.

Neuropsychological testing All subjects underwent the MHT in 1932 and 59 had repeat MHT at age 79. The MHT has previously been found to have a correlation of 0.8 with the Stanford Binet test.

Statistical analysis All analysis was carried out using Statistical Package for Social Sciences (SPSS 10).

Results

Table 1. Univariate analysis as below where WMH = white matter hyperintensity rating, BF = brain fraction, TICV = total intracranial volume and MHT = Moray House Test.

	N=59		**MHT age 79**	
Model	**Proxy of reserve**	**Measures of brain damage**	P	Partial Eta Squared
Active	Occupational Classification (GRO)	WMH	.003	.150
		BF	.011	.113
	Years of education	WMH	.016	.103
		BF	.056	.066
Passive	TICV	WMH	.391	.014

Using the general linear model, the passive reserve hypothesis was tested by examination of relationships between TICV (as a proxy for original brain size) and MHT aged 79, when childhood intelligence (MHT age 11) and brain damage (WMH) are accounted for, with gender as a fixed factor. No such relationship exists. The active reserve hypothesis, tested in the same way, shows significant relationships between both years of education and occupational score with MHT aged 79.

Conclusions

These results support the active or cognitive reserve hypothesis: that greater educational and occupational attainment are proxy measures of reserve and that this reserve is implemented via an active process.

References

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