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Effects of advanced aging on the neural correlates of successful recognition memory

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ABSTRACT

Functional neuroimaging studies have reported that the neural correlates of retrieval success (old > new effects) are larger and more widespread in older than in young adults. In the present study we investigated whether this pattern of age-related 'over-recruitment' continues into advanced age. Using functional magnetic resonance imaging (fMRI), retrieval-related activity from two groups (*N* = 18 per group) of older adults aged 84–96 years ('old–old') and 64–77 years ('young–old') was contrasted. Subjects studied a series of pictures, half of which were presented once, and half twice. At test, subjects indicated whether each presented picture was old or new. Recognition performance of the old–old subjects for twice-studied items was equivalent to that of the young–old subjects for once-studied items. Old > new effects common to the two groups were identified in several cortical regions, including medial and lateral parietal and prefrontal cortex. There were no regions where these effects were of greater magnitude in the old–old group, and thus no evidence of over-recruitment in this group relative to the young–old individuals. In one region of medial parietal cortex, effects were greater (and only significant) in the young–old group. The failure to find evidence of over-recruitment in the old–old subjects relative to the young–old group, despite their markedly poorer cognitive performance, suggests that age-related over-recruitment effects plateau in advanced age. The findings for the medial parietal cortex underscore the sensitivity of this cortical region to increasing age.

1. Introduction

A wealth of cross-sectional and longitudinal studies confirm the widely held impression that cognitive performance declines with age, especially for tests of speeded cognition, word generation and long-term memory (e.g. Light, 1991; Lindenberger & Baltes, 1997; Nilsson, 2003; Park et al., 1996, 2002; Schaie & Willis, 1993). Among these studies, some have characterized a trajectory of cognitive decline that accelerates as older adults enter their 8th decade (e.g. Park et al., 2002; Singer, Verhaeghen, Ghisletta, Lindenberger, & Baltes, 2003).

The focus of the present study is on the neural correlates of long-term memory performance in individuals aged 85 years or more, as indexed by functional magnetic resonance imaging (fMRI). The overriding majority of functional neuroimaging studies that have investigated the effects of age on memory functions have employed older adults with a mean age of around 70 years. To our knowledge, no studies have described such data in samples of individuals in their ninth decade and beyond. This is despite the facts that these individuals comprise a rapidly increasing proportion of the population in developed nations (Vaupel et al., 1998), and that cognitive decline accelerates with advancing age (see above).

Functional neuroimaging studies of the effects of age on the neural correlates of episodic memory have reported that, relative to young subjects, older individuals demonstrate greater and more widespread encoding- and retrieval-related cortical activity. This phenomenon of age-related 'over-recruitment' has been reported in studies that differ widely in methodology and in the specific details of their results (e.g. Cabeza et al., 1997; Cabeza, Anderson, Locantore, & McIntosh, 2002; Duverne, Habibi, & Rugg, 2008; Grady, McIntosh, & Craik, 2005; Madden et al., 1999; Maguire & Frith, 2003; Morcom, Good, Frackowiak, & Rugg, 2003; Morcom, Li, & Rugg, 2007; Rosen et al., 2002; Velanova, Lustig, Jacoby, & Buckner, 2007). The functional significance of these findings is unclear. Cabeza (2002) proposed that over-recruitment reflects engagement of additional neural resources that compensate for age-related decline in processing efficiency (see also Reuter-Lorenz & Cappell, 2008; Grady, 2008). By contrast, it has also been proposed that over-recruitment is a reflection of age-related cortical 'dedifferentiation', and has detrimental consequences for neural efficiency and, hence, cognitive performance (Buckner & Logan, 2002; Duverne et al., 2008; Logan, Sanders,

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Snyder, Morris, & Buckner, 2002; Morcom et al., 2003; Persson et al., 2006).

The present study did not seek to arbitrate between these competing perspectives on the functional significance of over-recruitment. Rather, it addressed the question of whether adults in their mid-80s or older, when compared to adults some 20 years younger, demonstrate an analogous pattern of over-recruitment. Such a finding would suggest that the forces propelling over-recruitment continue to increase with age, perhaps tracking decline in cognitive function. Thus, using a yes/no recognition memory task, we compared the neural correlates of 'retrieval success' in two groups of older adults ('old–old' – aged 84–96, and 'young–old' – aged 63–77) who would be expected on the basis of prior studies (e.g. Park et al., 1996; Park & Reuter-Lorenz, 2009; Singer et al., 2003) to differ markedly in their general level of cognitive function. Event-related fMRI[1] studies of recognition memory in young adults (reviewed in Rugg & Henson, 2002) have described a widespread network of cortical regions, including left lateral prefrontal cortex, and medial and lateral parietal cortex, where activity is enhanced for correctly detected 'old' items relative to correctly rejected 'new' items. Relative to young adults, the retrieval success effects of young–old subjects demonstrate over-recruitment in several of these regions (Daselaar, Veltman, Rombouts, Raaijmakers, & Jonker, 2003; Duverne et al., 2008; Morcom et al., 2007; van der Veen, Nijhuis, Tisserand, Backes, & Jolles, 2006).

In most prior studies of age-related differences in the neural correlates of retrieval the different age groups were not matched on retrieval performance. Without such matching the effects of performance and age are confounded, complicating the interpretation of between-group differences in neural activity (see Rugg & Morcom, 2005, for detailed discussion). Importantly, two event-related functional imaging studies that matched retrieval performance between age groups are among those to have reported age-related over-recruitment of retrieval success effects (Duverne et al., 2008; Morcom et al., 2007), although Duverne et al. (2008) reported substantially less widespread over-recruitment than did Morcom et al. (2007). Like these two prior studies, the present study utilized an event-related design and an experimental procedure that allowed memory performance to be matched between the two age groups.

2. Methods

2.1. Subjects

Eighteen subjects (11 female) aged between 64 and 77 years ('young–old', mean age: 70.2 years) and 18 subjects (11 female) aged between 84 and 96 years ('old–old', mean age: 87.4 years) participated in the experiment. Most subjects were recruited from the local Orange County community through newspaper advertisements and flyers. Other subjects were recruited from the control cohort of University of California, Irvine Alzheimer's Disease Research Center, and the study cohort of an on-going longitudinal study (the '90+' study; Whittle et al., 2007). Four additional subjects were excluded from the present dataset. One subject from each group was excluded because of inadequate behavioral performance, and the remaining two were excluded because of equipment malfunction.

All subjects were right-handed, English native speakers with normal or corrected-to-normal vision. The subjects had no history of significant neurological, cardiovascular, or psychiatric disease, had no contra-indications for MR imaging and were not taking CNS-active medications with the exception of the anti-hypertensive Lisinopril. No subjects were color-blind. All had MMSE scores of 26 or higher, and none scored more than two standard deviations below age-standardized means for each of the 5 sub-tests of the California Verbal Learning Test-II (CVLT). These means were available from the CVLT manual (Delis, Kramer, Kaplan, & Ober, 2000) in the case of the young–old subjects. Because the test manual does not provide standardized means above age 89, means for the old–old group were obtained from Whittle et al. (2007), who reported CVLT scores from a sample of 339 non-demented subjects aged 90 years or more. Eight young–old subjects and five of the old–old subjects were taking anti-hypertensive medication. The study was approved by the Institutional Review Board of the University of California, Irvine. Informed consent was obtained prior to participation in each experimental session.

2.2. Neuropsychological testing

A standardized neuropsychological battery was administered to all subjects in a session separate from the fMRI session. Long-term memory was assessed with the CVLT and the Immediate and Delayed NYU paragraph test (Kluger, Ferris, Golomb, Mittleman, & Reisberg, 1999). Short-term memory was assessed with the Digit Span Forward and Backward Test of the WAIS-R (Wechsler, 2001). General cognitive functioning was further assessed with the Digit/Symbol Coding test of the WAIS-R, Trail Making Tests A and B and letter fluency and category fluency tests. The Wechsler Test of Adult Reading (WTAR) provided an estimate of crystallized IQ. The Beck Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) was also administered. One 'old–old' participant declined to complete part B of the Trail Making Test and was given the maximum time possible (300 s) for this measure.

2.3. Overview of experiment

The experiment comprised a single study-test cycle, with both the study and test phases undertaken within the scanner. At study, subjects made animacy classifications on a series of pictures, half of which were presented once, and half of which were repeated after a few intervening items. During the test phase, the studied pictures were re-presented, intermixed with unstudied pictures, with the requirement to make a 'yes/no' recognition judgment on each test item. Data are reported here for the test phase only.

2.4. Materials

The experimental stimuli comprised 132 color pictures of common objects. For each subject, pictures were randomly sorted into 3 sets: 36 pictures were used in the 'easy' study condition, 36 pictures were used in the 'hard' study condition, and 60 pictures were reserved for the 'new' test condition. All stimulus lists contained an equal number of animate and inanimate pictures in each study and test block. Eighteen study/test list pairs were generated for each yoked 'young–old' and 'old–old' subject pair. Practice study and test lists were formed from items additional to those used to create the experimental lists described above.

2.5. Stimulus presentation parameters

The study phase was run as one block. A 2-min rest break was interposed in the middle of the block to allow functional data to download and the scanner to be re-started. The entire study phase duration was approximately 15 min. Study items were viewed via a mirror mounted on the scanner head coil that reflected a backprojected image displayed on a screen at the head of the scanner bore. The items were presented in central vision superimposed on a grey background (subtending a visual angle of $5.72^\circ \times 5.72^\circ$) that was continuously displayed in the center of an otherwise dark monitor. A fixation cross was continuously present at the center of the background other than during item presentation. The cross changed color from black to red 500 ms before the presentation of each item. The items were presented for a duration of 2 s, and were replaced by the black fixation cross. Excluding null events, stimulus onset asynchrony (SOA) was 4500 ms.

Half of the study items were presented once (hard condition), while the remainder were presented twice (easy condition). The repeated items were re-presented after a minimum of four and a maximum of nine intervening trials. Additionally, 38 null events (fixation only trials) were randomly interspersed between item presentations. The study block began with two filler items. An additional two fillers followed each mid-block break.

At test, 72 previously studied and 60 new pictures (along with 46 randomly interspersed null events) were presented in a single block in an identical manner to study with the exception that the presentation duration was 1.5 s. As in the study block, a two min break was given at the halfway point. The test phase duration was approximately 17 min.

2.6. Procedure

Prior to entering the scanner, subjects practiced the study and test tasks until each task requirement was fully understood. In addition, they underwent a brief test of visual acuity and were fitted if necessary with MRI-compatible corrective lenses for use within the scanner. For the final eight old–old and two young–old subjects, the pre-scan practice session was supplemented by a prior session that took place immediately after administration of the neuropsychological test battery. No practice materials were repeated in the experiment proper. Once inside the scanner, further short practice blocks were administered just before the study and test blocks.

At study, the task requirement was to make an animacy judgment about each item. Subjects were allowed to respond any time prior to the presentation of the

[1] Most prior studies that investigated age-related differences in the neural correlates of retrieval employed blocked experimental designs (e.g. Cabeza et al., 1997; Grady et al., 2005; Madden et al., 1999). Unlike event-related designs, these do not allow a distinction to be drawn between activity associated with a retrieval attempt, and activity associated with successful retrieval (see Rugg and Morcom, 2005 for a detailed discussion).