Is The Functional Anatomy Of Working Memory Affected By Cognitive Decline In Old Age?

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INTRODUCTION

Age related decline in working memory performance is apparent throughout the adult lifespan. Esposito et. al. (1) identified age related working memory deficits in cohorts of participants extending from 18-80 years. However little work has been done to investigate the working memory-related brain processing in those who age successfully, compared to those who suffer more cognitive decline on old age. The 1947 Scottish Mental Survey tested most eligible Scottish children born in 1936 and at school on 4th June 1947, using one of the Moray House Tests (2) of general intelligence used here to estimate baseline cognitive ability (age 11 IQ). We studied individual differences from this childhood baseline to cognitive performance in late mid-life.

METHODS

Participants: With ethical approval, 508 local residents who took part in the 1947 survey were recruited into a prospective, longitudinal study of brain aging and health, including a non-verbal measure of fluid type intelligence (Raven's Standard Progressive Matrices test [RPM]). From this sample, 52 individuals (aged 69/70) with an age 11 IQ between 85 and 115 volunteered for functional MRI.
Volunteers were grouped according to RPM score:

- A score of <34.1 (group mean – 0.5 SD) representing cognitive decline (decliners, n=15)
- a score of >41.6 (group mean + 0.5 SD) representing successful aging (sustainers, n=22).

Imaging: Using a 1.5-T scanner (NVi/CVi, General Electric Healthcare, Milwaukee, WI) and a quadrature head coil, functional images using BOLD contrast were collected. Working memory was assessed with a two-condition N-Back task.
Letters were presented every 3 s.

- In the low-load version of the N-Back task (0-back), participants were asked to press a button if a specific target, "X", appeared
- In the high-load version (2-back), participants determined whether an item was the same as one at two trials back and pressed a button.

The time-course fMRI image data were processed with SPM2 (3).

RESULTS

Behavioral Data: Of the 52 members of the ABC1936 group invited for fMRI scanning 15 were excluded from further analysis because they either fell below a pre-determined threshold of 8 correct responses out of a total of 16 for the high load task, or there were other problems associated with imaging such as poor image quality/movement. Those that did pass the threshold included a pre-defined *sustainer* group containing 22 participants (9 female), and a pre-defined *decliner* group containing 15 participants (7 female).

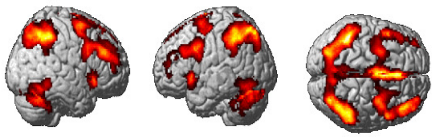

Figure 1. Areas of cortex showing main effect of working memory in the cohort as a whole, n=37 (thresholded at p<0.05 corrected at the cluster level)

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RESULTS cont..

Main effect of working memory: The results of the random effects analysis of all 37 participants are shown in Figure 1. Bilateral frontal and parietal areas were associated with an increase in activity during the high load working memory task. The cerebellum was also activated bilaterally. Investigating the *sustainer* and *decliner* groups (Figure 2) individually, it was found that the *decliner* group displayed a reduced frontal activation pattern compared to the *sustainer* group, although similar activation patterns were observed in the parietal and cerebellar regions. Performing a statistical analysis of the group differences, adjusting for childhood mental ability, (Figure 3), a left parietal region was found to be activated to a greater extent in the *decliners* group than the *sustainers* group. No significant regions were found for the comparison of *sustainers* greater than *decliners*.

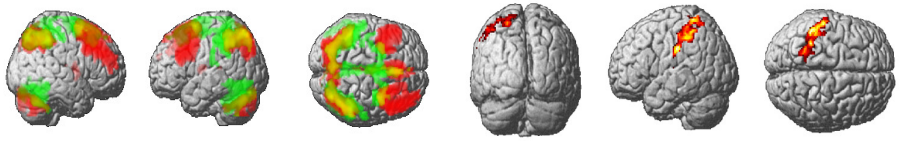

Figure 2. Areas of cortex showing main effect of working memory in sustainers (RED) and decliners (GREEN), with areas of over lap shown in yellow (thresholded at p<0.05 corrected at the cluster level).

Figure 3. Areas of cortex showing increased activity during the high load working memory task compared with rest in the decliners compared to the sustainers (thresholded at p<0.05 corrected at the cluster level).

DISCUSSION

In the largest study of its kind, to date, we have shown that a relatively simple working memory task (2-Back verbal identity monitoring) elicits an increased cognitive processing load in volunteers age 69/70 experiencing relative cognitive decline compared to their peers who have aged more successfully. The large bilateral frontal area present in those who age more successfully that is not present in those experiencing cognitive decline is, however, not significant at the cluster levels reported here.

CONCLUSION

These data add to the evidence that prefrontal, parietal and cerebellar cortical regions are important in maintaining working memory, and possibly general intelligence, as people age. Whether these patterns of activation represents an age-associated change, or alternatively, indicate a previously less well developed working memory system that is more vulnerable to ageing, is unclear though longitudinal studies may help illuminate this.

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