Cognition and the Middle-Aged Brain

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Chapter 3

A functional MRI study in young and middle-aged school teachers: The effects of age and cognitive fatigue on the neural correlates of successful memory encoding

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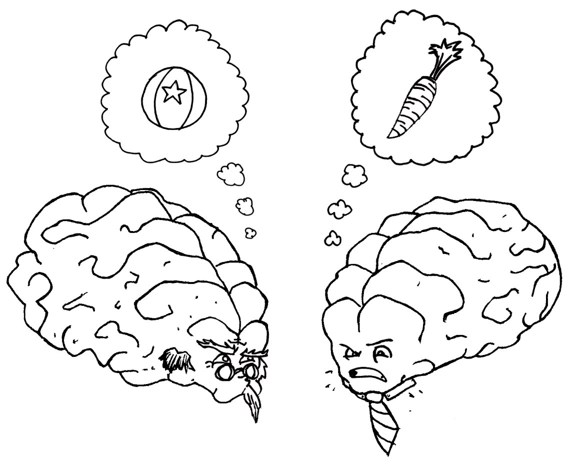

ABSTRACT

We used functional magnetic resonance imaging to investigate differences between young and middle-aged school teachers during successful memory encoding. Teachers were tested in a control condition and in an induced fatigue condition involving the sustained performance of cognitively demanding tasks. Results showed age-related brain activation differences underlying statistically equivalent behavioural performance including: 1) greater activation in middle-aged than young teachers in bilateral prefrontal cortex areas and 2) differential fatigue effects in the left anterior cingulate cortex and left hippocampal formation, with middle-aged teachers showing an activation decrease in the fatigue compared to control condition, whereas no change was evident in young teachers. Findings demonstrate ageing effects typically found in older adults, specifically the increased recruitment of neural resources, in middle age and indicate that ageing may also be associated with greater resource depletion following sustained task performance. Possible practical implications for middle-aged teachers are discussed.

* This chapter is based on data from fMRI study 1.

INTRODUCTION

Memory function declines across the adult lifespan (E.g., Bopp and Verhaeghen, 2005; Myerson et al., 2003; Park et al., 2002; Salthouse, 2003; Soei and Daum, 2008; Van der Elst et al., 2005), with episodic memory thought to be particularly affected (Reuter-Lorenz and Park, 2010; but see Ronnlund et al., 2005). However, the majority of ageing studies focus on differences between young and old adults (60+ years). Hence, although ageing effects can also be expected in middle age (40 – 60 years), little is known about the nature and impact of memory decline at this stage of life. The lack of studies including middle-aged adults may be attributed to the more subtle nature of the age-related decline in memory performance in this age group. Yet, the subtlety of age-related behavioural changes may belie more extensive brain activation changes; studies using functional magnetic resonance imaging (fMRI) have demonstrated significant brain activation differences between young and old adults underlying equivalent performance at the behavioural level (Dennis et al., 2007; Gutchess et al., 2005; Morcom et al., 2003; Park and Reuter-Lorenz, 2009). Moreover, these brain activation differences may have consequences with regard to the capacity for middle-aged adults to sustain performance on demanding tasks for a more prolonged period of time. Therefore, in the present study, we used fMRI to examine activation differences between young and middle-aged adults during episodic memory encoding in a control condition and in a 'fatigue' condition requiring the sustained performance of cognitively demanding tasks.

Unlike older, retired adults, middle-aged adults commonly still work fulltime and are consequentially faced with the challenge of maintaining a high level of performance throughout the workday. The impact of ageing on aspects of cognition, such as memory, in middle age is perhaps particularly relevant to occupations where workday cognitive demands are high. School teachers are a good example of an occupation group in which middle-aged adults must continue to perform at a high level during a workday with high cognitive demands despite the effects of age-related cognitive decline. The present study is, to the best of our knowledge, the first study to use fMRI to examine the neural correlates of cognitive processes in teachers.

Young and middle-aged teachers were compared in terms of successful memory encoding performance and brain activation using the subsequent memory paradigm (Paller and Wagner, 2002). In this paradigm, items studied during an encoding task are classified according to performance on a subsequent recognition task; items that were subsequently remembered are contrasted with items that were subsequently forgotten. Previous studies using the successful encoding paradigm have demonstrated activation differences including increased or more bilateral (Morcom et al., 2003) prefrontal cortex (PFC) recruitment sometimes coupled with reduced (left or bilateral) medial temporal lobe (MTL) activation (Gutchess et al., 2005) in old compared to young adults, despite equivalent performance at the behavioural level. These findings are commonly suggested to reflect the action of neural compensation processes (Dennis et al., 2007; Park and Reuter-Lorenz, 2009); increased and/or more dispersed PFC activation, indicative of increased recruitment of neural resources or the exertion of greater cognitive effort, is thought to facilitate the maintenance of a higher level of behavioural performance. We aimed to determine whether middle-aged teachers similarly rely on the increased recruitment of neural resources to maintain a similar level of performance to young teachers.

In demanding occupations, such as teaching, a typical workday commonly involves prolonged periods of demanding cognitive activity. Therefore, in the present study we not only compared middle-aged to young teachers at a baseline level (control condition), we also compared the two age groups following the sustained performance of cognitively demanding tasks (induced fatigue condition). The necessity to engage neural compensation processes in middle age may also influence the effect of such periods of demanding cognitive task performance. Specifically, the capacity for middle-aged teachers to sustain performance may be constrained by the limited nature of neural resources, and thus the limited capacity of age-related neural compensation processes (Park and Reuter-Lorenz, 2009). Several fMRI studies have provided support for the limited capacity of neural compensation by showing increased activation underlying equivalent task performance in older compared to younger adults when task demands were low, but relatively decreased activation coupled with performance declines in older adults when task demands were high (Cabeza et al., 2000; Cappell et al., 2010; Dennis et al., 2008; Schneider-Garces et al., 2010). The sustained performance of cognitive tasks requiring a high level of cognitive effort (DeLuca, 2005) is thought to result in a state of induced cognitive fatigue, as a result of the temporary depletion of limited cognitive resources (Persson et al., 2007; Smit et al., 2004). Aspects of this induced fatigue state include increased feelings of subjective fatigue, cognitive performance decrements and decreased amplitude of event-related potential components (E.g., Boksem et al., 2006; Kato et al., 2009; Lorist, 2008; Lorist et al., 2009; Lorist et al., 2005; Lorist et al., 2000; van der Linden et al., 2003). Hence, we hypothesised that the induced fatigue condition would result in a depletion of cognitive resources, evident as a decrease in brain activation and an associated performance decrement in both age groups. Furthermore, we hypothesised that decreased activation would be particularly evident in brain areas associated with cognitive control in memory, such as the left PFC (Badre and Wagner, 2007; Blumenfeld and Ranganath, 2007), as studies have shown that higher-level cognitive control functions are particularly sensitive to detrimental induced cognitive fatigue effects (Lorist et al., 2005; Lorist et al., 2000; van der Linden et al., 2003). However, we expected that a need to recruit increased neural resources to support age-related compensatory activation in middle-aged adults would be associated with greater subsequent exhaustion of cognitive resources in this age group than in young adults and, thus, greater performance decrements and brain activation decreases following the sustained performance of cognitively demanding tasks.

Investigating cognitive ageing effects in middle-aged adults in the context of challenging factors encountered during the workday, such as the sustained performance of cognitively demanding tasks, is an important step towards a better understanding of the real-life impact of cognitive decline in this age group. Findings from the present study provide insight into possible mechanisms underlying age-related differences in professional performance and work-related fatigue complaints, and thus provide avenues for research into interventions to improve workplace performance and satisfaction.

MATERIALS AND METHODS

Participants

Healthy, right-handed, young (14 participants aged 25-35 years) and middle-aged (18 participants aged 50-61 years) Dutch male school teachers (working fulltime) were recruited via advertisements placed in school bulletins, fliers distributed at schools or short information sessions for teachers. Volunteers were screened and those who suffered significant past or present physical or psychiatric illness, received medication (other than antihypertensives in two middle-aged adults), reported alcohol or drug abuse, or had MRI contraindications, were not included. We restricted our sample to males as our study concerned a less extreme age group comparison than most ageing studies. Testing males only increased sensitivity for the detection of age-related differences by increasing group homogeneity (improving functional co-localisation) and minimising variance between repeated measures, as females show increased fluctuation of cognition, mood and fatigue in relation to the menstrual cycle (Farage et al., 2008). The study was approved by the local medical ethical committee at Maastricht University academic hospital. Volunteers gave informed consent prior to their (paid) participation.

Procedure

Young and middle-aged teachers were compared in a to-the-tester-blind, randomised crossover study design. Participants completed a training session (in the week prior to the first test session) and two test sessions (administered on two consecutive weekends with both sessions starting at either 0900, 1100 or 1300 h). During the training session, participants completed a battery of neuropsychological tests and practiced the fMRI tasks in a dummy MRI scanner to become familiarised with the scanning environment and minimise practice effects.

During the test sessions, participants spent the first 1.5 h completing either the control or the induced fatigue manipulation outside the MRI scanner. They then entered the scanner where they were scanned during memory encoding and recognition tasks. An additional cognitive task (involving letters only, making interference with the present task unlikely) and a resting state measure were also completed in the MRI scanner, the results of which will be reported elsewhere. Each participant was therefore tested twice and the order of control or fatigue condition administration was randomised. Subjective fatigue levels were measured throughout the test sessions via a subjective rating scale. The researcher operating the scanner and providing instructions to participants during scanning was blind to the manipulation condition the participants had just completed.

Neuropsychological tests

A battery of standardised neuropsychological tests was administered to assess memory processes investigated in our fMRI tasks, other cognitive functions known to decline or remain stable with age, and the intelligence characteristics of the sample. The visual verbal Word Learning Test (WLT) (Van der Elst et al., 2005) was administered as a measure of immediate and delayed memory recall and recognition, whereas the Digit span (forward and backward) was administered to test short-term/working memory capacity (Lezak et al., 2004). General cognitive functions were tested using the Letter Digit Substitution Test (LDST) (van der Elst et al., 2006a) and the Letter verbal fluency test (Van der Elst et al., 2006b). Finally, the Dutch version of the National Adult Reading test (Nelson, 1991; Schmand et al., 1991) was administered as a measure of mental ability (intelligence) in adults based on vocabulary.

fMRI encoding and recognition tasks

During the fMRI encoding (6 min) and recognition (16 min) tasks, 100 words were presented one-by-one on the screen in pseudorandom order such that the proximity of highly semantically or phonetically similar words was minimised. Words were divided equally into four semantic categories: food (F), animals (A), utensils/tools (U) and landscape features (L). Two different word lists were constructed and used to create two versions of the task, which were then randomised in the repeated measures design. The two word lists were matched with regard to factors such as word length, the number of syllables in each word and frequency of use in everyday language.

During encoding, participants were instructed to indicate the category to which a word belonged by pressing the appropriate button, using the left- and right-hand middle and index fingers. The categories were displayed at the bottom of the screen as each word was presented (as: F A U L). Participants were aware that they would subsequently be required to remember the encoding task words.

During recognition, the same 100 'old' words were presented, plus an additional 100 'new' words. Participants were instructed to indicate with a button-press response whether they judged each word to be old or new, and how confident they were about this judgment. Response options therefore included: definitely old, probably old, probably new, and definitely new (displayed at the bottom of the screen as: Old 1 2 3 4 New). Encoding and recognition tasks were separated by a period of about 15 min, during which participants completed an unrelated task.

Encoding and recognition task words were presented in blocks of 8 stimuli followed by three null trials (consisting of a fixation point). Words were displayed in the centre of the screen for 2500 ms, followed by a jittered inter-trial interval (500 - 1250 ms). In the training session, the tasks were practiced with 200 words from the categories sport, country, city and occupation.

Control and fatigue manipulations

In the fatigue manipulation, participants performed the following tasks: 2 and 3-N-back task (3 x 10 min), Stroop task with additional auditory interference (2 x 10 min), mental arithmetic (20 min), and brain teasers/puzzles (20 min). These tasks were selected for the high demands they place on a range of executive functions also subsequently involved in the scanning tasks. During the control manipulation, participants watched a documentary style DVD and/or read a magazine (e.g., the National Geographic) at their leisure.

Subjective fatigue ratings

The fatigue subscale of the Dutch visual analogue scale (VAS: with scores ranging from 0 to 100) short version of the Profile of Mood States (POMS) was administered (Wald and Mellenbergh, 1990) at three time points: before the manipulation (time 0), between the manipulation and MRI scanning (time 1), and after scanning (time 2). The POMS fatigue subscale (consisting of six items) is a recommended measure of subjective fatigue in investigations that are short in duration (e.g., a few hours, O'Connor, 2006), and was administered to determine the effect of the fatigue manipulation on the 'mood of fatigue'. Mood of fatigue refers to "feelings of having a reduced capacity to complete mental or physical activities" (O'Connor, 2004, pp S7).

To assess longer-term feelings of fatigue in relation to the teaching profession and age-related memory and learning decline, we administered the following VAS questions during the training session: 'Do you have a fatiguing job?', 'Are your daily activities fatiguing?', and 'Does fatigue interfere with your ability to learn new things?'.

MRI data acquisition

Scans were made in a 3 Tesla Philips whole body scanner (Philips Achieva, Philips Medical Systems, Best, the Netherlands). A body coil was used for RF transmission with an 8-element SENSE head coil for signal detection. During the encoding task approximately 180 EPI scans were made (TR = 2.0 s, TE = 35 ms, number of slices = 32, image matrix = 64 x 64, voxel size = 4 x 4 x 3.5 mm). A T1-weighted anatomical scan was also acquired for anatomical reference and coregistration of the two test sessions (image matrix = 256 x 256, number of slices = 150, voxel size = 1 x 1 x 1 mm)

MRI data analysis

SPM8 (Statistical Parametric Mapping: Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London) was used to preprocess and analyse the fMRI data. Preprocessing steps included: slice time correction, realign and unwarp, coregistration (session 2 scans were coregistered to session 1 scans), spatial normalisation (MNI space using EPI template), and smoothing (FWHM 8 mm). Functional MRI data was analysed in an event-related analysis in which activity related to the various event types was modeled by convolving a vector of the onset times with the canonical hemodynamic response function within the context of the general linear model. Incorrectly categorised words during the encoding task were modeled separately as errors, whereas correctly categorised words were modeled based on subsequent memory performance during the recognition task as: (1) subsequently recognised (with high confidence) and (2) subsequently forgotten (including subsequently recognised with low confidence and subsequent misses) (Dennis et al., 2008; Duverne et al., 2009; Morcom et al., 2003). In addition, motion parameters were included to correct for motion-related activation.

Activation contrasts were computed for each participant in the control and fatigue conditions separately by contrasting subsequently recognised and subsequently forgotten events with null events (implicit baseline). The main effect of age group and fatigue condition, and the interaction between age group and fatigue condition were investigated by entering the individual activation contrasts into a second level two (control vs. fatigue condition) by two (young vs. middle-aged teachers) by two (subsequently recognised vs. forgotten events) Full Factorial model. Successful encoding was operationalised by the contrast: subsequent recognition > subsequent forgetting. Task-related activation (activation in the control condition associated with the successful encoding contrast across both age groups), age group and fatigue condition effects were examined at p(uncorrected) < .005, with a voxel threshold > 20, after masking with task-related activation associated with the successful encoding contrast at p < .05. Furthermore, given findings from previous studies, we focused on age and fatigue effects in the PFC and MTL (by small volume correcting using AAL regions defined using the SPM8 wfupickatlas toolbox: Maldjian et al., 2004; Maldjian et al., 2003; Tzourio-Mazoyer et al., 2002), further reducing the probability of false positives. Age and fatigue effects outside the PFC and MTL, but within areas showing task-related activation, were examined at a stricter threshold of p(uncorrected) < .001 with a voxel threshold > 10.

For the sake of completeness, the reverse of the successful encoding contrast (subsequently forgotten > subsequently recognised) was also examined. However, no significant task-related activation was found in association with this contrast, thus it was not investigated further. Additionally, the analysis was repeated using a contrast of subsequent recognition > subsequent misses (excluding low confidence subsequent recognition from the contrast); however, this did not change the main pattern of results.

Behavioural statistics

All behavioural analyses were carried out using PASWstatistics (version 18.0). Independent sample t-tests were used to compare scores between young and middle-aged teachers on each neuropsychological test and the additional longer-term fatigue VAS questions. Subjective fatigue ratings, subsequent recognition performance and encoding task RT were analysed using repeated measures analysis of variance (ANOVA) with age group as between-subjects factor and fatigue condition as within-subjects factor. Subsequent recognition task performance (indicative of successful encoding performance) was examined in terms of the number of high and low confidence subsequently recognised words, the number of false alarms (new words incorrectly judged as having been presented during the encoding task), and corrected recognition scores (subsequently recognised minus false alarms). Encoding task reaction time (RT) data were analysed in terms of RT to subsequently recognised and subsequently forgotten words. We additionally examined correlations between performance on each of the neuropsychological tests and successful encoding performance (using corrected recognition scores) in order to improve the interpretation of behavioural effects on the fMRI task (as fMRI tasks typically are not optimised for detection of behavioural effects and are not associated with normative behavioural data).

RESULTS

Three middle-aged teachers were excluded from the analysis due to intervening panic in the scanner, incorrect task execution, and a technical error during the encoding task, leaving 14 young (mean age = 30.6, standard deviation [SD] = 3.2, range = 25 – 35) and 15 middle-aged (mean age = 55.4, SD = 3.9, range = 50 – 61) teachers for group analysis. Additionally, due to a procedural error, the delayed cued recognition performance on the WLT was missing from one young participant.

Neuropsychological data

Scores on the neuropsychological tests are shown in Table 1. A trend (considered relevant due to the small sample sizes in the present study in relation to the detection of behavioural effects) was found for lower scores by middle-aged than young adults on the WLT immediate free recall subtest on ($t(27) = 2.03$, $p = .053$), but differences between the two age groups were not apparent on the WLT delayed free recall subtest, the WLT delayed cued recognition subtest or the Digit span test. Scores on the LDST did not differ statistically, although lower scores were observed in middle-aged than in young teachers. Scores were significantly higher in middle-aged than in young teachers on the Dutch adult reading test ($t(27) = 3.35$, $p = .003$) and the Letter fluency test ($t(27) = 2.44$, $p = .021$), suggesting higher intelligence in the middle-aged group despite matched education level and occupation type. Finally, a significant correlation was found between WLT delayed cued recall scores and corrected recognition scores on the fMRI recognition task in the control condition ($r = .50$, $p = .007$).

Table 1 | Neuropsychological test scores

	Young			Middle age		
	Mean	SD	Range	Mean	SD	Range
WLT immediate free recall	12.5	1.9	9 – 15	10.9	2.3	7 – 14
WLT delayed free recall	10.9	3.2	5 – 15	9.9	2.4	6 – 14
WLT delayed cued recall	14.4	0.8	13 – 15	14.3	1.1	12 – 15
Digit span	17.5	2.6	14 – 24	16.8	4.0	12 – 24
LDST	57.0	8.1	42 – 70	52.7	7.0	37 – 66
Letter fluency *	13.6	3.0	8 – 18	17.2	4.7	9 – 23
Dutch adult reading test **	80.9	7.8	65 – 90	88.9	4.7	82 – 96

Significant age group differences: * $p < 0.05$; ** $p < 0.01$.

Subjective fatigue ratings

There was a significant main effect of fatigue condition ($F(1, 27) = 16.87$, $p < .001$) as well as a significant interaction between fatigue condition and time point ($F(2, 54) = 5.30$, $p = .008$). Follow-up paired sample t-tests show that fatigue ratings were higher following the fatigue than the control manipulation at time 1 ($t(28) = 2.93$, $p = .007$) and at time 2 ($t(28) = 5.32$, $p < .001$). This indicates that the fatigue manipulation successfully induced greater feelings of fatigue in young and middle-aged participants compared to the control manipulation (Figure 1). Ratings did not differ significantly between young and middle-aged adults.

Significant differences were found between young and middle-aged adults in relation to feelings of fatigue associated with the teaching profession; middle-aged teachers (mean ratings = 69.7, 63.9, 38.3, SD = 16.5, 20.2, 19.1 respectively) rated their job (t(27) = 2.13, *p* .043) and daily activities (t(27) = 2.26, *p* = .032) as more fatiguing and indicated that fatigue interfered more with their ability to learn new things (t(27) = 2.32, *p* = .028) than young teachers (mean ratings = 51.2, 45.6, 24.0, SD = 29.0, 23.5, 13.4 respectively).

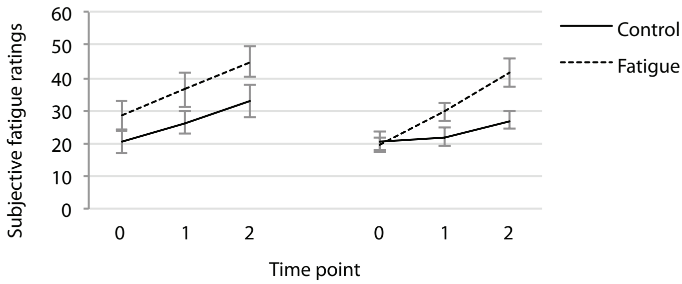

Figure 1 | Mean subjective ratings (± SE) before the manipulation (time 0), between the manipulation and the fMRI tasks (time 1), and after the fMRI tasks (time 2).

Encoding and recognition task behavioural results

Regardless of age group or fatigue condition, participants correctly categorised between 92 and 95 of the 100 words presented during the encoding task, and an average of 45 to 57 of these words were then subsequently recognised with high confidence on the recognition task (Table 2). The analysis of RTs to subsequently recognised and subsequently forgotten words during the encoding task (Table 2) revealed a significant main effect of encoding success (F(1, 27) = 6.96, *p* = .014), but no effect of age group or fatigue condition. This finding reflects slower RTs to subsequently recognised words than to subsequently forgotten words, indicating that the encoding processes benefitted from more prolonged study of word stimuli (i.e. more prolonged study during the encoding task was more likely to result in subsequent high confidence recognition). Some previous studies have reported a similar RT difference (Duverne et al., 2009; Morcom et al., 2003), whereas others have reported a lack of significant difference (Dennis et al., 2008). Importantly, this RT difference did not interact with age group or fatigue condition and is therefore unlikely to compromise our interpretations of age or fatigue effects.

Table 2 | Encoding task trials classified according to subsequent recognition task performance.

	Young		Middle age	
	Control	Fatigue	Control	Fatigue
Number of responses				
Subsequently recognised	55 (15)	57 (12)	45 (20)	47 (20)
Subsequently forgotten	37 (15)	34 (9)	46 (19)	46 (19)
Reaction time (ms)				
Subsequently recognised	1106 (149)	1106 (158)	1182 (124)	1187 (142)
Subsequently forgotten	1092 (125)	1087 (144)	1151 (141)	1145 (130)

Mean (SD).

Analysis of subsequent recognition task performance (Table 3) showed that performance in terms of corrected recognition scores did not differ between the two age groups or fatigue conditions, but that high confidence corrected recognition scores were significantly higher than low confidence scores ($F(1, 27) = 127.43$, $p < .001$). We then conducted repeated measures ANOVAs comparing subsequent recognition to false alarms per confidence level to investigate memory discrimination. Analysis of low confidence responses showed no significant difference between subsequently recognised words and false alarms (also reflected in low confidence corrected recognition scores, which were essentially zero), suggesting that low confidence responses represent guesses rather than reliable memory discrimination responses. Analysis of high confidence responses, on the other hand, showed significantly more high confidence subsequently recognised words than false alarms ($F(1, 27) = 290.14$, $p < .001$), suggesting that high confidence subsequent recognition generally reflected successful memory encoding. This finding supports our fMRI contrast classification of encoding task words into subsequently recognised words (with high confidence only) and subsequently forgotten words (including low confidence subsequent recognition in addition to subsequently missed words). Analysis of high confidence subsequently recognised words alone revealed a near-significant main effect of age group ($F(1, 27) = 4.15$, $p = .051$), showing less high confidence subsequently recognised words in middle-aged than in young teachers when scores were not corrected for false alarms.

Table 3 | Recognition task performance

	Young		Middle age	
Response type	Control	Fatigue	Control	Fatigue
Total misses	25 (9)	21(10)	31(15)	31(17)
High confidence				
Recognised	59 (16)	61 (12)	48 (22)	50 (21)
False alarms	14 (6)	17 (11)	9 (8)	9 (10)
Corrected recognition	45 (14)	44 (14)	39 (16)	41 (16)
Low confidence				
Recognised	15 (11)	16 (10)	17 (11)	16 (6)
False alarms	14 (10)	16 (10)	12 (8)	11 (7)
Corrected recognition	0 (11)	0 (7)	7 (14)	5 (8)

Mean (SD) number of responses. Corrected recognition = recognised minus false alarms.

Encoding task fMRI results

Task-related activation: Activation in the control condition associated with the successful encoding contrast in young and middle-aged adults was found in the left anterior cingulate cortex (ACC), left DLPFC, left ventrolateral PFC (VLPFC), bilateral orbital frontal cortex (OFC), left angular gyrus, and the left lateral temporal cortex (Table 4). This activation pattern is consistent with findings from two meta-analyses examining successful encoding

(Kim, 2011; Spaniol et al., 2009).

Main effect of age: A main effect of age was found, with middle-aged teachers showing greater successful encoding activation than young teachers in the bilateral dorsomedial PFC (DMPFC), bilateral DLPFC and left OFC (Table 5 and Figure 2a).

Main effect of fatigue condition: A main effect of fatigue condition was found in the right DLPFC, right ACC and right OFC, with greater activation evident in these areas in the control than in the fatigue condition (Table 6).

Age group and fatigue condition interaction: An interaction between age group and fatigue condition was found in the left ACC (peak coordinates x = -15, y = 15, z = 42; t-value = 3.31; cluster size = 31) and left hippocampal formation (peak coordinates x = -27, y = -24, z = -12; t-value = 3.17; cluster size = 27). Follow-up t-tests within each age group and fatigue condition using the interaction effect as an inclusive mask, indicated that middle-aged adults showed significantly reduced activation in the left ACC (t-value = 4.66) and left hippocampal formation (t-value = 3.84) in the fatigue compared to the control condition, whereas no significant activation change was found in these areas in young adults (Figure 2b).

Post-hoc correlations with task performance: Although corrected recognition scores showed equivalent performance in the two age groups, an examination of the number of high confidence subsequently recognised words alone revealed poorer performance in the middle-aged group (accompanied by greater variability on this measure in the middle-aged group than in the young group). Therefore, we also used regression analyses to examine the relationship between successful encoding-related activation and subsequent recognition task performance (using corrected recognition scores) within each age group and fatigue condition. Correlations were also masked with task-related activation and small volume corrected for MTL and PFC areas, with reported clusters significant at p(uncorrected) < .005 with a minimum of 20 contiguous voxels.

No significant correlations were found in the young group. In the middle-aged group, a significant negative correlation was found in the control condition in the left DMPFC (peak coordinates x = -24, y = -18, z = 57; t-value = 4.29; cluster size = 25) and right DLFPC (peak coordinates x = 24, y = 39, z = 33; t-value = 4.05; cluster size = 20), reflecting greater activation in these areas in association with poorer performance. On the other hand, significant positive correlations were found within the middle-aged group in the fatigue condition in the ACC (peak coordinates x = 3, y = 15, z = 48 and x = -12, y = 54, z = 3; t-value = 5.15, 5.11; cluster size = 122, 32), right DLPFC/VLPFC (peak coordinates x = 36, y = 42, z = 15 and x = 18, y = 48, z = 21 and x = 27, y = 45, z = 15; t-value = 7.53, 4.11, 3.15; cluster size = 63), right OFC (peak coordinates x = 30, y = 33, z = -9; t-value = 7.53; cluster size = 29) and left OFC (peak coordinates x = -42, y = 33, z = 3; t-values = 3.81; cluster size = 33), indicating greater activation in relation to better performance. We also examined correlations between RT to high confidence subsequently recognised words during the encoding task and brain activation, but did not find any effects.

Table 4 | Task-related brain activation associated with successful encoding

Region		BA	MNI coordinates x	y	z	t-value	Cluster size (voxels)
Anterior cingulate	L	32	-12	21	36	4.93	1720**
Dorsolateral PFC	L	46	-27	45	15	3.16	32
Ventrolateral PFC	L	44	-36	9	30	3.32	22
	L	*45*	*-48*	*27*	*18*	*4.19*	
Orbital frontal	L	47	-42	39	-3	4.10	469**
	R	47	36	33	-9	4.04	167
	R	*47*	*42*	*24*	*-3*	*3.47*	
	R	*45*	*36*	*36*	*9*	*3.35*	
Angular gyrus	L	39	-45	-72	30	3.27	42
Lateral temporal	L	20	-54	-30	-15	3.27	40

Abbreviations: L = left, R = right, BA = Brodmann area. Note: Italics are used to indicate additional activation peaks within a cluster. Cluster level significance: ** p(FWE) < .05, * p(FWE) < .1.

Table 5 | Greater successful encoding activation in middle-aged than young teachers

Region		BA	MNI coordinates x	y	z	t-value	Cluster size (voxels)
Middle age > Young							
Dorsomedial PFC	L	8	-6	33	57	3.09	22
	R	*8*	*3*	*30*	*57*	*3.04*	
Dorsolateral PFC	L	9	-30	27	45	3.26	37
	L	*8*	*-24*	*21*	*45*	*3.15*	
	L	9	-6	51	36	3.31	79
	L	*32*	*-9*	*42*	*30*	*3.06*	
	R	9	39	21	48	3.22	30
Orbital frontal	L	45	-48	42	-3	3.41	27

Table 6 | Greater successful encoding activation in the control than the fatigue condition

Region		BA	MNI coordinates x	y	z	t-value	Cluster size (voxels)
Control > Fatigue condition							
Dorsolateral PFC	R	46	30	45	12	3.33	21
Orbital frontal	R	47	39	39	-6	3.47	27
Anterior cingulate	R	32	15	39	18	4.35	71
	R	*46*	*24*	*42*	*21*	*3.24*	

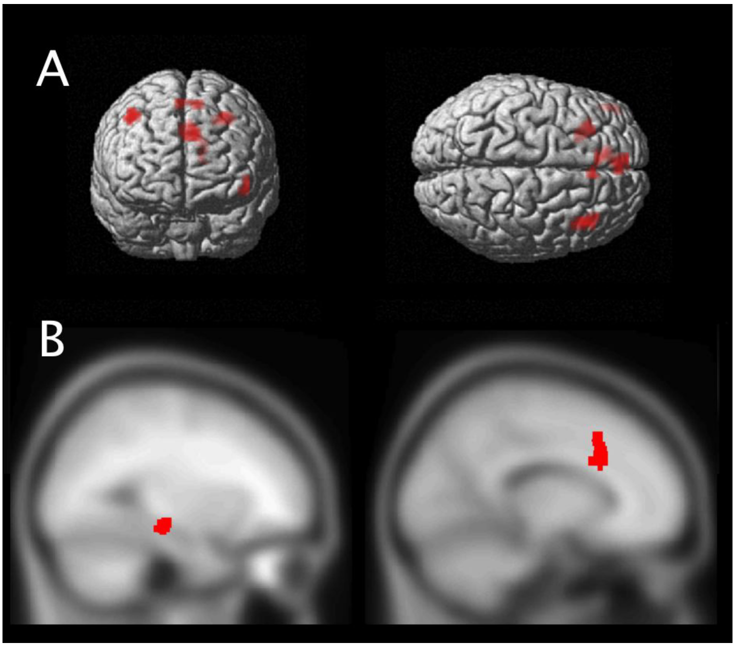

Figure 2 |

(A): Main effect of age: Increased activation in middle-aged compared to young teachers during successful memory encoding.

(B): Hippocampal formation and anterior cingulate cortex areas showing greater activation decreases in the fatigue compared to the control condition in middle-aged adults.

DISCUSSION

In the present study we examined the effects of age and induced cognitive fatigue on brain activation associated with the subsequent memory operationalisation of successful encoding in young and middle-aged school teachers. This investigation resulted in several main findings. Firstly, a main effect of age group was evident. Greater activation was found in middle-aged than in young teachers in bilateral PFC areas. Secondly, a main effect of fatigue condition was found. The fatigue condition resulted in reduced activation compared to the control condition in the right PFC. Thirdly, an interaction was found between age group and fatigue condition in the left ACC and left hippocampal formation. Activation in these areas decreased in the fatigue compared to the control condition in middle-aged teachers, but did not change significantly in young teachers. Finally, increased activation in middle-aged teachers in PFC areas including the right DLPFC was associated with poorer memory performance in the control condition, but with better memory performance in the fatigue condition.

Age-group differences

Behavioural performance on the neuropsychological WLT test and the association with subsequent recognition performance on the fMRI task reflected the typical pattern of ageing effects on memory; memory recall showed signs of age-related cognitive decline in middle-aged teachers, whereas recognition performance remained relatively unaffected (Yonelinas, 2002). Middle-aged teachers also had slightly lower scores on the LDST and showed slower responding (a 76 ms difference) during the encoding task than young teachers, consistent with an age-related general slowing of processing speed.

As expected, significant brain activation differences between young and middle-aged teachers were found to underlie these subtle differences at the behavioural level. Our findings demonstrated the presence of similar age-related activation differences between young and middle-aged teachers to those found in previous studies comparing young and old adults (Dennis et al., 2007; Gutchess et al., 2005; Morcom et al., 2003). Our results are particularly consistent with findings by Morcom et al. (2003) of increased bilateral DLPFC recruitment in older adults (young adults selectively activated the left DLPFC only), but no MTL activation differences. The age-related increase in bilateral DLPFC recruitment is in keeping with the 'Hemispheric Asymmetry Reduction in Older Adults' (HAROLD) model of cognitive ageing that proposes an age-related decrease in activation lateralisation (Cabeza, 2002). However, our findings do not provide support for the proposal that an age-related increase in DLPFC activation functionally compensates for reduced MTL function (Dennis et al., 2007; Gutchess et al., 2005), as no age-related decreases in MTL activation were evident. Correlational analyses indicated that greater activation in the right DLPFC was related to poorer recognition performance by middle-aged teachers on the subsequent recognition task. This finding is congruous to the finding that poor performing old adults show greater activation in the right PFC than young adults, whereas higher performing older adults do not show increased recruitment of this area (Duverne et al., 2009). This association between greater bilateral PFC activation and poorer performance is in line with the suggestion that recruitment of right PFC is inefficient and deleterious to performance, rather than fulfilling a beneficial neural compensatory role (Rajah and D'Esposito, 2005; Spreng et al., 2010). Hence, the present study provides support for the proposal that bilateral PFC recruitment is more likely to result from inefficient cortical dedifferentiation effects than performance supporting neural compensation effects (Buckner and Logan, 2002; Logan et al., 2002).

Increased activation in middle-aged compared to young teachers was also found in the left DLPFC. However, activation in this area did not correlate significantly with task performance. Dennis et al. (2007) suggested that a similar increase in left DLPFC activation in older adults in relation to successful encoding might reflect deeper or more elaborate semantic processing. On the basis of a meta-analysis examining age-related differences across multiple cognitive domains, Spreng et al. (2010) suggested that increased left DLPFC activation in older adults might be attributable to a greater reliance on strategic control. Either or both of these explanations may therefore also account for increased DLPFC activation in middle-aged teachers in the current study.

Overall, results from the present study point towards similarities between age-related brain activation differences in middle-aged teachers to those previously reported in old adults. Surprisingly, given that we expected a high level of performance in our homogeneous sample of school teachers, these similarities extended to congruous findings in association with poorer performance in middle-aged teachers and poor performing old adults. In relation to this finding, it should be noted that memory performance in the middle-aged group did not correlate with age within this group, thus performance correlations were not attributable to a dichotomy within the middle-aged group of 'young' middle-aged and 'old' middle-aged participants. Future studies are therefore warranted in order to remedy the relative lack of insight currently available regarding the effects of age-related cognitive decline in middle age. Furthermore, future studies should consider testing a larger group of middle-aged adults in order to facilitate a comparison of low and high performers.

Fatigue condition effects

Subjective fatigue ratings were higher in all participants in the fatigue compared to the control condition, indicating that the fatigue manipulation successfully induced a state of increased fatigue. As expected, the fatigue condition was associated with a decrease in brain activation, indicating a fatigue-related depletion of cognitive resources. However, this decreased activation was not evident in the hypothesised left PFC suggesting that processes other than the cognitive control of memory were more sensitive to induced fatigue effects. In relation to the hypothesised differential effects of the fatigue condition in young and middle-aged teachers, the interaction effect showed additional brain activation decreases in middle-aged than in young teachers suggestive of greater resource depletion in the middle-aged group.

Activation in the ACC was reduced in the fatigue compared to the control condition. In an event-related potential study, Lorist et al. (2005) also reported reduced ACC activity in young adults as a result of induced cognitive fatigue. Lorist et al. (2005) attributed this finding to impaired cognitive control, resulting in compromised error monitoring and inadequate performance adjustment. In the present study, reduced ACC activation was associated with poorer recognition performance in middle-aged teachers, in line with impaired cognitive control. An association between ACC activation and reduced performance was not evident in young teachers. This is perhaps unsurprising given that the decrease in ACC activation was less extensive in young than in middle-aged teachers, as indicated by the interaction effect. Nevertheless, somewhat of an increase in the number of false alarms was apparent in young teachers, perhaps reflecting slightly poorer performance resulting from decreased performance monitoring and/or a more lenient response criterion.

The fatigue condition also resulted in decreased activation in the right DLPFC, VLPFC and OFC. In middle-aged teachers, greater activation in these areas in the fatigue condition was actually associated with better subsequent recognition performance. Thus, this correlation was in the opposite direction to the correlation found in the right DLPFC in the control condition in middle-aged teachers. Therefore, it appears that while poorer performance by middle-aged adults in the control condition was associated with greater right DLPFC recruitment, poorer performance in the fatigue condition was associated with a greater decrease in right DLPFC recruitment. On the basis of these findings, we speculate that the overall decrease in right DLPFC activation in the fatigue compared to the control condition may have been driven by significant activation decreases in a sub-group of poorer performing middle-aged adults who previously relied more heavily on right DLPFC in the control condition. This suggestion is in line with the expected increased effect of fatigue-related cognitive resource depletion on middle-aged adults characterised by a greater age-related utilisation of cognitive resources in the control condition. Unfortunately, samples sizes in the present study preclude further investigation of this proposal by examining low- and high-performing middle-aged adults separately.

The investigation of the interaction between age group and fatigue condition also showed significantly reduced activation in the left hippocampal formation in the fatigue compared to the control condition in middle-aged teachers, whereas young teachers did not show a change in activation in this area. The hippocampus is known to play a crucial role in memory encoding, with left hippocampal activation in particular thought to be predictive of subsequent recognition success (Fletcher et al., 2003; Ulrich et al., 2010). It can therefore be expected that decreased activation in this area would lead to poorer subsequent recognition performance. However, in the present study we found no relation between hippocampal activation and subsequent recognition performance. Therefore, we can only speculate as to the nature of the decrease in left hippocampal activation in middle-aged teachers. To do just that, one possibility is that middle-aged teachers may have adopted an alternative task strategy in response to the fatigue condition. This alternative strategy may have involved reduced reliance on 'deep' encoding processes recruited by the left hippocampus and greater reliance on 'shallow' encoding processes that were nevertheless sufficient to maintain performance (Fletcher et al., 2003).

The differential effects of the sustained performance of cognitively demanding tasks on young and middle-aged teachers suggests that age-related performance and brain activation differences may vary throughout a demanding workday. In particular, differences evident during short cognitive tasks in non-fatigued participants may underestimate differences in more challenging situations. Insight into the mechanisms utilised by ageing adults in response to various challenging situations is essential to our understanding of consequences of cognitive ageing.

Limitations

Interestingly, despite equivalent education level and occupation type in the two age groups, middle-aged teachers were characterised by significantly higher letter fluency and Dutch adult reading test scores. This finding suggests higher verbal intelligence in the middle-aged group, as letter fluency in particular has been shown to decline with age (Van der Elst et al., 2006b). However, since letter fluency and reading test scores did not correlate with performance on the fMRI task, we consider it unlikely that this difference significantly influenced fMRI findings. We also note that, although the fatigue condition provides greater insight into age-related differences by examining them in the context of induced fatigue, a factor encountered during the workday, future studies may extend the ecological validity of this investigation to more real-world conditions, such as fatigue induced by a real-life workday. Furthermore, although we chose to focus on males in order to minimise unwanted variance in our small sample group, future studies should consider examining these effects in larger samples including females.

Implications for school teachers

Findings from the present study suggest that middle-aged teachers recruit greater neural resources than younger teachers in relation to similar levels of cognitive performance. The increased recruitment of the left PFC is indicative of the exertion of increased cognitive control or effort in middle age, whereas increased recruitment of the right PFC seems more likely to reflect neural inefficiency. Furthermore, our findings are indicative of a greater depletion of cognitive resources in middle-aged than in young teachers as a result of the sustained performance of cognitively demanding tasks.

What might these findings mean for the middle-aged school teacher in practice? Middle-aged teachers have the benefit of greater experience and knowledge with regard to numerous aspects of their job, allowing them to perform many tasks intuitively. However, cognitive ageing effects may mean that other aspects of teaching require the exertion of increased cognitive effort and result in greater subsequent cognitive fatigue effects in middle-aged than in young teachers. Hence, in line with subjective ratings in the present study, middle-aged teachers may experience greater fatigue in relation to their job than young teachers. Challenging situations may arise for middle-aged teachers when they are unable to rely on previous experience and must instead engage processes affected by age-related cognitive decline in order keep up-to-date with changing educational practice. For example, implementing the use of new technologies in the classroom may require extra effort by middle-aged compared to young teachers. Indeed, this suggestion is, in our experience, a difficulty commonly expressed by middle-aged teachers and is again in line with subjective ratings in the present study indicating that middle-aged teachers felt that fatigue interfered more with their ability to learn new things than young teachers did. The increased effort required by such tasks in middle age, in the context of an already highly demanding occupation, is probably also an important contributor to greater resistance to change in this age-group (Hargreaves, 2005).

We suggest that middle-aged teachers may therefore benefit from workday interventions that focus on providing support with regard to tasks that they find more demanding than young teachers, as well as the minimisation of the sustained performance of demanding tasks. For example, change management strategies may be tailored to meet the needs of middle-aged teachers. Such change management strategies may include working one-on-one with middle-aged teachers to provide coaching or mentoring in difficult areas, as well as providing a plan for the step-by-step implementation of changes. Similarly, the encouragement of collaborations between young and older teachers within the professional learning community may foster working relationships in which each teacher benefits from the strengths of the other. Minimising the sustained performance of demanding tasks may be achieved by improved planning of the workday, or specific lessons, such that demanding classes are followed by a break, or a less demanding class, and teachers alternate between demanding and less demanding teaching strategies within a lesson. Recognising the differing strengths and weaknesses of young and middle-aged teachers, and adjusting performance expectations and support strategies accordingly, is not only important to enhancing workplace performance, it is probably also an important step towards addressing the relatively high incidence of burnout in the teaching profession (Hakanen et al., 2006).

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