Cognition and the Middle-Aged Brain

Klaassen, E.B.

2012

document version
Publisher's PDF, also known as Version of record

Link to publication in VU Research Portal

citation for published version (APA)
Klaassen, E. B. (2012). *Cognition and the Middle-Aged Brain: Functional MRI studies examining demand, fatigue and caffeine effects*.

Chapter 1

General Introduction

Middle-age defn. - Between young adulthood and old age. A period of great productivity. The stage of life when one has a great knowledge of the how and why of things, but keeps forgetting where they left them.

BACKGROUND AND RATIONALE

Cognitive ageing: What about middle age?

As we get older we start to notice changes, such as increased forgetfulness or greater difficulty learning new things and keeping up with new technologies. These changes are so pervasive in the healthy population that they are an accepted part of getting older. Indeed, research has shown us that cognitive decline is a natural part of the ageing process. The implications of age-related cognitive decline may be particularly obvious to us when we watch Grandma or Grandpa struggling to send an email or use their new mobile phone, but cognitive decline has already begun well before this stage of life. Studies indicate that cognitive ageing begins as early as the 20's (Bopp and Verhaeghen, 2005; Park et al., 2002; Salthouse, 2003, 2009; Van der Elst et al., 2005, 2006b, c). Yet, while cognitive changes in old adults (60+ years) have been quite extensively investigated, changes in middle-aged adults (40 - 60 years) have received far less attention (with the exception of a limited number of large scale ageing studies including the Maastricht Ageing Study: MAAS, Jolles et al., 1995; Van der Elst et al., 2005, 2006a, b; Van der Elst et al., 2006c; Van Dijk et al., 2008).

Age-related cognitive changes can be expected to be subtler in middle age than in old age. However, it is important to consider that these subtle changes occur in a different context to changes occurring in old adults. While older adults are commonly winding down their career and heading into retirement, middle-aged adults often find themselves at the peak of their career in high profile, high demand jobs. Hence, subtle cognitive decline is paired with considerable cognitive challenge. This leads us to the primary focus of this thesis: age-related cognitive decline in middle age in the context of cognitive challenge. Yet, we do not expect that all middle-aged adults will respond equally to challenge. Therefore, we also investigated factors underlying individual differences in this age group. The effects of cognitive decline in middle-aged professionals have implications for a large proportion of our ageing workforce. However, the busy lifestyles of individuals in this population group make them somewhat difficult to recruit, especially for participation in studies requiring a substantial time investment. Hence, this thesis provides important insights into this little studied population.

MRI insights

Magnetic resonance imaging (MRI) techniques have facilitated considerable developments in the field of cognitive ageing research. Structural MRI techniques have provided insight into age-related changes in grey and white matter volume and integrity. Functional MRI has provided insight into age-related changes in neural activity associated with cognition. MRI involves the use of a strong static magnetic field combined with changing magnetic gradients and oscillating electromagnetic fields to produce images of different tissue types in the body (Huettel et al., 2008). Functional MRI studies primarily rely on an indirect measure of neural activity, namely the blood oxygenation level-dependent response (BOLD). The BOLD response is based on changes in the magnetic properties of blood following oxygenation or deoxygenation of the haemoglobin molecule elicited in response to neural activation.

Although the BOLD response is not without its limitations, it is nevertheless an invaluable tool for the investigation of the neural correlates of cognitive processes (Huettel et al., 2008). The neural correlates of age-related cognitive changes have been relatively extensively investigated in older adults. A finding from these studies of particular relevance to studies in middle age, is that differences in brain activation can underlie statistically equivalent behavioural performance (task accuracy) (Park and Reuter-Lorenz, 2009). Thus, while cognitive changes may appear subtle and difficult to detect at the behavioural level in middle-aged adults, they may be accompanied by significant changes in underlying brain activation (Grady et al., 2006; Mathis et al., 2009). The present thesis describes findings from two fMRI studies examining brain activation during learning and memory tasks in middle-aged adults.

Cognitive demand, effort and fatigue

Healthy, motivated individuals commonly respond to greater cognitive challenge or ‘demand’ by exerting increased cognitive effort (DeLuca, 2005). When sufficient cognitive resources are available to support cognitive effort, task demands can be met and performance maintained. However, cognitive resources are limited. Thus, as task demands increase, cognitive resources become depleted and performance starts to decline (Persson et al., 2007; Smit et al., 2004).

Cognitive ageing theories state that ageing is associated with the recruitment of greater cognitive resources at lower levels of tasks demand (Park and Reuter-Lorenz, 2009). In this way older adults may be able to ‘compensate’ for age-related cognitive decline. However, this ‘over-recruitment’ of neural resources at lower levels of task demand also entails an earlier exhaustion of resources in older individuals as demands increase (Reuter-Lorenz and Cappell, 2008). Functional MRI studies have provided support for this theory by demonstrating increased and more dispersed brain activation, primarily in prefrontal cortex areas, in older adults (than in younger adults) underlying equivalent behavioural performance at relatively low levels of task demand, but relatively decreased activation and performance decrements at higher levels of task demand (Cabeza et al., 2000; Cappell et al., 2010; Dennis et al., 2008; Nagel et al., 2009; Schneider-Garces et al., 2010).

Functional MRI studies have typically investigated activation differences between young and old adults during relatively short cognitive tasks (commonly around 15 minutes). However, during a typical workday, for example, we are required to perform demanding tasks for a much more prolonged period of time. The prolonged performance of cognitive tasks requiring sustained mental efficiency leads to an exhaustion of cognitive resources and a state of cognitive fatigue (DeLuca, 2005; Lorist, 2008). This induced fatigue state is associated with subjective feelings of exhaustion and fatigue, cognitive performance decrements and changes in event-related potential components (Boksem et al., 2006; Kato et al., 2009; Lorist, 2008; Lorist et al., 2005; van der Linden et al., 2003).

The increased recruitment of neural resources in older adults during short tasks may, therefore, lead to earlier resource exhaustion when prolonged performance is required. Hence, even minor differences between young and middle-aged adults on short tasks may be exacerbated when prolonged task performance is required. However, very little is known about how the necessity to perform demanding tasks for a prolonged period of time may interact with age-related cognitive decline.

A cup of coffee

In situations where we feel fatigued, many of us turn to a cup of coffee to get us through the workday. The caffeine in coffee alleviates feelings of tiredness and fatigue, and increases subjective energy. However, studies into the effects of caffeine on learning and memory show somewhat inconsistent results (Nehlig, 2010; Snel et al., 2004). Furthermore, very few studies have examined the effect of caffeine on brain activation underlying learning and memory (Koppelstaetter et al., 2008). Insight into the effect of caffeine on brain activation may reveal mechanisms underlying inconsistent behavioural effects. Moreover, in relation to the effects of caffeine consumption in middle age, there is some indication that caffeine can exert a more pronounced enhancement of cognition in older individuals (Nehlig, 2010). Therefore, the possible memory enhancing effects of caffeine are of particular interest in this age group; middle-aged adults may stand to benefit more from caffeine in terms of work-related performance enhancement than working young adults (or retired old adults in whom daily cognitive demands are probably reduced). In the present thesis we used fMRI to investigate the effects of induced cognitive fatigue and caffeine on learning and memory-related brain activation in middle-aged adults.

THESIS OUTLINE

Aims

The over-arching aim of this thesis is the visualisation of age-related brain activation differences underlying learning and memory in middle age using fMRI. We take the novel approach of investigating cognitive ageing in the context of factors commonly encountered during a workday including the fatigue-inducing sustained performance of cognitively demanding tasks and the attempt to alleviate fatigue effects with a cup of coffee. By examining ageing effects in different contexts we aimed to gain a more 'real-life' picture of the effects of cognitive ageing in middle age.

Approach

The present thesis is based on data from two experimental fMRI studies conducted at Maastricht University. In the first study, young (25 – 35 years) and middle-aged (50 – 60 years) male school teachers (recruited from schools in the Limburg region) were tested in an induced fatigue condition and in a control condition. At present, school teaching in the Netherlands is a good example of a profession where daily cognitive demands are high. Hence, the interaction between ageing and the effects of cognitive demand is particularly relevant to school teachers. Furthermore, school teaching is a relatively well-defined profession, conferring homogeneity in terms of education level, cognitive performance and experience with cognitively demanding tasks. In the second study, middle-aged (40 – 60 years) male, white-collar professionals who habitually consumed approximately three to six cups of coffee (recruited from the Limburg region) were tested in a non-withdrawn state in a caffeine condition (100 mg caffeine) and in a placebo condition. Testing habitual caffeine consumers in a non-withdrawn state is more reflective of the effects of caffeine as it is consumed in daily life and ensures that caffeine effects are not due to the resolution of caffeine withdrawal.

In both studies participants were scanned using fMRI during a working memory maintenance task and a verbal episodic memory task. The working memory task we used was a letter Sternberg task. This task required encoding (presentation of a target letter string for memorization), maintenance (retention/maintenance of the letters over a delay period) and retrieval (response indicating whether a probe letter was part of the target or not). The verbal episodic memory task involved the administration of a word encoding task followed fifteen minutes later by a recognition task. In both studies we also obtained neuropsychological data and subjective measurements of fatigue, effort and mental demand. Furthermore, we obtained saliva samples for the determination of cortisol levels in the first study and caffeine levels in the second study.

Chapter overview

Using data from the first fMRI study, we aimed to determine the effects of age (young vs. middle-aged school teachers) and induced fatigue (control vs. fatigue condition) on a) working memory task performance and brain activation (Chapter 2), b) episodic memory encoding performance and brain activation (Chapter 3), and c) functional connectivity during resting state (Chapter 4). In Chapter 5, we examined individual differences in the effect of induced fatigue on episodic memory encoding and recognition in relation to the elicitation of a cortisol-indexed stress response. Data from the second study were used to examine the effect of caffeine (compared to placebo) on working memory load-related activation in middle-aged coffee drinkers (Chapter 6). Finally, in Chapter 7 we combined data from the first (control session) and second (placebo session) study to investigate individual differences within this larger sample of middle-adults with regard to episodic memory encoding performance and brain activation. Chapter 8 reflects on the findings, implications and limitations of this thesis.

REFERENCES

Boksem, M.A., Meijman, T.F., Lorist, M.M., 2006. Mental fatigue, motivation and action monitoring Biol Psychol 72, 123-132.

Bopp, K.L., Verhaeghen, P., 2005. Aging and verbal memory span: a meta-analysis. J Gerontol B-Psychol 60, 223-233.

Cabeza, R., Anderson, N.D., Houle, S., Mangels, J.A., Nyberg, L., 2000. Age-related diferences in neural activity during item and temporal-order memory retrieval: A positron emission tomography study. J Cognitive Neurosci 12, 197-206.

Cappell, K.A., Gmeindl, L., Reuter-Lorenz, P.A., 2010. Age differences in prefontal recruitment during verbal working memory maintenance depend on memory load. Cortex 46, 462-473.

DeLuca, J., 2005. Fatigue, Cognition and Mental Effort, in: DeLuca, J. (Ed.), Fatigue as a window to the brain. MIT Press, Cambridge, Mass.; London, pp. 37 - 58.

Dennis, N.A., Hayes, S.M., Prince, S.E., Madden, D.J., Huettel, S.A., Cabeza, R., 2008. Effects of aging on the neural correlates of successful item and source memory encoding. J Exp Psychol Learn 34, 791-808.

Grady, C.L., Springer, M.V., Hongwanishkul, D., McIntosh, A.R., Winocur, G., 2006. Age-related changes in brain activity across the adult lifespan. J Cogn Neurosci 18, 227-241.

Huettel, S.A., Song, A.W., McCarthy, G., 2008. Functional Magnetic Resonance Imaging, 2nd Edition. Sinauer Associates, Inc., Sunderland, Massachusetts USA.

Jolles, J., Houx, P., van Boxtel, M.P., Ponds, R., 1995. Maastricht Aging Study: determinants of cognitive aging. Neuropsych Publishers, Maastricht.

Kato, Y., Endo, H., Kizuka, T., 2009. Mental fatigue and impaired response processes: event-related brain potentials in a Go/NoGo task. Int J Psychophysiol 72, 204-211.

Koppelstaetter, F., Poeppel, T.D., Siedentopf, C.M., Ischebeck, A., et al., 2008. Does caffeine modulate verbal working memory processes? An fMRI study. Neuroimage 39, 492-499.

Lorist, M.M., 2008. Impact of top-down control during mental fatigue. Brain research 1232, 113-123.

Lorist, M.M., Boksem, M.A., Ridderinkhof, K.R., 2005. Impaired cognitive control and reduced cingulate activity during mental fatigue. Brain Res Cogn Brain Res 24, 199-205.

Mathis, A., Schunck, T., Erb, G., Namer, I.J., Luthringer, R., 2009. The effect of aging on the inhibitory function in middle-aged subjects: a functional MRI study coupled with a color-matched Stroop task. Int J Geriatr Psychiatry 24, 1062-1071.

Nagel, I.E., Preuschhof, C., Li, S.C., Nyberg, L., Backman, L., et al., 2009. Performance level modulates adult age differences in brain activation during spatial working memory. Proc Natl Acad Sci USA 106, 22552-22557.

Nehlig, A., 2010. Is caffeine a cognitive enhancer? Journal of Alzheimer's disease: JAD 20 Suppl 1, S85-94.

Park, D.C., Lautenschlager, G., Hedden, T., Davidson, N.S., Smith, A.D., et al., 2002. Models of visuospatial and verbal memory across the adult life span. Psychol Aging 17, 299-320.

Park, D.C., Reuter-Lorenz, P., 2009. The adaptive brain: aging and neurocognitive scaffolding. Ann Rev Psychol 60, 173-196.

Persson, J., Welsh, K.M., Jonides, J., Reuter-Lorenz, P.A., 2007. Cognitive fatigue of executive processes: interaction between interference resolution tasks. Neuropsychologia 45, 1571-1579.

Reuter-Lorenz, P.A., Cappell, K.A., 2008. Neurocognitive aging and the compensation hypothesis. Curr Dir Psychol Sci 17, 177-182.

Salthouse, T.A., 2003. Memory aging from 18 to 80. Alzheimer Dis Assoc Disord 17, 162-167.

Salthouse, T.A., 2009. When does age-related cognitive decline begin? Neurobiol Aging 30, 507-514.

Schneider-Garces, N.J., Gordon, B.A., Brumback-Peltz, C.R., Shin, E., Lee, Y., et al., 2010. Span, CRUNCH, and Beyond: Working Memory Capacity and the Aging Brain. J Cogn Neurosci 22, 655-669.

Smit, A.S., Eling, P.A., Coenen, A.M., 2004. Mental effort causes vigilance decrease due to resource depletion. Acta Psychol 115, 35-42.

Snel, J., Lorist, M., Tiegers, Z., 2004. Coffee, Caffeine, and Cognitive Performance, in: Nehlig, A. (Ed.), Coffee, Tea, Chocolate, and the Brain. CRC Press, Florida, pp. 53-72.

van der Elst, W., van Boxtel, M.P., van Breukelen, G.J., Jolles, J., 2005. Rey's verbal learning test: normative data for 1855 healthy participants aged 24-81 years and the influence of age, sex, education, and mode of presentation. JINS 11, 290-302.

van der Elst, W., Van Boxtel, M.P., Van Breukelen, G.J., Jolles, J., 2006a. The Concept Shifting Test: adult normative data. Psychol Assessment 18, 424-432.

van der Elst, W., van Boxtel, M.P., van Breukelen, G.J., Jolles, J., 2006b. The Letter Digit Substitution Test: normative data for 1,858 healthy participants aged 24-81 from the Maastricht Aging Study (MAAS): influence of age, education, and sex. J Clin Exp Neuropsychol 28, 998-1009.

van der Elst, W., Van Boxtel, M.P., Van Breukelen, G.J., Jolles, J., 2006c. Normative data for the Animal, Profession and Letter M Naming verbal fluency tests for Dutch speaking participants and the effects of age, education, and sex. JINS 12, 80-89.

van der Linden, D., Frese, M., Meijman, T.F., 2003. Mental fatigue and the control of cognitive processes: effects on perseveration and planning. Acta Psychol 113, 45-65.

van Dijk, K.R., Van Gerven, P.W., Van Boxtel, M.P., Van der Elst, W., Jolles, J., 2008. No protective effects of education during normal cognitive aging: results from the 6-year follow-up of the Maastricht Aging Study. Psychol Aging 23, 119-130.