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Navigational Strategy Switching in Ageing

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Abstract

With advancing age, many cognitive faculties deteriorate, and navigation abilities may be among those most affected. The majority of previous work investigating navigation impairments in ageing has focused on allocentric processing, attributing deficits to hippocampal dysfunction. However, real-world navigation is dependent upon numerous different strategies, as well as the ability to flexibly switch between them. Outside the context of navigation, it has been demonstrated that strategy switching, thought to be coordinated by regions of prefrontal cortex and the locus coeruleus-noradrenergic system, is also susceptible to the effects of ageing. Deficits in navigational strategy switching, and prefrontal or noradrenergic dysfunction, are therefore also likely to contribute to age-related navigation impairments. The work presented in this thesis aimed to explore age-related impairments in strategy switching within the context of navigation, and the underlying neural mechanisms in terms of a prefrontal-noradrenergic model of switching.

The studies presented in Chapter Three assessed the use of allocentric and egocentric navigational strategies by young and older people. Older participants tended to use an egocentric strategy where an allocentric strategy was required, possibly due to a difficulty in switching to the appropriate allocentric strategy. In Chapter Four, I provide an account of two studies directly assessing navigational strategy switching, using two different tasks based in virtual reality. The first study utilised a virtual adaptation of the plus maze task, involving switching between an allocentric place strategy and an egocentric response strategy, and demonstrated that older participants were specifically impaired at switching to the place strategy. The second study used a more realistic task set in a virtual town environment, which involved switching from an egocentric route-following strategy to an allocentric wayfinding strategy, and also demonstrated an age-related deficit in switching to an allocentric strategy.

In Chapter Five, I begin to explore the mechanisms underlying impaired navigational strategy switching in ageing. Firstly, I describe a further behavioural study that used variants of the virtual plus maze and a navigational gambling task to demonstrate a

contribution of impaired decision making to the deficit in switching to an allocentric strategy. This indicates that the deficit can be attributed, at least in part, to prefrontal dysfunction. A second study presented in the same chapter demonstrated that practising orienteering does not protect against decline in navigational strategy switching ability with ageing. Chapter Six provides an account of my direct assessment of the neural bases of navigational strategy switching using functional magnetic resonance imaging. In young subjects, I found some evidence in support of the roles of prefrontal regions in navigational strategy switching. However, I was unable to complete development of a task suitable for assessing age differences in functional activation of brain regions involved in navigational strategy switching.

The final experimental study, included in Chapter Seven, assessed pupil size and heart rate as physiological correlates of noradrenergic activity during performance of the virtual plus maze. Both young and old participants demonstrated a noradrenergic response to all strategy changes, suggesting that impairments are more likely attributable to dysfunction of prefrontal cortex than of the locus coeruleus, although some subtle effects suggested that noradrenergic dysfunction does have some effect on navigational strategy switching deficits. In the same chapter, I report the results of a meta-analysis of data from five of the preceding studies, suggesting that deficits in both strategy switching and allocentric processing combine to produce a greater impairment in switching to an allocentric strategy.

The main finding of this series of studies is that navigational strategy switching is impaired in ageing, which may contribute to the more widely reported difficulties that older people have with navigation. My work also provides evidence in support of a prefrontal-noradrenergic model of navigational strategy switching, and suggests that dysfunction of prefrontal cortex and, to a lesser extent, the locus coeruleus-noradrenergic system is responsible for decline in navigational strategy switching ability with ageing. In conclusion, this thesis draws attention to the important role of deficient executive processing and dysfunction of extra-hippocampal brain regions in age-related navigation impairments.

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Publications

The following publications arose from studies presented as part of this thesis:

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Wiener, J.M., de Condappa, O., Harris, M.A. & Wolbers, T. (2013). Maladaptive bias for extrahippocampal navigation strategies in aging humans. *Journal of Neuroscience*, 33: 6012-6017.

Harris, M.A. & Wolbers, T. (2014). How age-related strategy switching deficits affect wayfinding in complex environments. *Neurobiology of Aging*, 35: 1095-1102.

Two further papers are currently under preparation:

Harris, M.A., Wolbers, T. Pupillary responses in older people during navigational strategy switching suggest deficits are not due to locus coeruleus-noradrenergic dysfunction.

Harris, M.A., Gauld, O.M., Zangemeister L.J.A. Decision making deficits and impaired navigational strategy switching in ageing.

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Abbreviations

ACC	Anterior cingulate cortex
ANOVA	Analysis of variance
ASST	Attentional set-shifting task
ATT	Alternative approach task
BL	Blocks learned
BOLD	Blood oxygen level dependent
BPS	British Psychological Society
CANTAB	Cambridge Neuropsychological Test Automated Battery
CBF	Cerebral blood flow
CBV	Cerebral blood volume
CCNS	Centre for Cognitive and Neural Systems
CDF	Cumulative distribution function
CMT	Cogntive mapping test
CRF	Corticotropin-releasing factor
dlPFC	Dorsolateral PFC
DNAB	Dorsal noradrenergic bundle
DZNE	German Center for Neurodegenerative Diseases
EPI	Echo planar imaging
fMRI	Functional MRI
FWE	Familywise error
gLM	General linear model
GLM	Generalised linear model
hMT+	Human motion complex
HR	Heart rate
HRF	Haemodynamic response function
HRT	Hormone replacement therapy
HSD	Honestly significant difference
IDED	Intra-dimensional/extra-dimensional set-shifting subtest of CANTAB
IGT	Iowa Gambling Task
LC	Locus coeruleus

LDT	Landmark direction test
LPT	Landmark position test
M	Mean
MCI	Mild cognitive impairment
MMSE	Mini Mental State Examination
MoCA	Montreal Cognitive Assessment
mPFC	Medial PFC
MRI	Magnetic resonance imaging
MVPA	Multi-voxel pattern analysis
NA	Noradrenaline
NART	National Adult Reading Test
NGT	Navigational gambling task
No-DM	No decision making
OFC	Orbitofrontal cortex
PD	Parkinson's disease
PFC	Prefrontal cortex
PMd	Dorsal premotor cortex
PME	Perceived mental effort
PPLS	School of Philosophy, Psychology and Language Sciences
PS	Pupil size
RF	Radio frequency
RFX	Random effects
RLT	Route learning task
ROI	Region of interest
R-P	Reverse place
R-R	Reverse response
RSC	Retrosplenial cortex
RSPM	Raven's Standard Progressive Matrices
SD	Standard deviation
SEM	Standard error of the mean
S-P	Switch to place
S-R	Switch to response

ST	Stable trials
SVC	Small volume correction
SWMT	Spatial working memory task
TC	Trials correct
TMT-B	Trail-Making Test Part B
TR	Repetition time
UCSB	University of California Santa Barbara
V1	Primary visual cortex
VE	Virtual environment
vmPFC	Ventromedial PFC
VPM	Virtual plus maze
VNAB	Ventral noradrenergic bundle
VR	Virtual reality
WCST	Wisconsin card sorting task

Chapter One – Introduction

1.1 Cognitive ageing

1.1.1 Normal ageing

Ageing refers to a degenerative process experienced in later life, characterised by the deterioration of physical and mental health and ability. It is associated with greatly increased incidence of many serious diseases and disorders, including cardiovascular disease, cancer and dementia (Gao et al., 1998; Sniderman & Furberg, 2008; Gerashchenko, 2010; Niccoli & Partridge, 2012). However, age-related decline occurs even in the absence of such diseases. For instance, muscle strength declines to around 80% of its peak level at age 25 by age 65, and to around 50% by age 95 (Beenakker et al., 2010). Athletic performance also declines gradually until around 65 years, and then exponentially thereafter (Tanaka & Seals, 2003). Similarly, cognitive decline is observed in the absence of dementia and other neurodegenerative diseases. The Seattle Longitudinal Study made repeated measurements of many facets of cognitive ability, and demonstrated a gradual decline until age 60, followed by an increasingly steep decline throughout later life (Schaie et al., 2004; Schaie & Willis, 2010). Such changes are regarded as aspects of normal ageing, which is generally considered an inevitable part of life. The progressive, deteriorative process of normal ageing has been said to universally affect everyone, as influenced by endogenous factors (Strehler, 1977; Viña et al., 2007).

However, there are substantial individual differences in rate of decline (Poehlman et al., 1993; Wilson et al., 2002; Raz et al., 2010), which do seem to relate to environmental and behavioural factors, such as area of residence, diet and physical activity (Morgan et al., 2000; Roberts & Schoeller, 2007; Archer et al., 2011; Santangelo et al., 2011). An ever-increasing volume of research has therefore focused on the mechanisms underlying the process of normal ageing. Developing theories generally attribute physical and mental decline to cell death, whether this in turn is programmed by genetic factors (Kuro-o, 2000; Davidovic et al., 2010) and

moderated by endocrine or immune function (Walford, 1964; Tatar et al., 2003); caused by general wear and tear (Weissman, 1891; Pearl, 1928; Viña et al., 2007), exposure to free radicals (Harman, 1956; Finkel & Holbrook, 2000), or accumulation of gene mutations and epigenetic changes (Kanungo, 1975; Freitas & de Magalhães, 2011); or attributable to a limit on the number of cell replications imposed by the shortening of telomeres (Hayflick & Moorhead, 1961; Jiang et al., 2007). Some of these theories suggest that ageing may be avoidable (Rapp & Amaral, 1992; de Grey et al., 2002), or at least amenable to treatment (Weinert & Timiras, 2003; Niccoli & Partridge, 2012). Recent research therefore aims to contribute not only to our further understanding of the ageing process, but also to the mitigation and prevention of the deleterious effects of normal ageing.

1.1.2 Cognitive decline

Cognitive abilities and brain regions affected by ageing

Cognitive decline is an important aspect of normal ageing, which, sooner or later, affects us all. However, there is substantial variability in the effects of ageing across cognitive abilities and supporting brain regions, as well as between individuals. Some abilities, including vocabulary, some numerical abilities and general knowledge, are less susceptible to the effects of ageing, whereas processing speed, reasoning, executive functioning, memory and spatial abilities begin to deteriorate even before old age (Deary et al., 2009; Salthouse, 2010). Generally, measures affected by ageing reflect processing efficiency in old age, whereas unaffected measures reflect the acquisition of information earlier in life (Salthouse, 2010). Cattell (1943) categorised abilities that were and were not prone to age-related decline as fluid and crystallised intelligence, respectively. Others have subsequently demonstrated an ageing-related distinction between the two. For example, Cunningham, Clayton and Overton (1975) administered Raven's Standard Progressive Matrices (RSPM), a test of non-verbal reasoning and of fluid intelligence, and the Wechsler Adult Intelligence Scale (WAIS) vocabulary subtest, as a test of crystallised intelligence, to 35 young (aged ~19) and 40 older (aged 60-

79) participants. As would be predicted by decline in fluid but not crystallised intelligence, the correlation between the two was significantly weaker within the older group than in the young. A much larger-scale study of 1500 adults (aged 17-94) also demonstrated that, while four measures of fluid intelligence demonstrated steady decline throughout middle age and rapid decline in old age, four measures of crystallised intelligence only showed moderate decline in old age (Kaufman & Horn, 1996).

Cognitive decline is accompanied by substantial neurophysiological changes, most noticeably an overall decrease in brain volume (Scahill et al., 2003; Deary et al., 2009; Takao et al., 2012), although various regions are differentially affected by ageing-related atrophy. The most substantial volume decreases are evident in prefrontal cortex (PFC), the medial temporal lobe, and the cerebellum (Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011). Deterioration of hippocampus and PFC in particular has been directly associated with decline in memory and executive functioning, respectively (Yankner et al., 2008; Kaup et al., 2011). Cerebellar atrophy may underlie age-related decline in physical coordination (Kennedy & Raz, 2005; Seidler et al., 2010). There is also a specific association between cognitive decline and reductions in prefrontal white matter volume and integrity (Raz et al., 2005; Hinman & Abraham, 2007; Deary et al., 2009), suggesting that reduced functional connectivity between regions may be important in cognitive ageing (O'Sullivan et al., 2001; Gunning-Dixon et al., 2009).

Rate of cognitive decline and mediating factors

In 1956, Warner Schaie began the Seattle Longitudinal Study, a large-scale assessment of changes in cognitive ability (Schaie, 1989; Schaie et al., 2004; Schaie & Willis, 2010). He first tested 500 participants of various ages on measures of inductive reasoning, numeric ability, verbal ability, verbal memory and spatial orientation; Thurstone's primary mental abilities (Thurstone, 1938; Schaie, 1989). At seven-year intervals, he and others then tested as many of these original participants as possible again on the same measures, and later on additional measures of

perceptual speed (Schaie et al., 2004). They also introduced a cohort of several hundred new participants at each stage, who were then also retested at seven-year intervals thereafter. While decline was observed in all measures (*figure 1.1 top*), those of fluid intelligence, such as numeric ability and perceptual speed, showed the greatest and earliest decline, beginning even in early adulthood and accelerating throughout middle and old age. Verbal ability, as a measure of crystallised intelligence, continued to increase throughout adulthood, and declined by less throughout old age, up until very old age, at which point it showed equivalent or even greater decline. Inductive reasoning, verbal memory and spatial orientation were also maintained or improved throughout adulthood, but then declined increasingly rapidly throughout old age. Others have confirmed that rate of cognitive decline increases exponentially throughout ageing (Wilson et al., 2002; Finkel et al., 2007; Mitnitski & Rockwood, 2008). Neurodegeneration also accelerates with ageing (*figure 1.1 bottom*), in terms of both changes in whole brain volume (Deary et al., 2009; Fjell et al., 2009; Takao et al., 2012) and atrophy of particularly susceptible regions, including the hippocampus, PFC and cerebellum (Jernigan et al., 2001; Raz et al., 2005, 2010). Furthermore, rate of atrophy is directly related to rate of cognitive decline (Mungas et al., 2005; Sluimer et al., 2008).

Studies of the Lothian Birth Cohort 1936 have assessed cognitive ability, environmental factors and genetic make-up in a large group of older people who were also tested on the Moray House Test in 1947 at age 11 (Deary et al., 2007). The genes APOE, COMT, PRNP, DISC1, BDNF have all been identified as contributing to rate of cognitive decline (Harris et al., 2005; Kachiwala et al., 2005; Thomson et al., 2005; Harris et al., 2006). Those with allele E4 of the APOE gene in particular, which has also been associated with dementia risk, show greater decline in perceptual speed, episodic memory and executive functioning (Deary et al., 2009). Endocrine function has also been associated with rate of cognitive decline, and hormone replacement therapy (HRT) may in fact alleviate the effects of cognitive ageing (Sherwin, 2002). There is a degree of interdependence between cognitive and physical ageing, as, for example, cardiovascular ageing can affect cerebral blood flow (CBF) and thereby impair neurocognitive functioning (Rafnsson et al., 2007;

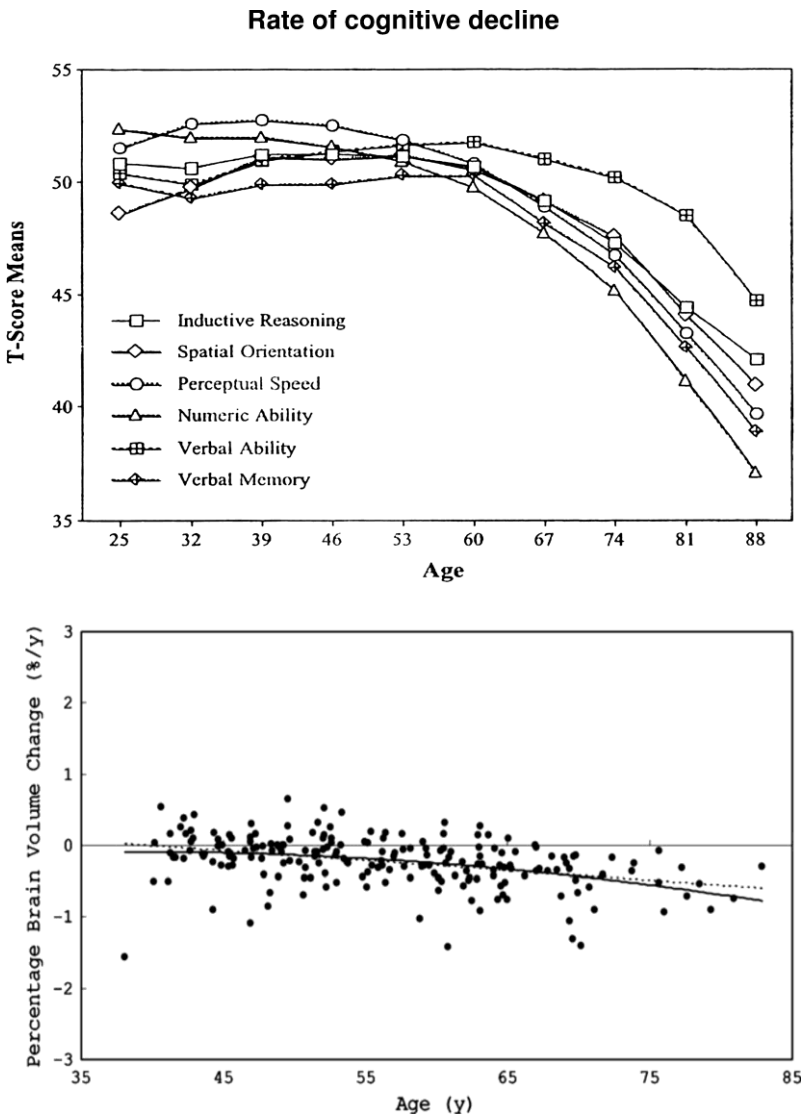

Figure 1.1 Rate of cognitive decline. *Top:* measures of inductive reasoning, spatial orientation, perceptual speed, numeric ability, verbal ability and verbal memory by age, each demonstrating an exponential rate of decline. From Schaie et al. (2004). *Bottom:* annual change in whole brain volume by age, also showing an exponential rate of decline. From Takao et al. (2012).

Haley et al., 2009; Okonkwo et al., 2010).

Rate of cognitive decline also seems to depend upon intelligence in early life (Leibovici et al., 1996; Snowdon et al., 1996; Deary et al., 2000), years or level of education (Leibovici et al., 1996; Alley et al., 2007; Kaufman et al., 2009), and occupational status (Dartigues et al., 1992; Finkel et al., 2009). In combination, such

factors may contribute to a 'cognitive reserve', which can reduce the effects of neurobiological decline on cognitive performance (Stern, 2003; Whalley et al., 2004; Allen et al., 2005). Many lifestyle factors may also improve or exacerbate cognitive decline, including diet (Solfrizzi et al., 2003; Van Dyk & Sano, 2007), exercise (Yaffe et al., 2001; Kramer et al., 2004; Sofi et al., 2011), social interaction (Krueger et al., 2009; James et al., 2011), sleep (Jelicic et al., 2002; Keage et al., 2012), smoking (Anstey et al., 2007; Nooyens et al., 2008) and alcohol consumption (Ganguli et al., 2005; Sabia et al., 2014).

1.1.3 Impact

Cognitive ageing can have subtle or even severe effects on the lives of older individuals. Older people may find it more difficult to perform everyday tasks (Burton et al., 2006; Gross et al., 2011), to interact as effectively with others (Phillips et al., 2011; Moran et al., 2012) and even to find their way around their environment (Kirasic, 2000; Moffat, 2009). This last point, perhaps being particularly problematic in old age, is discussed in more detail later in this chapter, and is considered throughout the rest of this thesis. Cognitive decline may also impact on important life decisions, regarding, for example, finances and medical treatment (Moye & Marson, 2007). The combined effects of cognitive decline upon the lives of older individuals make it more difficult for them to remain independent, and many require care from family members, as well as social and health care organisations, thereby contributing to the social and economic burden associated with ageing (Deary et al., 2009). As the population ages (Lutz et al., 2008), the implications of cognitive ageing for individuals and society are becoming increasingly important.

1.1.4 Interventions

The individual and global impact of cognitive ageing make it ever more important to identify potential methods of preventing, mitigating or remedying cognitive decline. One method that has been trialled is cognitive training. Specific training regimens include learning mnemonic strategies (Ball et al., 2002; Brehmer et al., 2008),

practising visual searching and problem solving (Gräsel, 1994; Ball et al., 2002), and playing commercially available 'brain training' games (Gates & Valenzuela, 2010; McDougall & House, 2012; Nouchi et al., 2012). Such interventions have alleviated age-related decline in memory (Brehmer et al., 2008; McDougall & House, 2012; Maseda et al., 2013), reasoning (Ball et al., 2002; Boron et al., 2007), executive functioning (Basak et al., 2008; Nouchi et al., 2012), and processing speed (Ball et al., 2002; Nouchi et al., 2012; Wolinsky et al., 2013), although some research suggests that benefits are limited to the abilities that are trained (Ball et al., 2002; Park & Bischof, 2013). However, cognitive training can also preserve hippocampal volume (Lövdén et al., 2012), prevent deterioration of cortical thickness and white matter integrity (Belleville & Bherer, 2012) and even produce increases in neural volume (Park & Bischof, 2013), which is likely to provide a more general advantage. Pharmacological interventions have also been developed, achieving some success (Landfield et al., 1981; Andrade & Radhakrishnan, 2009; Koh, 2012), and, as mentioned above, HRT may protect against the effects of cognitive ageing.

Physical exercise has also been associated with increases in hippocampal volume and neurogenesis (Ahlskog et al., 2011; Erickson et al., 2011), as well as retention of prefrontal grey matter volume (Colcombe et al., 2006; Ahlskog et al., 2011). Meta-analyses of numerous intervention trials suggest that physical exercise mitigates decline in processing speed, executive function and memory (Smith et al., 2010; Ahlskog et al., 2011). Even short-term exercise interventions have been shown to produce improvements in cognitive functioning (Aguiar et al., 2011; Chapman et al., 2013). As mentioned earlier, other aspects of lifestyle – such as sleeping, social interaction, smoking and alcohol consumption – seem to affect the ageing process, so active management of these factors may also provide benefits. However, while the continued exploration of interventions is important, the future management of age-related decline also critically depends upon improving our understanding of the underlying mechanisms.

1.2 Navigation

1.2.1 Spatial cognition

Spatial cognition refers to the ability to learn and use information about the three-dimensional (3D) properties of objects and the spatial relations between them. As mentioned in the previous section, spatial abilities are among those that are particularly susceptible to the effects of cognitive ageing. Small-scale spatial cognition, or visual-spatial ability, usually revolves around the visualisation and manipulation of objects, such as in drawing or constructing a model (Mervis et al., 1999). It is generally assessed using tasks that require participants to replicate a spatial configuration, or visualise a spatial transformation. For example, in block design tasks, participants view an image of a configuration of blocks, then must produce that configuration from a number of patterned blocks (Wechsler, 1958; Schorr et al., 1982). Mental rotation tasks involve viewing images of 3D shapes from different angles, usually comparing two images and judging whether they feature the same 3D shape (Shepard & Metzler, 1971; Vandenberg & Kuse, 1978; *figure 1.2*). Studies using block design and mental rotation tasks have implicated visual, motor and premotor cortex and the superior parietal lobule in spatial cognition (Vingerhoets et al., 2002; Wanzel et al., 2007; Bölte et al., 2008). Visual-spatial ability is involved in a variety of everyday tasks (Mervis et al., 1999) and is important for specialist occupational skills such as performing surgery (Wanzel et al., 2002).

Spatial cognition also encompasses navigation, the process by which we move around our environment. More specifically, navigation involves the use of various external and self-motion cues, together with existing knowledge of the environment, in order to plan a route to a target location, and then coordinate movement along the planned route (Burgess, 2008; Wolbers & Hegarty, 2010). While many animals, particularly humans, rely heavily on visual landmarks (Muller & Kubie, 1987; Etienne et al., 1996; Riecke et al., 2002), we may also make use of auditory (Walker & Lindsay, 2006; Watanabe & Yoshida, 2007) and olfactory (Porter et al., 2007; Moessnang et al., 2011) cues, and some animals also rely on other information, such

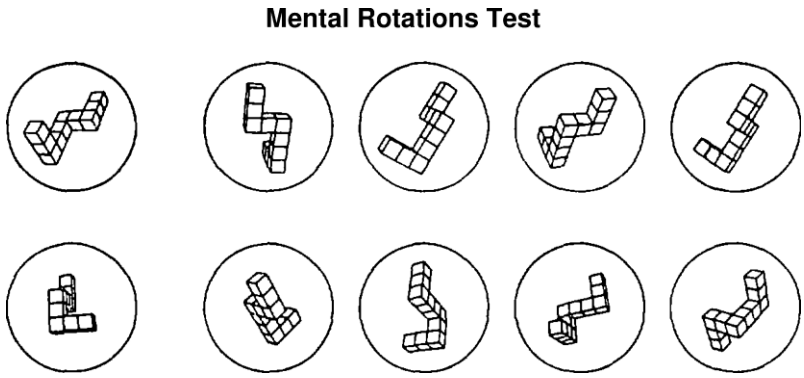

Figure 1.2 Mental Rotations Test. Participants must identify which of the four images on the right depict the same 3D shape as the image on the left from an alternative orientations. In the first example, the first and fourth alternatives are correct, whereas the others are mirror images of the stimulus shape. In the second, the second and third are correct, while the others are different shapes. From Vandenberg & Kuse (1978).

as magnetic fields (Cain et al., 2005; Putman et al., 2014). Self-motion cues come from the vestibular system, which provides information on head orientation and acceleration (Angelaki & Cullen, 2008; Zeng & Zhao, 2011), proprioceptive sensors, which monitor musculoskeletal position and provide feedback on bodily movements (Kelso et al., 1980; Hasan & Stuart, 1988), and optic flow, which refers to the rate of movement of visual information across the retina, providing information on movement speed (Koenderink, 1986; Lappe et al 1999). Existing knowledge of the environment may include egocentric or allocentric representations of landmarks, specific routes or the spatial layout of the environment (Siegel & White, 1975; Burgess, 2008; Chrastil, 2013), all of which are discussed in further detail in the next section. Although navigation operates on a much larger scale than visual-spatial processes, it still depends on knowledge of 3D spatial properties, and has been shown to relate to tests of small-scale spatial ability (Kirasic, 2000; Malinowski, 2001). Further, while navigation may involve travelling complex routes over great distances, even moving to the next room depends upon navigational processing, illustrating just how essential spatial cognition is to everyday life.

1.2.2 Navigational processes

Path integration

One of the most fundamental purposes of navigation, from an evolutionary perspective, is to find food, or rather, after having found food, to determine the way back home. This can be achieved by path integration, which describes the continuous and automatic monitoring of an animal's position and orientation relative to a fixed home base, based on cues derived from self-motion (Loomis et al., 1999; Etienne & Jeffery, 2004; Kubie & Fenton, 2009). By integrating information about movements, animals can compute a homing vector, so that when they do find food, they can then follow a direct course home. Experiments with ants have found that, if transposed at a food location, the ants still try to return to their origin by following the same homing vector, as if their origin had also been transposed by the same amount (Wehner et al., 2002; Andel & Wehner, 2004). As it had not, of course, ants then circle around until they find their original starting position, the inefficiency of which demonstrates how useful path integration can be. Some studies of mammals also provide evidence of dependence upon path integration (Mittelstaedt & Mittelstaedt, 1980; Etienne & Jeffery, 2004; Kubie & Fenton, 2009).

Human path integration has been studied using triangle completion tasks, which involve guiding participants along the first two sides of a triangular path, then asking them to return to their starting position, thus completing the triangle. Participants complete the task blindfold or in darkness in order to eliminate visual cues, although this does also exclude self-motion information usually received via optic flow. Still, such experiments demonstrate that humans can also navigate by path integration, over short distances at least (Loomis et al., 1993; Marlinsky, 1999; Kearns et al., 2002). Allen, Kirasic, Rashotte and Haun (2004) had participants complete a triangle completion task both blindfold and in a wheelchair, thereby eliminating proprioceptive as well as visual cues, and showed that participants could still find their way back towards their starting position using only vestibular information. Experiments in virtual reality (VR) have also demonstrated that triangle completion

task performance is possible relying solely on optic flow (Mahmood et al., 2009; Wan et al., 2010; Harris & Wolbers, 2012), although, when other self-motion cues are also available, they tend to have more of an influence on path integration performance (Kearns et al., 2002).

Over greater distances, errors accumulate quickly, and humans cannot navigate by path integration as effectively (Loomis et al., 1999; Etienne et al., 1996; Etienne & Jeffery, 2004). However, animals use visual landmarks to correct errors in path integration (Collett, 1996; Etienne et al., 1996, 2004) and human path integration performance is vastly improved by the additional availability of landmark information (Riecke et al., 2002). When navigating familiar environments, humans rely primarily on cognitive maps, discussed below; however, path integration is still useful in navigating unfamiliar environments, and plays an important role in the formation of cognitive maps (Gallistel & Cramer, 1996; Montello, 1998; Loomis et al., 1999; Wolbers & Hegarty, 2010). This also applies to spatial updating, an extension of path integration, which updates egocentric vectors to multiple locations, rather than just a single origin (Burgess, 2008; Wolbers et al., 2008).

Route navigation

Path integration provides some animals with an efficient way of finding their way back home. However, humans are unable to compute accurate homing vectors over large distances, and even if we were, we would rarely be able to follow them through the urban and cultivated environments we usually navigate. Furthermore, while some animals are content to spend most of their lives randomly foraging for food, humans generally are not. We prefer to visit the same locations routinely, such as our places of work, for which path integration does not provide a suitable mechanism. Instead, we remember information about routes between familiar locations, so that we may take the same route the next time we make the same journey. A familiar route is encoded as a procedural sequence, i.e. in terms of a series of movement responses required at decision points (Foo et al., 2005; Waller & Lippa, 2007; Wiener et al., 2012). For example, *figure 1.3* depicts the route from my house to the local shop (in

red). I can encode this route as follows: from my front door, turn left; at the big oak tree, turn right; at the next T-junction, turn left; and at the post box, turn right. This kind of route navigation operates in an egocentric reference frame (Iglói et al., 2009; Wolbers & Hegarty, 2010; Wiener et al., 2012), as the route representation is described in terms of my own position and movements.

The benefit of route navigation is that it requires very little cognitive effort, with route knowledge consisting of very little to remember (Hartley et al., 2003; Foo et al., 2005; Iglói et al., 2009). In the above example, a route covering half a mile is reduced to three simple associative responses. The major disadvantage of route knowledge is that it is inflexible, applying only to one specific route (Hartley et al., 2003; Wolbers & Hegarty, 2010). For example, knowledge of the route from my house to the local shop will not help me get to any other location. If the local shop does not have everything I need and I then have to go to the supermarket, doing so by the same navigational process would depend on another separately encoded procedural sequence (shown in green). In fact, being encoded as a sequence, i.e. in one particular direction, the original route representation does not even get me back home from the local shop. It is sometimes possible to retrace a route that has just been traversed by following the same landmarks (Whishaw et al., 2001; Waller & Lippa, 2007), but only if they are also visible from the opposite direction, and from the preceding decision point along the return route. Otherwise, retracing my route would depend upon objective knowledge of the spatial relationships between elements of the route, i.e. an allocentric representation (Wiener et al., 2012). Furthermore, if I wanted to take a direct route home from the supermarket (shown in blue), and if I had not previously travelled this route, this would require an even more extensive allocentric representation of my village, known as a cognitive map.

Cognitive mapping

A cognitive map is an allocentric internal representation of an environment, which encodes the positions of landmarks and locations within the environment in relation to each other (O'Keefe & Nadel, 1978; Gallistel & Cramer, 1996; Foo et al., 2005).

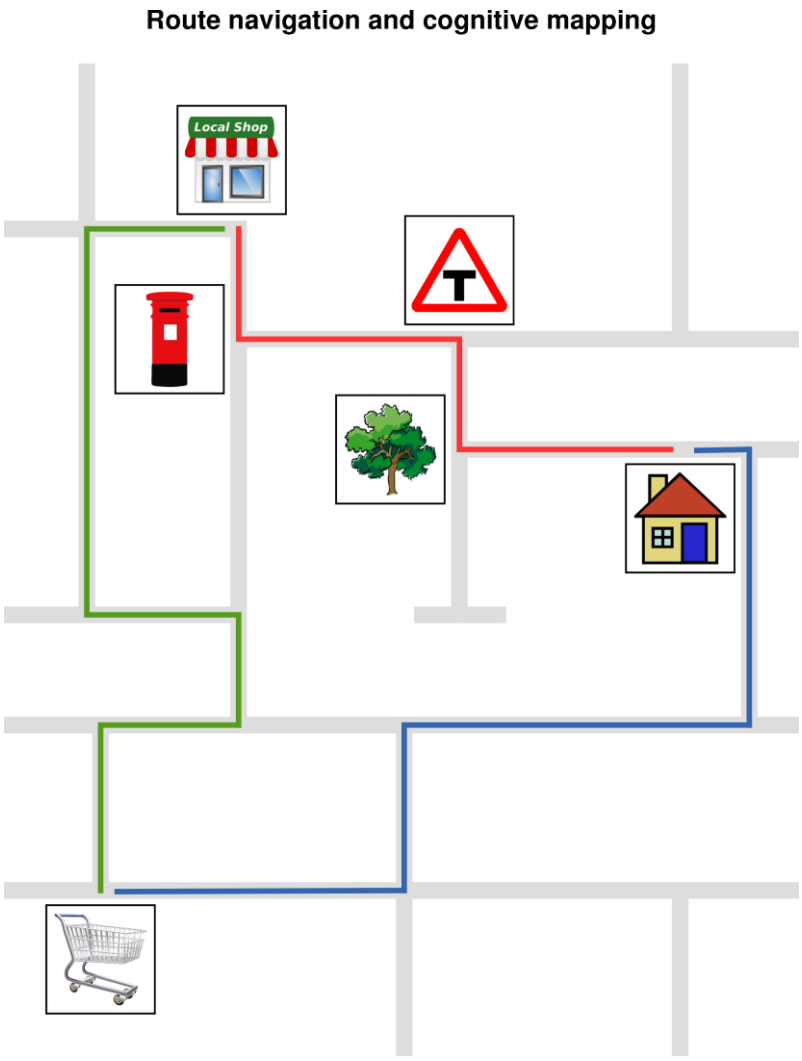

Figure 1.3 Route navigation and cognitive mapping. The route from my house to the local shop (in red) can be encoded as a sequence of movements required at specific points; the oak tree, the T-junction and the post box. The route from there to the supermarket (in green) can be encoded as another egocentric procedural sequence. Calculating the shortest route home from there (in blue) would require a cognitive map of the environment.

The concept was first proposed by Tolman (1948), who argued that rodent navigation of complex mazes required more than just stimulus-response learning. In contrast to route knowledge, cognitive maps feature metric information about the distances and directions between places, and integrate knowledge of various spatial regions (Foo et al., 2005; Jeffery & Burgess, 2006; Wolbers & Hegarty, 2010). They therefore provide a much more flexible navigational mechanism, which allows animals and humans to draw inferences about the spatial relations between locations they have

not travelled between, facilitating the efficient computation of novel routes, shortcuts and detours (Bennett, 1996; Foo et al., 2005; Wolbers & Hegarty, 2010). In the example given in the previous section and shown in *figure 1.3*, allocentric knowledge of the routes from my house to the local shop and from the local shop to the supermarket, and more importantly, the integration of this knowledge into the same allocentric representation of my village, allows me to take a direct route home from the supermarket, even if I have not travelled the route before.

Numerous studies have provided evidence that animals and humans navigate using a cognitive map. For example, Morris (1981) used a water maze to demonstrate that once rats had found a submerged platform, they were then able to swim directly to it from novel locations on subsequent trials. This suggests that the position of the platform had been encoded in a map-like representation of the maze environment. Chapuis and Varlet (1987) trained dogs on separate routes from a starting point to two food locations. During testing, the dogs visited both locations in turn by following a novel route from one to the other. This shows that they had combined knowledge of the two routes into an allocentric representation of the environment. The discovery of supporting cell types, discussed in the next section of this chapter, also provide evidence of navigation using a cognitive map (O'Keefe & Dostrovsky, 1971; Hafting et al., 2005; Moser et al., 2008). While some argue that simpler mechanisms can explain some of the evidence proposed to demonstrate use of a cognitive map (e.g. Bennett, 1996), it is still thought to be one of the primary mechanisms underlying human spatial navigation.

Animals cannot navigate using a cognitive map until they have formed such an allocentric representation of the environment. The classic model of cognitive map formation suggested that animals first learn information about landmarks, then develop knowledge of the routes between them, and finally integrate this route knowledge into a survey representation of the environment (Hart & Moore, 1973; Siegel & White, 1975; Dabbs et al., 1998). More recently, it has been proposed that acquisition of landmark, route and survey knowledge occurs simultaneously, with no qualitative shift from one representation to another (Montello, 1998; Ishikawa &

Montello, 2006). However, while acquisition of each form of spatial information may begin at the same time, encoding of cognitive maps, being more complex and extensive, may take the longest to complete. During the exploration of novel environments, distal landmarks and self-motion cues are important for the encoding of direction and distance information (Gallistel & Cramer, 1996; Montello, 1998; Loomis et al., 1999; Wolbers & Hegarty, 2010). Gradually, as a cognitive map begins to form, inferences about the spatial relations between familiar locations can be made in order to produce a more complete representation of the environment.

1.2.3 Navigational systems

Place, grid and head direction cells

Some brain cells are specialised for guiding navigation. So far, three types of navigational cell have been identified: place cells, grid cells and head direction cells. Place cells were first discovered in rodent hippocampus by O'Keefe and Dostrovsky (1971). They recorded electrophysiological signals from hippocampal cells during rats' free exploration of a square platform, and found that certain cells fired whenever the rats were in a particular place on the platform (*figure 1.4 top left*). These place cells fired independently of a rat's orientation, suggesting that they represented its position within an allocentric reference frame. Hippocampal place cells are therefore thought to represent the neural basis of the cognitive map (O'Keefe & Nadel, 1978; Maguire et al., 1999; Moser et al., 2008). They also exhibit prospective coding of future and potential trajectories (Ferbinteanu & Shapiro, 2003; Johnson & Redish, 2007; Ferbinteanu et al., 2011), showing that they are involved in navigational planning and decision making (Johnson et al., 2007; Catanese et al., 2012; Chersi & Pezzulo, 2012). Numerous other studies have confirmed the existence of hippocampal place cells in both animals (Muller & Kubie, 1987; Breese et al., 1989; Sharp et al., 1995) and humans (Ekstrom et al., 2003; Miller et al., 2013).

Grid cells were discovered more recently in entorhinal cortex (Hafting et al., 2005). As an animal moves around, these cells fire at regular intervals, along the lines of a

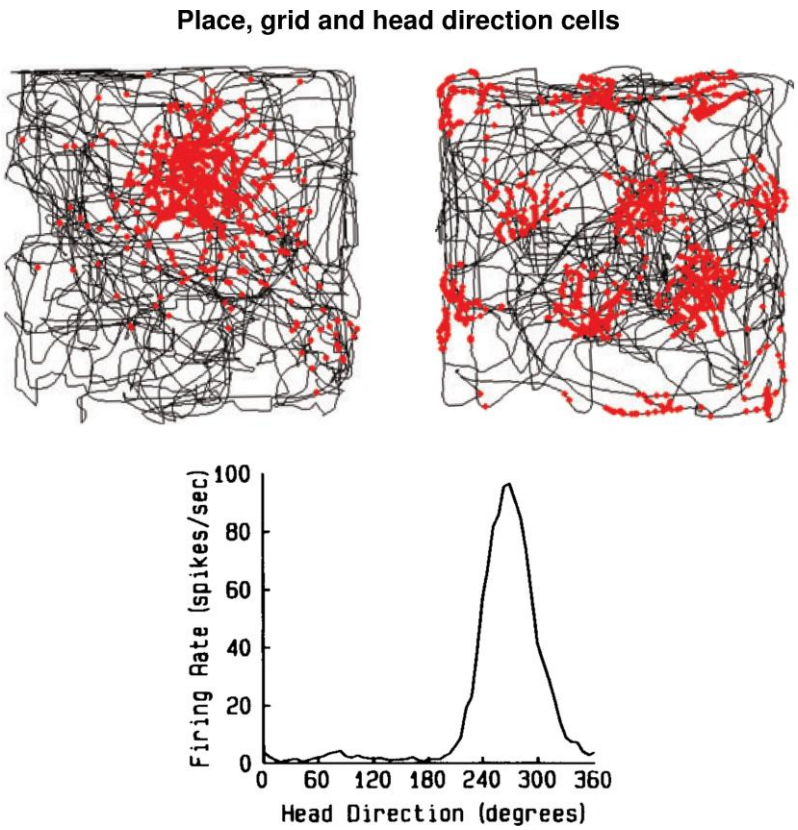

Figure 1.4 Place, grid and head direction cells. *Top*: locations at which a hippocampal place cell (*left*) and a medial entorhinal grid cell (*right*) fired during a rat's free exploration of a square platform (movement represented by black lines). From Moser et al. (2008). *Bottom:* a rodent head direction cell's firing rate by allocentric heading direction during free exploration. From Taube et al. (1990a).

triangular grid (*figure 1.4 top right*), based primarily on self-motion cues (Burgess, 2008; Wolbers & Hegarty, 2010). Furthermore, grid cells vary in terms of grid scale, or in terms of the spatial frequency at which they fire, which increases from ventral to dorsal entorhinal cortex (Hafting et al., 2005). This means that, while individual grid cells can represent distance information, the signals from multiple grid cells can, in combination, represent specific places (Solstad et al., 2006; Moser et al., 2008). In this way they are thought to drive hippocampal place cells, which entorhinal lesion studies also support (Brun et al., 2008; Van Cauter et al., 2008). The regular organisation of grid cells in entorhinal cortex produces a macroscopic signal that is detectable using functional magnetic resonance imaging (fMRI), providing evidence of grid cells in humans (Doeller et al., 2010). Single-cell recordings in humans have

found evidence of grid cells in entorhinal cortex that also encode direction information (Jacobs et al., 2010), most likely from head direction cells (Yoder et al., 2011).

Head direction cells are found in a number of brain regions, including postsubiculum, retrosplenial cortex and thalamus (Taube et al., 1990a; Taube, 1995; Epstein, 2008; Yoder et al., 2011). Taube, Muller and Ranck (1990a, 1990b) found that, as an animal freely explores its environment, these cells fire whenever the animal is facing in a certain direction, with firing rate peaking at a specific orientation (*figure 1.4 bottom*). The direction information provided by head direction cells – discerned from both self-motion cues and visual landmarks (Blair & Sharp, 1996; Knierim et al., 1998), particularly distal landmarks (Zugaro et al., 2001) – is thought to integrate with distance information provided by grid cells within entorhinal cortex (Yoder et al., 2011). Head direction cells have not yet been identified in humans, although there is some evidence to suggest (and good reason to believe) that they do exist (Takahashi et al., 1997; Baumann & Mattingley, 2010).

Other brain regions

Place, grid and head direction cells work together to guide navigational behaviour. As above, direction and distance information are combined as head direction cells in postsubiculum, retrosplenial cortex, dorsal thalamus and other regions pass information on to entorhinal grid cells (Yoder et al., 2011). This is demonstrated by the directional information encoded by some grid cells in deeper layers of medial entorhinal cortex (Sargolini et al., 2006; Jacobs et al., 2010; Si & Treves, 2013). The postsubiculum and retrosplenial cortex have also been implicated in processing landmark information (Epstein, 2008; Auger et al., 2012), while a region designated the parahippocampal place area appears to be responsible for processing the geometric properties of environments (Epstein & Kanwisher, 1998; Epstein, 2005). This information may also be combined with direction and distance information in entorhinal cortex, contributing to the more extensive cognitive map in hippocampus (Yoder et al., 2011). Numerous studies have demonstrated that the hippocampus does

support allocentric navigation (Morris et al., 1982; Packard & McGaugh, 1996; Hartley et al., 2003; Iaria et al., 2003).

In order to guide movement during navigation, allocentric information must be translated into an egocentric reference frame. Posterior parietal cortex is thought to support this translation (Byrne et al., 2007; Burgess, 2008), as well as other navigational processes that do not depend on an allocentric representation of the environment (Stein, 1989; Byrne et al., 2007; Wolbers et al., 2008). Additionally, a number of animal studies (Cook & Kesner, 1988; Devan et al., 1996; Packard & McGaugh, 1996; Fouquet et al., 2013) and human studies (Maguire et al., 1998; Hartley et al., 2003; Iaria et al., 2003; Head & Isom, 2010) have implicated the caudate nucleus of the striatum in aspects of egocentric navigation, such as route following and spatial stimulus-response associations. Many of these studies compared egocentric response-based and allocentric place-based forms of navigation, demonstrating that striatal and hippocampal systems are separately responsible for coordinating the two. PFC also seems to play an important role in navigation (de Bruin et al., 2001; Ciaramelli, 2008; Doeller et al., 2008; Martinet et al., 2011), but I will discuss this in further detail later on in the chapter.

1.2.4 Navigation in ageing

As mentioned earlier, navigation abilities decline with ageing, and allocentric navigation seems to be particularly affected. For example, aged rats are impaired at performance of the Morris water maze (Gage et al., 1984; Begega et al., 2001; Wilson et al., 2003), as are older people tested on virtual adaptations of the task (Moffat & Resnick, 2002; Driscoll et al., 2003; Antonova et al., 2009), which is thought to depend on cognitive map formation. More specifically, Iaria, Petrides, Dagher et al. (2009) found that older people require longer to form a cognitive map, and subsequently make more mistakes when using this representation to navigate. Moffat and Resnick (2002) also demonstrated that older people's cognitive maps contain less information than those of young controls. Path integration is impaired by ageing too, whether based on vestibular cues (Allen et al., 2004) or optic flow

(Mahmood et al., 2009; Harris & Wolbers, 2012). These effects are thought to be produced by atrophy and other degenerative changes that occur in ageing within supporting brain regions, such as the hippocampus (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009) and entorhinal cortex (Du et al., 2003, 2006). In fact, impaired allocentric navigation has been directly associated with dysfunction of hippocampal place cells (Rosenzweig et al., 2003; Wilson et al., 2003, 2004) – particularly in subregion CA3 (Wilson et al., 2005) – in rats, and with reduced hippocampal volume (Driscoll et al., 2003; Nedelska et al., 2012) and activation (Moffat et al., 2006; Antonova et al., 2009) in humans.

The caudate nucleus is also affected by age-related neurodegeneration (Raz et al., 2005; Hasan et al., 2008) but to a much lesser extent than the hippocampus (Jernigan et al., 2001; Fjell et al., 2009; Raz et al., 2010). As a result, although there is still some evidence of route learning impairments in ageing (Wilkniss et al., 1997; Head & Isom, 2010), generally, egocentric route navigation abilities remain relatively intact in comparison to allocentric cognitive map-based navigation. For example, Begega, Cienfuegos, Rubio et al. (2001) found that, while aged rats were impaired on an allocentric water maze task, they performed just as well as young controls on an egocentric T-maze task. Jansen, Schmelter and Heil (2010) trained young and older people on a virtual maze and demonstrated that, although older people take longer to learn routes, once learned, they are able to recall and follow routes just as well as young people. In another virtual navigation study, Wiener, Kmecova and de Condappa (2012) demonstrated much greater age-related deficits in route retracing, dependent upon allocentric processing, than in recalling the route in its original direction. Perhaps as a result, older animals (Nicolle et al., 2003) and people (Rodgers et al., 2012) exhibit a preference for egocentric strategies. Konishi, Etchamendy, Roy et al. (2013) confirmed that this preference for egocentric navigational strategies is associated with increased reliance on caudate nucleus over hippocampus. However, as egocentric representations are far less flexible than allocentric, depending on egocentric strategies is not always practical in real-world situations, so this preference may contribute to the navigational difficulties experienced by older people.

1.3 Strategy switching

1.3.1 Executive functioning

Overview of executive functions

Executive functions include a range of higher level processes involved in the conscious control of other cognitive systems for performing complex tasks (Brocki et al., 2008; Robbins & Arnsten, 2009). They coordinate goal-directed problem solving in situations where habitual or automatic responses are inefficient or ineffective (Marcovitch & Zelazo, 2009; Stoet & Snyder, 2009; Leh et al., 2010). Aspects of executive control integrate information from multiple other cognitive systems and select the most appropriate behavioural response for a given situation (Robbins, 1996; Stoet & Snyder, 2009). They also monitor behavioural outcomes and adapt behaviour accordingly, in order to optimise performance (Robbins, 1996; Marcovitch & Zelazo, 2009). Individual executive functions include planning, working memory, attentional control, inhibition, behavioural monitoring, error correction, and task and strategy switching (Robbins, 1996; Brocki et al., 2008; Marcovitch & Zelazo, 2009; Stoet & Snyder, 2009). Of particular relevance to my research, strategy switching – also referred to as set shifting – will be discussed further in the next section.

Executive functions are essential to a wide range of cognitive processes and are therefore of particular importance to a range of everyday behaviours. Subtle and relatively severe impairments in various activities of daily living have been associated with executive dysfunction in disorders such as Parkinson's disease (PD; Foster & Hershey, 2011; Lanni et al., 2014), schizophrenia (Jovanovski et al., 2007; Puig et al., 2012), mild cognitive impairment (MCI) and dementia (Razani et al., 2007; Aretouli & Brandt, 2010; Allain et al., 2013), as well as normal cognitive ageing (Tomaszewski Farias et al., 2009; McAlister & Schmitter-Edgecombe, 2013), discussed further later on. Executive functioning has also been shown to predict everyday behavioural performance in non-clinical samples (Isquith et al., 2004; Gerstorf et al., 2008; Takeuchi et al., 2013).

Neural bases of executive functions

Executive control is supported primarily by PFC (Funahashi, 2001; Arnsten & Li, 2005; Brocki et al., 2008), particularly dorsolateral PFC (MacPherson et al., 2002; Leh et al., 2010), although different subregions having been associated with specific executive processes (Robbins, 1996; Stuss, 2011). For example, performance at delayed response tasks, dependent on spatial working memory, is impaired in non-human primates with lesions to dlPFC (Sawaguchi et al., 1989; Levy & Goldman-Rakic, 1999), whereas lesions to and activation of medial PFC (mPFC) indicate that it is involved in response inhibition (Broersen & Uylings, 1999; Menon et al., 2001; Hester et al., 2004). Orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) appear to be responsible for monitoring behaviour, with OFC implicated in reward processing (Tremblay & Schultz, 1999; Schultz et al., 2000; Rolls, 2000) and the ACC in error detection (Carter et al., 1998; Botvinick et al., 2004; Carter & van Veen, 2007). The Wisconsin Card Sorting Test (WCST; Berg, 1948) – discussed in further detail in the next section and illustrated in *figure 1.6* – is widely used to assess executive functioning in general, but is specifically a test of strategy switching. A number of non-human primate studies using an adaptation of the WCST have demonstrated that the principle sulcus of dlPFC is involved in coordinating strategy switching (Mansouri et al., 2006; Moore et al., 2009).

As executive functions depend on the integration of information from numerous cognitive systems, they are also dependent upon interconnectivity of prefrontal subregions, as well as connectivity between PFC and parietal and temporal cortices, hippocampus, thalamus and striatum (Robbins, 1996; Funahashi, 2001; Brocki et al., 2008). During early childhood, executive functions are thought to emerge as these prefrontal connections develop, indicated by increases in dendritic and synaptic density (Brocki et al., 2008), with further development throughout adolescence relating to synaptic plasticity (Selemon et al., 2013). An analogous reduction in white matter integrity seems to underlie executive dysfunction in ageing (Buckner, 2004; Charlton et al., 2008; Gunning-Dixon et al., 2009). Of particular relevance, white matter integrity has been directly associated with performance on measures of

cognitive flexibility, such as the Trail-Making Test Part B (TMT-B; Takahashi et al., 2004; Perry et al., 2009; Sudo et al., 2013), which involves connecting dots in sequence, switching between numbers and letters.

Executive functioning also seems to depend upon innervation of PFC by noradrenaline (NA), dopamine (DA) and other neurotransmitters (Robbins, 1996; Arnsten & Li, 2005; Robbins & Arnsten, 2009). For example, Li and Mei (1994) injected various adrenoceptor antagonists into monkey dlPFC and produced executive deficits, indicating that NA, as an adrenoceptor agonist, may be important to certain executive processes. Executive dysfunction in PD, characterised by DA depletion, also suggests a role for DA (Owen, 2004; Leh et al., 2010), although NA dysfunction does occur in PD too (Scatton et al., 1983; Fornai et al., 2007). It is worth noting that PFC exerts control over NA and DA systems, which in turn innervate many forebrain regions (Robbins & Arnsten, 2009), suggesting that these neurotransmitters may be utilised by PFC to coordinate executive control throughout prefrontal subregions and other brain regions.

1.3.2 Switching behaviour

Strategy switching

Strategy switching is an executive function describing the ability to change between different methods of performing a task. It is part of a hierarchy of functions relating to cognitive flexibility (Derrfuss et al., 2005; Kehagia et al., 2010), as a lower level process than changing between different tasks (task switching), but a higher level process than changing between specific responses using the same strategy (strategy reversing). However, the distinction between task and strategy switching is unclear, and both have also been referred to as set shifting. Cognitive flexibility has been assessed in rodents using the attentional set-shifting task (ASST; Birrell & Brown, 2000), illustrated in *figure 1.5*. In this task, rodents are required to find a reward at the bottom of one of two reward wells, each filled with a different digging medium and scented with a different odour, with the location of each of these cue types varied

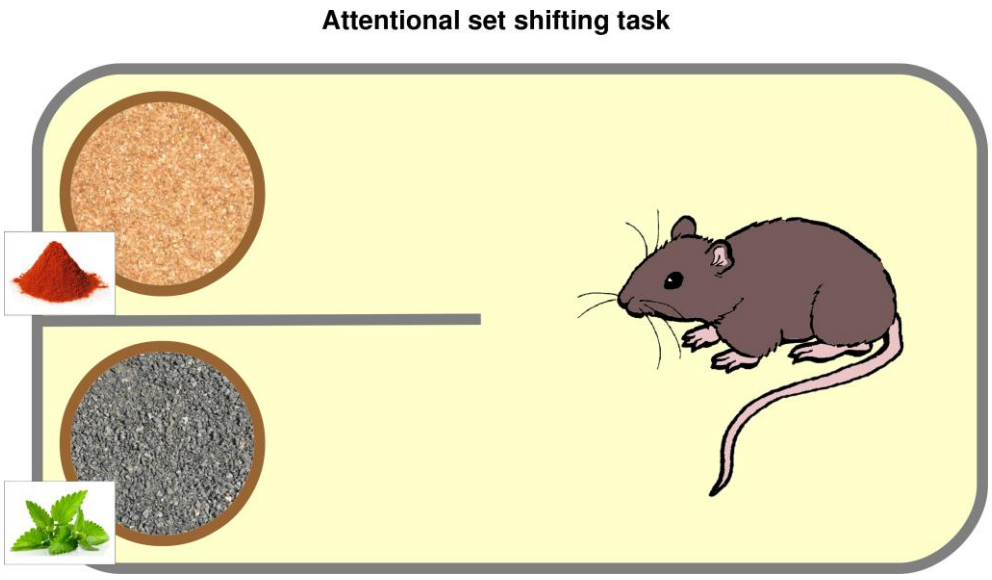

Figure 1.5 Attentional set shifting task. One of the two reward wells at one end of the enclosure contain a reward, buried under a scented substrate. Rodents rely on either the odour (e.g. paprika or mint) or the digging medium (e.g. sawdust or gravel) to find the reward. Every so often, rodents must switch between an odour-response strategy and a digging medium-response strategy.

independently across trials. After a number of trials throughout which digging in a particular medium was rewarded, a rat may then be required to change to responding to a particular odour, representing an extra-dimensional shift, or strategy switch. The same task can be used to assess reversals, when reward associations are changed, for example, from one digging medium to another. Studies using the ASST have demonstrated that strategy switching is coordinated by PFC and NA (Lapiz & Morilak, 2006; Tait et al., 2007; McGaughy et al., 2008; Snyder et al., 2012), and that it is impaired in ageing (Barense et al., 2002; Young et al., 2010; Tanaka et al., 2011).

In humans, strategy switching is measured using tasks such as the TMT-B (de Oliveira-Souza et al., 2000; Perry et al., 2009), the intra-dimensional/extra-dimensional set-shifting subtest (IDED) of the Cambridge Neuropsychological Test Automated Battery (CANTAB; Jazbec et al., 2007; McKirdy et al., 2009), design fluency tests (McDonald et al., 2005; Hurks, 2013) and the WCST, as mentioned above. The WCST, shown in *figure 1.6*, uses a large number of cards, each depicting

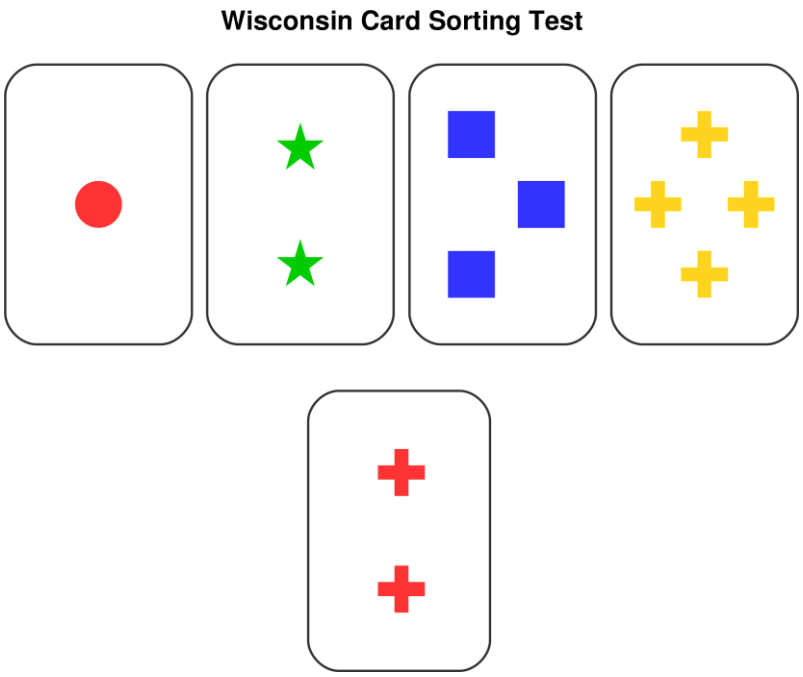

Figure 1.6 Wisconsin Card Sorting Test. Participants must sort cards based either on shape, colour or number. In the above example, the test card (at the bottom) could be placed on the first, second or fourth pile (of the top row), depending on the current sorting strategy. Every so often, participants must switch strategies based on experimenter feedback.

one to four instances of one of four basic shapes in one of four colours. Participants are required to sort cards based on colour, shape or number of shapes, periodically switching between these three strategies based on experimenter feedback. Studies using the WCST have been used to show that strategy switching is impaired by frontal lobe damage (Owen et al., 1993; Pantelis et al., 1999; Stuss et al., 2000). Hampshire and Owen (2006) used another task dependent on switching between stimulus dimensions and fMRI to show that strategy switching in humans is specifically mediated by dlPFC. More specifically, and also as mentioned earlier, adaptations of the WCST for use with non-human primate subjects have been used to show that it is the principle sulcus of dlPFC that is involved in coordinating strategy switching (Mansouri et al., 2006; Moore et al., 2009). Cognitive flexibility is also thought to depend upon monoaminergic modulation (Alexander et al., 2007; Kehagia et al., 2010; Logue & Gould, 2013).

Adaptive gain theory

As above, various studies have demonstrated that neurotransmitters such as NA and DA are involved in executive functioning. However, Aston-Jones and Cohen (2005) propose a key role for NA in the adaptive regulation of behaviour. NA is produced by the locus coeruleus (LC), which projects to almost every other region of the brain, (Loizou, 1969; Jones et al., 1977). In an extensive review, Aston-Jones and Cohen discuss LC function in terms of two modes of noradrenergic output: phasic and tonic. In phasic mode, LC outputs NA in short bursts in response to task-relevant stimuli, whereas in tonic mode, LC outputs NA stably and consistently. They also discuss evidence suggesting that phasic LC-NA activity is associated with task performance and focused attention, or the continued use of a current behavioural strategy. On the other hand, they point out that tonic LC-NA activity, although associated with poorer performance of a single task and increased distractibility, is important for the exploration of alternative behavioural strategies, i.e. for switching strategies. Based on previous functional and structural findings, Aston-Jones & Cohen suggest that LC output mode changes in response to information reflecting the utility of a current behaviour, received from ACC and OFC. They also suggest that, through projections to PFC, tonic LC activity facilitates disengagement from a current behaviour and the sampling of alternative behaviours, and phasic LC activity then promotes engagement of one of these alternatives. Thus, the adaptive gain theory suggests that strategy switching is coordinated by a PFC-LC network (*figure 1.7*).

Bouret and Sara (2005) also presented a theory of LC-NA function and its role in switching behaviour. They suggested that phasic LC output promotes the organisation of brain regions into functional networks used to perform specific tasks. This reflects the engagement of a new strategy, while disengagement of a previous strategy may relate to dissolution of functional networks, mediated by tonic LC activity. A number of studies provide evidence in support of this NA hypothesis of strategy switching. For example, Lapiz and Morilak (2006) demonstrated that administration of atipamezole (an α_2-adrenergic autoreceptor antagonist) improved rodents' performance of extra-dimensional shifts (strategy switches) on the ASST,

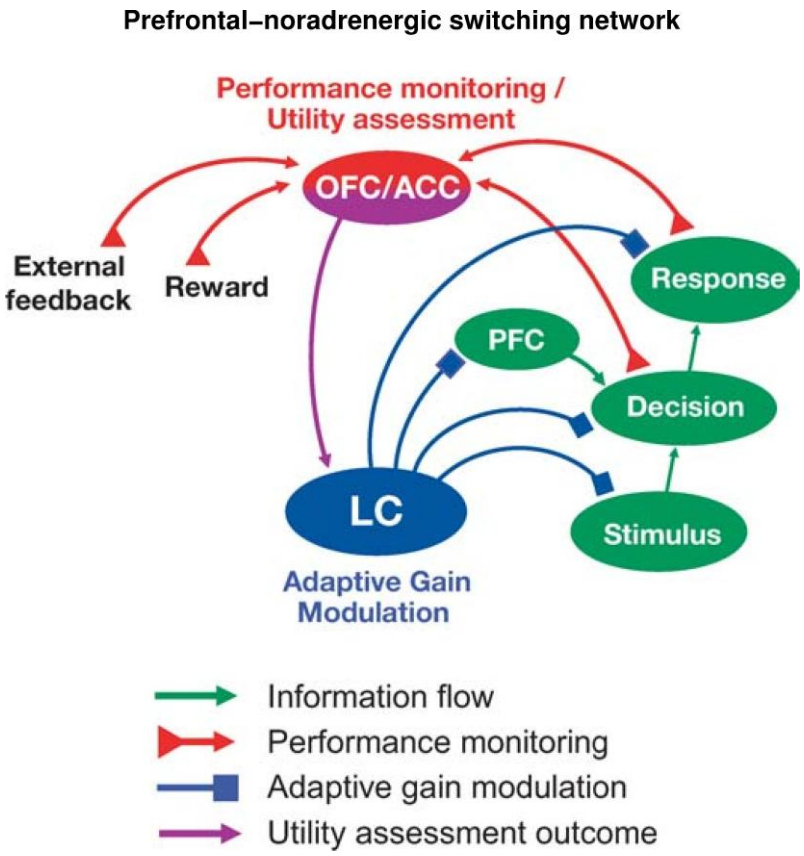

Figure 1.7 Prefrontal-noradrenergic switching network. According to the adaptive gain theory, prefrontal cortex (PFC) and locus coeruleus (LC) coordinate switching behaviour in response to reward monitoring and error detection information from orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC). From Aston-Jones & Cohen (2005).

while infusion of an α_1-adrenergic receptor antagonist into mPFC (the rodent analogue of primate dlPFC; DeVito et al., 2010) blocked this effect. Injection of corticotropin-releasing factor (CRF) directly into LC, prompting a shift into high tonic mode, has also been shown to benefit cognitive flexibility (Snyder et al., 2012). Also testing rats on the ASST, Tait, Brown, Farovik et al. (2007) demonstrated strategy switching impairments following lesions to the dorsal noradrenergic bundle (DNAB), which carries NA to PFC, among other regions. Other methods of depleting prefrontal NA have produced similar effects (McGaughy et al., 2008). In humans, pharmacological manipulation of LC output mode has confirmed that higher phasic LC-NA activity improves task performance by increasing task-relevant neural activity (Minzenberg et al., 2008). Several studies have also demonstrated an

association between changes in pupil size, a known correlate of LC activity, and switching behaviour (Gilzenrat et al., 2010; Jepma & Nieuwenhuis, 2011; Jepma et al., 2011).

1.3.3 Strategy switching in ageing

Frontal ageing hypothesis

As discussed earlier, PFC is particularly prone to neurodegeneration in ageing (Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011). The frontal ageing hypothesis highlights this prefrontal degeneration as the most important aspect of brain ageing, suggesting that it can account for many of the observed cognitive deficits (Dempster, 1992; West, 1996). Specifically, Dempster proposed that frontal lobe ageing impairs inhibition, or resistance to interference, which he argued was a major factor underlying cognitive ability. He reviewed the performance of children, older adults and patients with frontal lobe damage on various tests of inhibition, although many of these also assessed other aspects of executive functioning. However, it was West who applied the hypothesis to other areas of cognitive performance dependent upon prefrontal function. As executive functioning is associated primarily with PFC (Robbins, 1996; Funahashi, 2001; Arnsten & Li, 2005), the frontal ageing hypothesis therefore predicts executive dysfunction in ageing. Deficits in working memory, attentional control and other aspects of executive functioning have indeed been demonstrated in ageing (Schneider-Garces et al., 2010; Bizon et al., 2012; Hedden et al., 2012), and they generally occur together, perhaps reflecting decline in a general factor of overall executive control (Rodríguez-Aranda & Sundet, 2006). Further, prefrontal and executive dysfunction in turn has a wider impact on many cognitive abilities and everyday behaviours. Dysfunction of dlPFC may be particularly important in ageing (MacPherson et al., 2002), and is likely associated with impairments in strategy switching, and in turn navigation, as discussed below.

Strategy switching in ageing

Strategy switching impairments have been demonstrated in older animals and humans. For example, as mentioned earlier, rodents tested on the ASST show deficits in performance of extra-dimensional set shifts, or strategy switches, but not reversals (Barense et al., 2002; Young et al., 2010; Tanaka et al., 2011). In non-human primates conceptual set shifting – for example, switching between responding to colours and responding to shapes – is also impaired in ageing (Moore et al., 2003; Picq, 2007; Hara et al., 2011). These tasks are comparable to the WCST, which has been used to demonstrate similar strategy switching impairments in ageing humans (Rodríguez-Aranda & Sundet, 2006; Ashendorf & McCaffrey, 2008; Gamboz et al., 2009). These findings are consistent with evidence of age-related impairments in the comparable process of task switching (Kramer et al., 1999; Smith et al., 2001).

Other tasks that involve switching between dimensions of more complex and less abstract stimuli also provide evidence of strategy switching deficits in older people. For example, Hampshire, Gruszka, Fallon and Owen (2008) tested participants on a task using pairs of images, each composed of superimposed images of a face and a building. Participants responded to a particular face or a particular building, and periodically performed reversals, intra-dimensional shifts or extra-dimensional shifts. Older participants were significantly impaired at switching between face and building response strategies. Maintenant, Blaye and Paour (2011) used a task that required participants to identify which of three visual stimuli did not match a semantic rule. The semantic rule determining which was the odd one out changed periodically, so that participants had to switch between categorisation strategies. Older people took significantly longer to switch to a taxonomic categorisation strategy. Considered in terms of the NA hypothesis of switching behaviour (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005), all of these findings are consistent with evidence of PFC (Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011) and LC-NA (Manaye et al., 1995; Grudzien et al., 2007) dysfunction in ageing.

1.3.4 Navigational strategy switching

A role for strategy switching in navigation

As described in section 1.2.2, navigation is supported by numerous different processes, such as path integration, route navigation and cognitive mapping. During navigation, people can use either allocentric or egocentric strategies – dependent on the hippocampus and caudate nucleus, respectively (Hartley et al., 2003; Iaria et al., 2003; Head & Isom, 2010) – and have been shown to spontaneously switch between them (Iglói et al., 2009). Hippocampal and striatal strategies rely upon different environmental and bodily cues, the availability and reliability of which change during movement around the environment. For example, landmarks may become obscured, and self-motion information becomes less reliable over greater distances. During real-world navigation, our navigational goals often change, which may also necessitate reliance upon another navigational system. For example, we may have to correct deviation from a route, detour around unexpected obstacles, or simply revise our target location. Due to changes in cues and goals, successful navigation depends critically upon the ability to switch between hippocampal and striatal strategies (Foo et al., 2005; Wolbers & Hegarty, 2010). Furthermore, PFC is involved in real-world navigation (Spiers & Maguire, 2006; Tranel et al., 2007), which is consistent with the idea that navigation is dependent upon strategy switching, and that, as in other contexts, it is mediated by PFC. Allocentric processing and route navigation mechanisms are thought to operate in parallel (Bohbot et al., 2007; Iglói et al., 2009), with PFC determining which actually guides behaviour by reweighting inputs from hippocampus and striatum (Doeller et al., 2008).

In rodents, navigational strategy switching has been studied using the plus maze task (e.g. Ragozzino, 2007; Rich & Shapiro, 2007; *figure 1.8*). Briefly, the task involves finding a reward at the end of one of two opposing goal arms of a plus-shaped maze, starting from one of the two other maze arms. Animals are rewarded for using either an allocentric 'place' strategy, visiting the same place on each trial regardless of which direction it is in from the start arm, or an egocentric 'response' strategy, turning

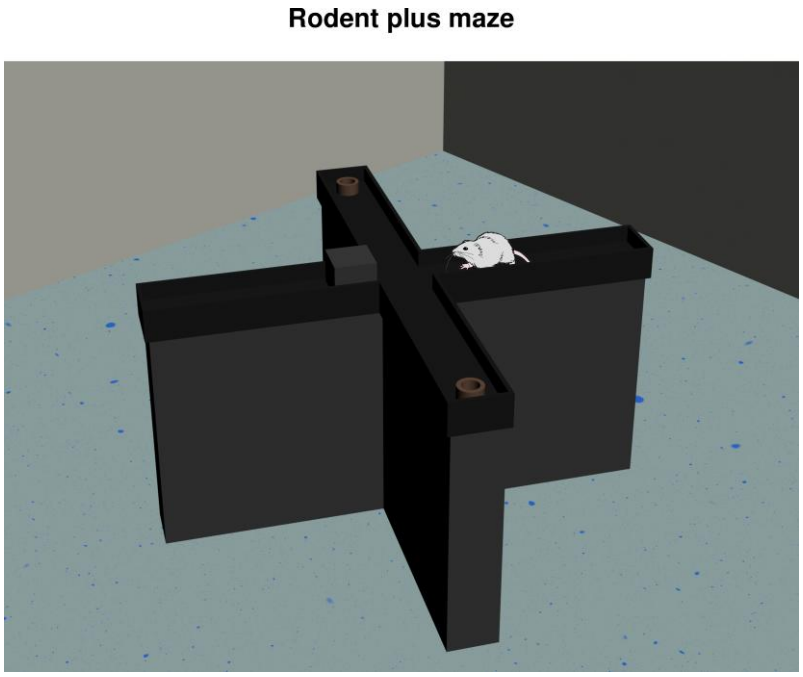

Figure 1.8 Rodent plus maze. A rat performing the plus maze task on an elevated plus maze, with reward wells at two opposing goal arms and a blockade at the entrance to the arm opposite the current start arm. Some versions of the plus maze also feature opaque or transparent walls around the maze, or just the goal arms.

the same direction on each trial, regardless of which goal arm this leads them to. Between periods or sessions of using the same strategy, animals must perform either a strategy switch (e.g. from place to response) or a reversal (e.g. from 'turn left' to 'turn right'). The plus maze is described in further detail in section 2.3.3. Several studies using the task have confirmed that specific regions of rodent mPFC are responsible for coordinating navigational strategy switching (Ragozzino et al., 1999; Rich & Shapiro, 2007; Young & Shapiro, 2009). This suggests that in primates, navigational strategy switching is coordinated by dlPFC (DeVito et al., 2010).

Navigational strategy switching in ageing

As strategy switching is both impaired in ageing (Ashendorf & McCaffrey, 2008; Hampshire et al., 2008; Gamboz et al., 2009; Maintenant et al., 2011) and involved in navigation (Foo et al., 2005; Iglói et al., 2009; Wolbers & Hegarty, 2010), the navigational difficulties experienced by older people may be, at least in part,

attributable to deficits in strategy switching. For example, impaired performance on allocentric tasks (Moffat & Resnick, 2002; Driscoll et al., 2003; Antonova et al., 2009; Iaria et al., 2009), although associated with hippocampal degeneration (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009), may also reflect a diminished capacity to switch to an allocentric strategy. Similarly, the preference for egocentric strategies among older animals and humans (Nicolle et al., 2003; Rodgers et al., 2012; Konishi et al., 2013) may reflect a decrease in switching between strategies. A small number of studies have indicated that prefrontal dysfunction does contribute to navigation impairments in ageing (Moffat et al., 2007; Antonova et al., 2009), and that there is a relationship between executive dysfunction and navigational decline (Taillade et al., 2013). However, previous work has not focused explicitly on the effects of ageing on navigational strategy switching, which was therefore the main objective of my doctoral research.

1.4 Thesis overview

At the beginning of my PhD, I set out to investigate the effects of ageing on the ability to switch between navigational strategies, considered in terms of the impact that any deficits would have on navigation in general. I also aimed to explore the neural mechanisms underlying navigational strategy switching, as well as age-related changes in the functionality of these mechanisms, with the long-term aim of contributing to the alleviation of age-related decline in navigation. I originally planned to use human behavioural and neuroimaging studies, as well as parallel rodent behavioural and lesion studies, to assess navigational strategy switching. In the end, my work focused solely on human participants, but also incorporated some behavioural studies of navigational strategy preferences, as well as a study assessing physiological measures as correlates of neural activity.

The studies of navigational strategy preferences are reported first, in Chapter Three. Study 1 assessed use of an allocentric strategy and two egocentric strategies by young and old participants, using a task that depended upon use of the allocentric

strategy. This first study aimed to demonstrate a greater preference for egocentric strategies among older people, even when an allocentric strategy was required. Study 2 followed on from Study 1 by investigating age-related deficits in use of the two egocentric strategies. This study was based on the hypothesis that older participants are impaired at using an associative cue strategy, but not a beacon strategy. Chapter Four includes my first two behavioural studies of navigational strategy switching. Study 3 used a virtual plus maze (VPM) to explore deficits among older participants in switching between an allocentric and an egocentric strategy. Study 4 used a shortcutting task in a virtual town environment, specifically designed to assess age differences in navigational strategy switching in a more realistic context.

Two further behavioural studies of navigational strategy switching are presented in Chapter Five. Study 5 used two variations of the VPM and a navigational decision making task to explore the association between ageing-related impairments in navigational strategy switching and decision making, relating to dysfunction of PFC. Study 6 assessed navigational strategy switching in older people involved in orienteering, aiming to identify whether practice could protect against the effects of ageing on navigational strategy switching. My neuroimaging work is documented in Chapter Six. In Study 7, I attempted to use fMRI data collected from young participants during performance of the VPM to confirm that dlPFC, OFC and ACC are involved in navigational strategy switching. I had planned a second fMRI study, which was to assess the activation of these regions and LC during VPM performance in young and old participants. Although I did not complete the second fMRI study, pilot testing is also presented in this chapter as Study 8.

In my final experimental chapter, Chapter Seven, I provide a report of the physiological study of LC-NA activity during navigational strategy switching. In Study 9, I monitored pupil size and heart rate throughout VPM performance in young and old participants. I expected changes in these measures to reflect changes in LC-NA activity, and age differences in functionality of the LC-NA system to relate to deficits in navigational strategy switching. I finish with a short meta-analysis of five of the studies in which I used the VPM to assess navigational strategy switching,

presented as Study 10. The results of this analysis were useful in formulating my final conclusions, which are then discussed in Chapter Eight.

Chapter Two – Methods

2.1 Participants

2.1.1 Sample information

Groups and sizes

Most studies assessed differences between two groups of participants – a young group and an old group. For such studies, I usually aimed to recruit 25 participants for each of these two groups, with actual group sizes ranging from 23 to 28 throughout Studies 1, 4, 5 and 9. In each case, age group sizes were exactly or approximately equal. Study 3, due to difficulties with recruitment, included slightly fewer participants; 18 young and 20 old. Studies 2 and 6 each involved two conditions, with two participant sub-groups per age group. Groups were therefore slightly smaller, with 17 to 22 participants in each. For these two studies, the number of participants in each age group, as well as the numbers of each age group assigned to each condition, were exactly or approximately equal. Study 7, an fMRI study, assessed only eight young participants. Study 8, a short pilot study, assessed only four young and six older participants.

Age and gender

In general, young participants were aged between 18 and 31 years, while older participants were aged between 60 and 86 years, although the majority of young participants were in their early twenties and most older participants were in their late sixties or seventies. For those studies with more than one condition, young and old participants assigned to each condition were approximately the same age. More detailed information on participant ages by study is included in *table 2.1*. Age (and condition) groups were also approximately balanced in terms of gender. Where groups were not exactly gender balanced, there were usually one or two more females than males. Further details are included in the respective methods sections of

Participant ages

Study	Young			Old		
	Min	Max	Mean	Min	Max	Mean
1	18	23	20.7	65	86	74.3
2	18 | 18	25 | 28	19.8 | 20.6	65 | 67	85 | 83	73.4 | 74.5
3	20	29	22.2	60	84	68.6
4	20	25	21.8	65	85	68.7
5	20	24	21.9	65	80	71.4
6	18 | 20	25 | 24	21.0 | 21.0	65 | 65	80 | 78	68.6 | 71.0
7	19	31	23.1	-	-	-
8	23	30	25.5	63	78	70.3
9	19	30	22.6	60	79	70.2

Table 2.1 Participant ages. Minimum, maximum and mean age for each group that participated in Studies 1-9. For Study 2, figures on the left represent those assigned to the associative cue condition, those on the right to the beacon condition. For Study 6, orienteers are on the left, controls on the right.

each study reported in subsequent chapters. However, throughout the majority of my studies, I found no evidence of gender differences in navigational strategy switching performance.

Health and cognitive abilities

I only recruited participants in good overall health, with no known cognitive deficits or neurological disorders. As detailed in section 2.3.1, I also screened for signs of mild cognitive impairment (MCI), particularly among old participants, excluding any that did show signs of MCI from all following data analyses. Participants selected for Study 7 had prior experience of magnetic resonance imaging (MRI), but were also screened for metal implants, pregnancy, claustrophobia and other conditions that would have rendered them unsuitable for functional MRI (fMRI). While recruiting participants for Study 9, I also excluded any with known heart conditions. Throughout all studies, participants were required to have normal or corrected-to-normal vision (and to wear corrective lenses if necessary), as well as to speak

English to a native standard.

2.1.2 Recruitment

Old participants

Most of the experiments reported in later chapters were conducted at the University of Edinburgh, at which the School of Philosophy, Psychology and Language Sciences (PPLS) holds a database of people who have volunteered to participate in psychological research. Almost all of the older participants who I tested in Edinburgh were recruited from this database. The database includes the results of prior screening tests, including information on health conditions, neuropsychological disorders and sensory acuity, which I used for selecting suitable participants, although I also checked this information with all participants who were selected. As all of my studies involved using a computer to navigate a virtual environment (VE), I made sure that recruits had some experience of using computers, and that they would feel comfortable completing a computer-based experiment. I conducted three studies in collaboration with a research group at Bournemouth University, and while most of the older participants for each of these studies were tested in Edinburgh, those who were not were selected from a similar database at Bournemouth University. For Studies 5 and 6, some of the older participants were recruited from the local community through a number of clubs and associations. Some of the older participants recruited for the short pilot study, Study 8, had previously been tested on the virtual plus maze (VPM), but not for some time.

Young participants

Most young participants were students at the University of Edinburgh, or, for Studies 2 and 3, Bournemouth University. Participants tested in Edinburgh were recruited through advertising on the university's careers and employment website, which quickly garnered a large number of responses. Advertisements specified that applicants must be in good general health, with no known neurological or cognitive

disorders, and with English to a native standard. From the large number of responses, only those who met these criteria were selected. Participants tested in Bournemouth were recruited through a similar system. For Study 8, the four young pilot participants were doctoral students and postdoctoral associates at the Centre for Cognitive and Neural Systems (CCNS) in Edinburgh and the German Center for Neurodegenerative Diseases (DZNE) in Magdeburg.

Imaging participants

Study 7 was conducted at the University of California Santa Barbara (UCSB), using eight young participants from the Brain Imaging Center's database of volunteers for imaging research. All of these participants were deemed suitable to participate in an fMRI experiment, having previous experience of MRI, and no conditions that might preclude them from undergoing MRI, such as metal implants, pregnancy or claustrophobia.

Orienteers

Study 6 assessed the effect of orienteering practice on age-related decline in navigational strategy switching performance. In this study, I tested young and old control participants, who were recruited as above, but also young and old orienteers, who were recruited using information from Scottish Orienteering and through the following local orienteering clubs: Clydeside Orienteers, East Lothian Orienteers, Edinburgh Southern Orienteering Club, Edinburgh University Orienteering Club, Forth Valley Orienteers, Interlopers Orienteering Club, Kingdom of Fife Orienteers, Roxburgh Reivers Orienteering Club, Tayside Orienteers and Tinto Orienteering Club.

Reimbursement

Participants were reimbursed for their time at an hourly rate exceeding the UK national minimum wage. For some of the earlier studies I conducted, participants

were paid an equivalent of £6/hr, whereas for later studies they were paid £7/hr. Rate of reimbursement was the same for all who participated in any given study, and did not depend on performance or even on completion of the experiment. While participants were informed of the rate of reimbursement at recruitment, it was not deliberately offered as an incentive.

2.2 Ethical conduct

2.2.1 Ethical approval

Each of the experimental studies presented in this thesis was separately approved by the relevant ethics committee. For Studies 1-6 and Study 9, I applied with full details of the studies to the Psychology Research Ethics Committee in Edinburgh, who approved the studies before I began testing. Studies 1-3 were also approved by the University Research Ethics Committee in Bournemouth. Study 7 was approved by the Institutional Review Board at UCSB. I also applied to the University Medical Centre in Magdeburg for ethical approval to conduct an fMRI study at the Leibniz Institute of Neurobiology in collaboration with the DZNE. Although I never completed this study, the pilot testing (presented as Study 8) was conducted in accordance with its ethical approval, as well as that of prior VPM studies in Edinburgh.

2.2.2 Participant information

Participants were given a general overview of the study at recruitment, and were provided with more detailed information at the beginning of their testing session. This included a full description of the tasks they would be required to perform, including any potential risks involved, the expected duration of the experiment, and the rate of reimbursement. Importantly, participants were also made well aware that their data would be completely anonymised, and that they were free to withdraw from the study at any time, without penalty and without having to give a reason.

Participants were also given the opportunity to ask any questions about the general nature of the study or about what they were expected to do before beginning. They then provided signed confirmation of their informed consent.

While participants were not deceived, small details of certain tasks were sometimes withheld. For example, in Study 2, participants were trained and tested on a route through a number of junctions featuring two landmarks. A cycle of training and testing was repeated six times, followed by a seventh in which three of the pairs of landmarks had switched positions. Participants were not told that the seventh repetition was any different from the preceding six. Also, while participants were otherwise fully informed about the nature of the study they were participating in, the aims and hypotheses of each study were not discussed until after participants had completed the experiment. At this stage, they were also given the opportunity to ask any further questions about the study, which could be answered freely.

2.2.3 Procedures

All studies were conducted in accordance with the ethical guidelines of the approving ethics committees, of the British Psychological Society (BPS), and, where relevant, the Declaration of Helsinki. As most studies were behavioural and conducted in virtual reality (VR), they were not associated with any major risks. One minor risk of virtual navigation is that, due to the discrepancy between visual perception of movement and proprioceptive and vestibular sensations of remaining stationary, it can induce motion sickness. In order to minimise this risk, I made sure that rotational movement in VR tasks was performed slowly. I also warned participants of the potential risk and asked them to stop immediately if they started to feel dizzy or sick – but none did. As I was testing older participants on something at which I expected them to be impaired, I was also cautious of their being embarrassed about their performance. I always provided encouraging feedback at the end of the experiment, attributing any self-reports of poor performance to task difficulty.

Due to its use of fMRI, Study 7 was associated with more potential risks, although

most of these related to unsuitability for MRI, which was thoroughly screened for prior to scanning. Participants were asked to change into provided clothes and to take out all piercings, in order to ensure that they had no metal on their persons. They were also fitted with earplugs to reduce any discomfort caused by the noise of the scanner. Although participants were screened for claustrophobia and had previous experience of MRI, they were also warned that the confined space could cause stress or discomfort. They were asked if they were comfortable and willing to continue during every break between sessions, and were given an emergency button to press if this changed or if anything else happened during a session. For Study 9, participants were required to wear eye-tracking and heart rate (HR) monitoring equipment throughout the equipment. Participants fitted the HR monitor electrodes themselves (after being instructed how and where to fit them) and, before beginning, I ensured that both pieces of equipment were fitted comfortably. As for other studies, I also told participants that they should stop if they became uncomfortable.

2.3 Behavioural measures

2.3.1 Screening tests

Mini Mental State Examination

The Mini Mental State Examination (MMSE; Folstein et al., 1975) was designed to quickly assess the cognitive abilities of psychiatric patients, particularly elderly patients with delirium or dementia. The test consists of 11 items, administered verbally, with some responses given on paper. These items assess orientation, memory, attention, language and copying, producing a total score out of a possible 30. The MMSE has proved useful as a screening test for dementia, indicated by a score of 23 or less (Folstein et al., 1975; Mitchell, 2009), and more recently MCI, indicated by a score of 24 to 27 (Mitchell, 2009; De Marchis et al., 2010). I used the MMSE to screen for MCI in Studies 5 and 6, but all those who were tested scored 28 or higher.

Montreal Cognitive Assessment

The Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) is a similar measure to the MMSE, but was developed more recently, with the specific aim of screening for MCI. The test consists of 12 items, assessing visuospatial abilities, executive functioning, attention, concentration, working memory, arithmetic, language and orientation. Like the MMSE, the MoCA is administered verbally and on paper, and scored out of a possible total of 30. Nasreddine, Phillips, Bédirian et al. (2005) originally proposed a critical score of 26, with those scoring 25 or below identified as cognitively impaired. Using this cut-off, the MoCA demonstrated far greater sensitivity to MCI than the MMSE, although less specificity. The first time I used the MoCA, I administered it to young participants as well as old. In addition to several older participants, two young participants (who were both university students) were also identified as showing signs of MCI! Due to the known and observed non-specificity of the MoCA, I therefore chose to use a lower critical score of 23, as recommended by Luis, Keegan and Mullan (2009). I used the MoCA with the lower cut-off to screen for MCI in Studies 1, 4 and 7, detecting only one possible case of MCI in all three studies. This person was excluded from all data analyses.

2.3.2 Control measures

Computer experience

Older people are generally less experienced with computers, having grown up without them and having been educated before they were introduced into schools. Some may even have reached the end of their careers before computers were commonplace in working environments. As all of my experimental studies required participants to use a computer to navigate VR, age differences in computer experience may have had a substantial effect on performance. In Studies 2 and 3, as well as in another VR study I conducted before my PhD (Harris & Wolbers, 2012), I therefore asked participants to rate their level of experience with computers and computer games on a nine-point scale. Their responses were combined as a single

score representing computer experience. In each case, there were significant age differences in computer experience, as expected. However, in all three studies, regression analyses indicated that computer experience did not have a significant bearing upon performance. Other than at recruitment, as above, I did not assess computer experience in later studies.

Spatial working memory task

While the main tasks I used were designed to assess navigational strategy use and strategy switching, they were also dependent, to a certain degree, upon spatial working memory. In Studies 1 and 3, I used a custom spatial working memory task (SWMT), specifically designed by a laboratory colleague, Alexander Enoch, using Autodesk (San Rafael, CA, USA) 3ds Max and WorldViz (Santa Barbara, CA, USA) Vizard 3.0. The SWMT assessed place recall and route recall, as well as reward sensitivity. Place recall trials were set in a VE consisting of an open field surrounded by mountain scenery, with six positions in a central circle marked by a well (*figure 2.1*). Participants were automatically moved to three of the six positions, returned to the origin and reoriented, then asked to revisit the same three positions in any order. Route recall trials were set in a grid like maze shrouded in fog to restrict visibility. Participants were first directed along a route through five junctions by arrows appearing at each one, before being asked to retrace the same route without directions. Throughout place and route encoding phases, a reward signal (a yellow ball, as used in the earlier versions of the VPM) would sometimes appear from a well or at a junction. While revisiting the places and retracing the routes, participants also had to indicate whether or not a reward had appeared at each location. These responses produced a measure of reward sensitivity. The task included 10 place recall trials and 10 route recall trials, alternating between the two types. As for computer experience, place recall, route recall and reward sensitivity were not identified as significant predictors of virtual navigational performance. Also as for computer experience, these measures had not predicted performance in my earlier virtual navigation study (Harris & Wolbers, 2012).

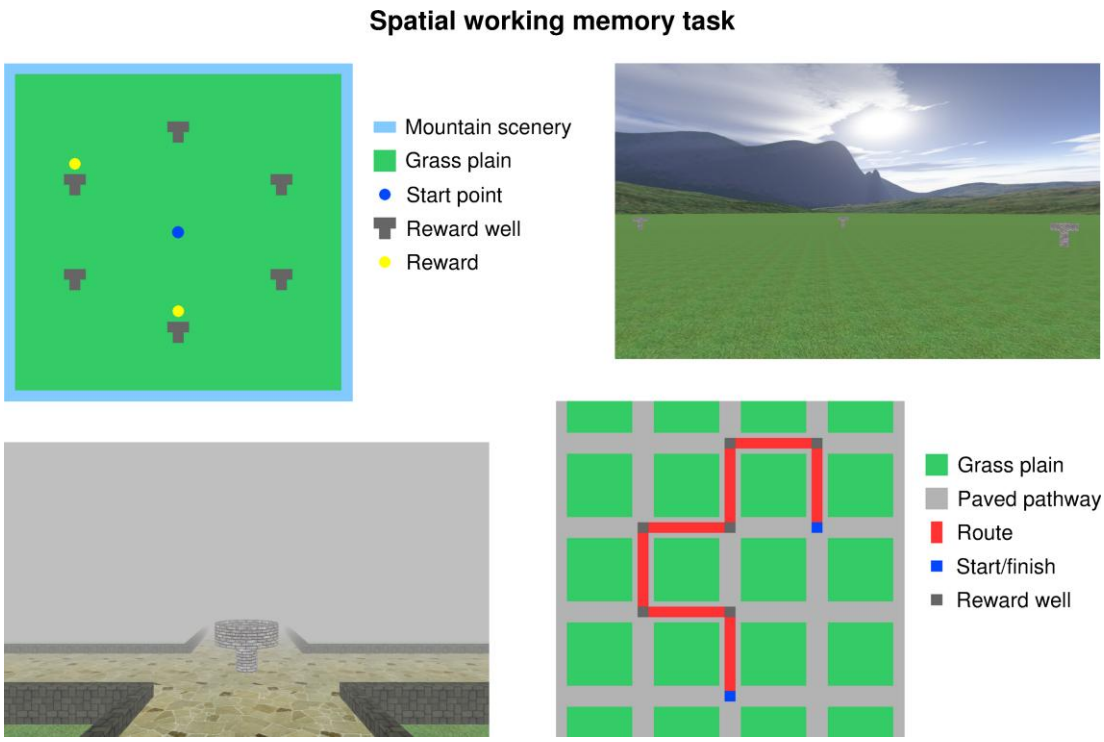

Figure 2.1 Spatial working memory task. Diagrams and screen images of the place recall (*top*) and route recall (*bottom*) phases of the task.

Corsi blocks task

In subsequent studies, I asked participants to complete a much briefer test of spatial working memory, a computerised Corsi blocks task. I developed this task in Vizard, based on Corsi's (1972) original block-tapping test and on standard block positions and sequences provided by Kessels, Zandvoort, Postma et al. (2000). The task revolved around a spatial array of nine blocks, or rather on-screen squares, as shown in *figure 2.2*. The program presented spatial sequences by illuminating each block in the sequence in turn. Participants then had to repeat the sequence by clicking on the same blocks in the same order. The first sequence featured only two blocks, but each time participants successfully repeated a sequence, they progressed to a sequence that was one block longer, up to a maximum of nine blocks. If participants made a mistake while repeating a sequence, they were given a second chance to repeat a sequence of the same length. If they made a mistake again, the task ended. Their score, or 'block span', was the number of blocks in the longest sequence they were

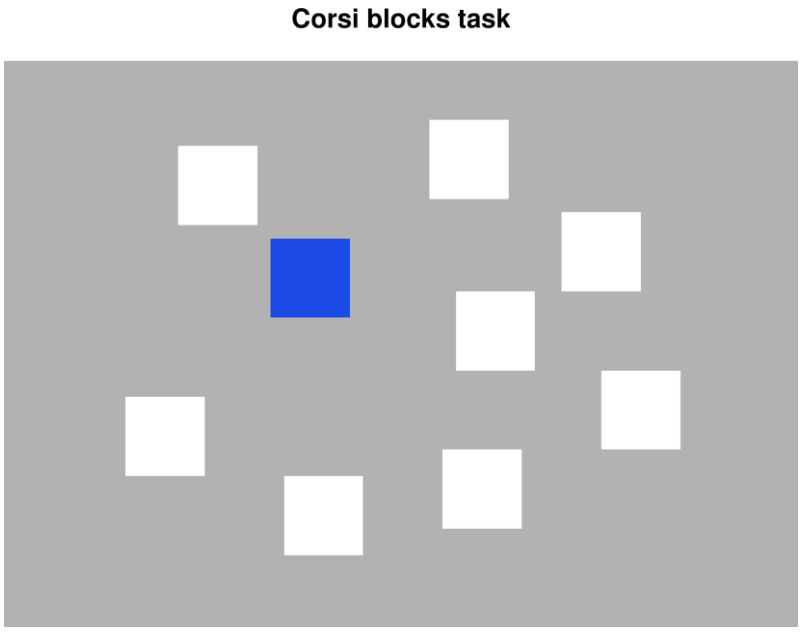

Figure 2.2 Corsi blocks task. In this computerised version of Corsi's block-tapping test, spatial sequences were presented and repeated using an array of nine squares. The blue square represents the current block in a presented sequence.

able to repeat correctly. In Studies 4 and 6, this measure was not found to significantly predict navigational strategy switching performance.

Other control measures

In Study 4 only, I briefly assessed crystallised intelligence using the National Adult Reading Test (NART; Nelson, 1982), which simply involves reading aloud a list of 50 words with irregular pronunciations. This measure demonstrated that older participants performed slightly better than young, indicating that the observed age effects of interest were not due to a pre-existing lower level of ability. Furthermore, other studies have also demonstrated higher verbal knowledge in older people (Lövdén et al., 2005, Strauss et al., 2006, Bates & Wolbers, 2014), suggesting those who participated in this study were a representative sample of older people.

Study 4 also controlled for allocentric processing ability using a cognitive mapping test (CMT), which required participants to label a map of the VEs that they navigated

throughout the main shortcutting task. Participants were given a diagram of each VE, similar to those shown in *figure 4.6*, with landmark positions marked, along with a list of landmark names. They had to match landmark names to the positions, scoring a point for each correct match. There were 17 landmarks altogether, but scores were corrected for the fact that it was not possible to make only one mistake for each VE, producing totals out of 15.

In Study 9, I assessed mental effort applied during navigational strategy switching using a self-report measure. Following completion of the VPM, participants were asked to rate on a scale from 0 to10 how much mental effort they felt they had to apply throughout the task in general, and specifically following a change in strategy. The difference between the two responses was taken as a measure of perceived mental effort (PME) applied to navigational strategy changes. I planned to control for PME when assessing age differences in pupillary and cardiac responses to strategy changes. However PME did not correlate with changes in pupil size (PS) or heart rate (HR), and there were no age differences in PS or HR changes.

2.3.3 Virtual plus maze

Rodent plus maze task

The VPM was an adaptation of a rodent task, previously used by Ragozzino and colleagues (Ragozzino et al., 1999; Ragozzino, 2007) and Shapiro and colleagues (Rich & Shapiro, 2007, 2009; Young and Shapiro, 2009, 2011) to assess navigational strategy switching. In such studies, rats are placed on the end of one arm of an elevated plus-shaped maze, surrounded by visual cues (*figure 1.7*). The entrance to the opposite arm is blocked, producing a T-maze, with reward wells at the ends of the other two arms. Only one reward well represents a correct response and contains a food reward. Which arm the animal is initially placed on (and which opposing arm is blocked) is changed regularly. For example, Rich & Shapiro (2007), changed the start arm after two consecutive correct responses during the first stage of training, then pseudorandomly (ensuring that no more than three consecutive trials used the

same start arm) during the second stage.

Changing the start arm means that subjects can use one of two kinds of strategy to find a reward. Rats can either use an allocentric place strategy, which takes into account the start arm, which may be inferred from the surrounding visual cues, and leads them to adjust their response accordingly, so that they still enter the same goal arm and reach the same reward well. Alternatively, animals may use an egocentric response strategy, which does not take into account their current starting position, but leads them to simply make the same response, regardless of which goal arm and reward well they visit as a result. Rich and Shapiro (2007) initially trained rats on one strategy until they reached a criterion of six consecutive correct trials. During subsequent training sessions, rats completed 24 trials from pseudorandomly selected start arms, and continued with this training until they achieved a criterion of at least 20 trials correct in two consecutive sessions. In the following session, the rewards changed, so that rats had to perform either a strategy switch (e.g. from a place strategy to a response strategy) or a reversal (e.g. from 'turn left' to 'turn right'), as illustrated in *figure 2.3*. Navigational strategy switching performance can be assessed in terms of correct responses during the session following the switch, responses consistent with the previous strategy (perseverative errors), and the number of sessions required to reach the performance criterion using the new strategy.

Original VPM

I developed the VPM in Vizard, based on the rodent plus maze task and on a similar VR task developed by Alexander Enoch. I used existing 3D models of a plus-shaped pathway, with light brown stone paving and grey brick kerbs, and a light grey brick well. I also used images of sky and mountain scenery, rendered on the inside surface of a vast box in 3ds Max, which was placed over the entire VE to provide a continuous background. Additional aspects of the VE were created in Vizard, including transparent walls around the edge of the maze, a large grass-textured plain surrounding the maze, a sign with directions indicating available responses (and the associated key presses required) that appeared at the central junction, and a yellow

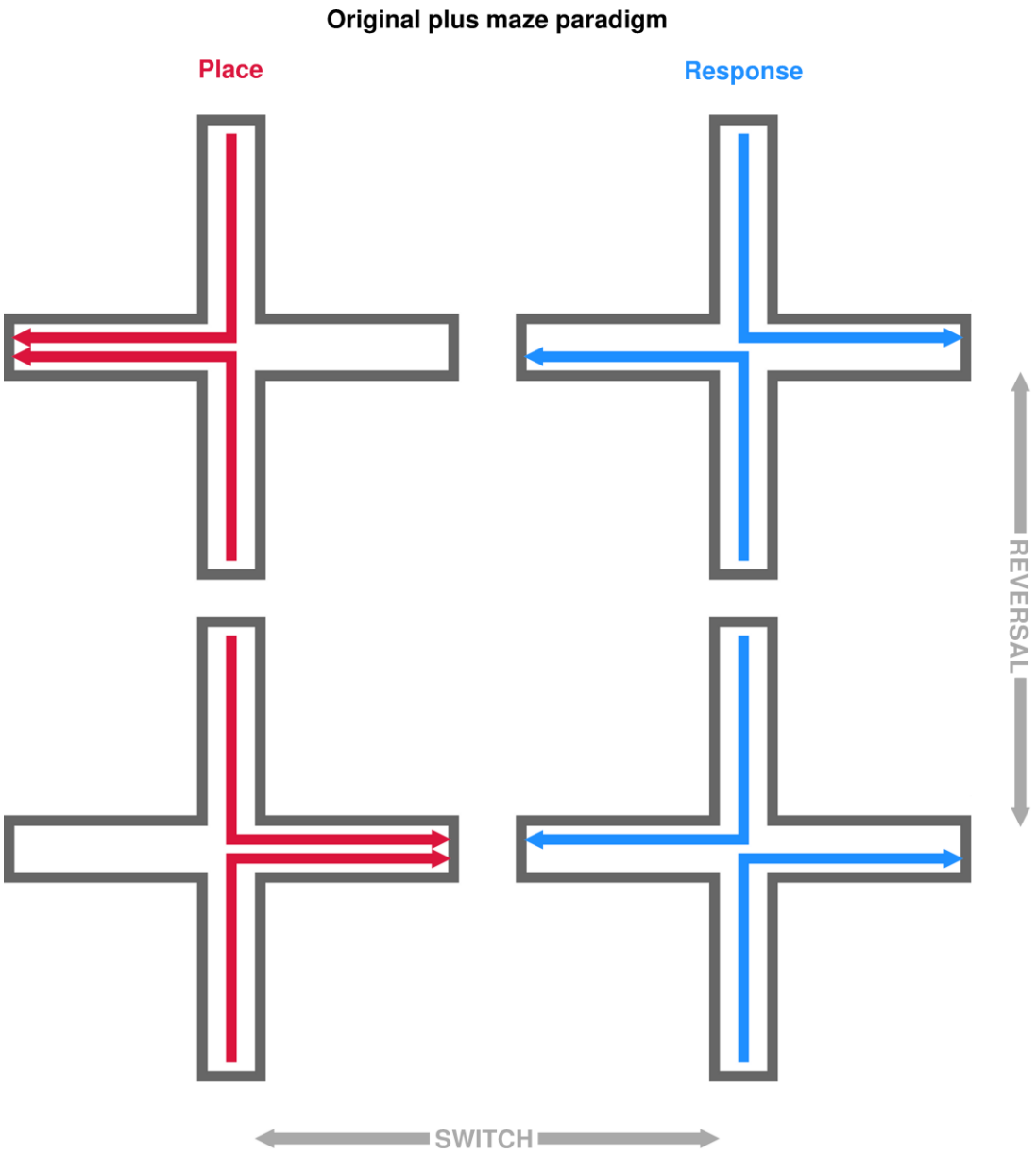

Figure 2.3 Original plus maze paradigm. The rodent plus maze task used opposing start arms and a two-way choice (left/right). This meant that, if animals continued to use the previous strategy following a strategy switch, they were still rewarded on 50% of trials.

ball that served as a reward signal. The participant's current score (in virtual money) was also displayed in the top right corner of the screen throughout the task.

Each trial began with the participant positioned at the end of either the north or south arm of the maze, facing towards the central junction. They initiated movement

forward to the central junction by pressing the up arrow key, or any button on a four-button pad used during fMRI. At the central junction, a sign appeared, featuring arrows indicating that the participant could turn left or right. In Study 7, these arrows appeared at the top and bottom of a tall sign, corresponding to the top and bottom buttons of the four-button pad used in the scanner. Which button participants had to press to turn in each direction (and the corresponding position of the arrows on the sign) varied randomly across trials, so that use of a response strategy did not produce a motor response-related activation signal. If participants did not respond within 3s, the trial was aborted without continuing through the central junction to either goal arm. However, if participants did press the left or right arrow key (or the top or bottom button) in time, the sign disappeared and they turned through the central junction and moved down the chosen east or west goal arm. Movement stopped just before the reward well, from which a yellow ball appeared as a reward signal if participants had responded in accordance with the current navigational strategy. A correct response also increased the total virtual money displayed in the top right corner of the screen. If participants did not respond in accordance with the current strategy, they received no reward signal and their virtual money balance did not increase. At the end of each trial, the view of the VE faded out so that participants could be instantly repositioned at a start arm, ready for the next trial to begin. Images of the VPM at four stages throughout a typical trial are included in *figure 2.4*.

Whether the participant received a reward depended on the current strategy. As in the rodent plus maze task (*figure 2.3*), participants could be rewarded for using a place strategy, which involved going to either the east or west goal arm, or a response strategy, turning either left or right. However, unlike the rodent task, participants were rewarded for using the same strategy only throughout blocks of 20 trials, with multiple blocks in the same session. Between trial blocks, there was either a strategy switch (e.g. from place to response), a reversal (e.g. from left to right) or no change. Following a strategy change, the only indication that participants were required to adopt a new strategy was the change in reward. Participants were then expected to try other strategies, monitoring the rewards they received, until they successfully learned the new strategy. When there was no change, participants simply continued to use the

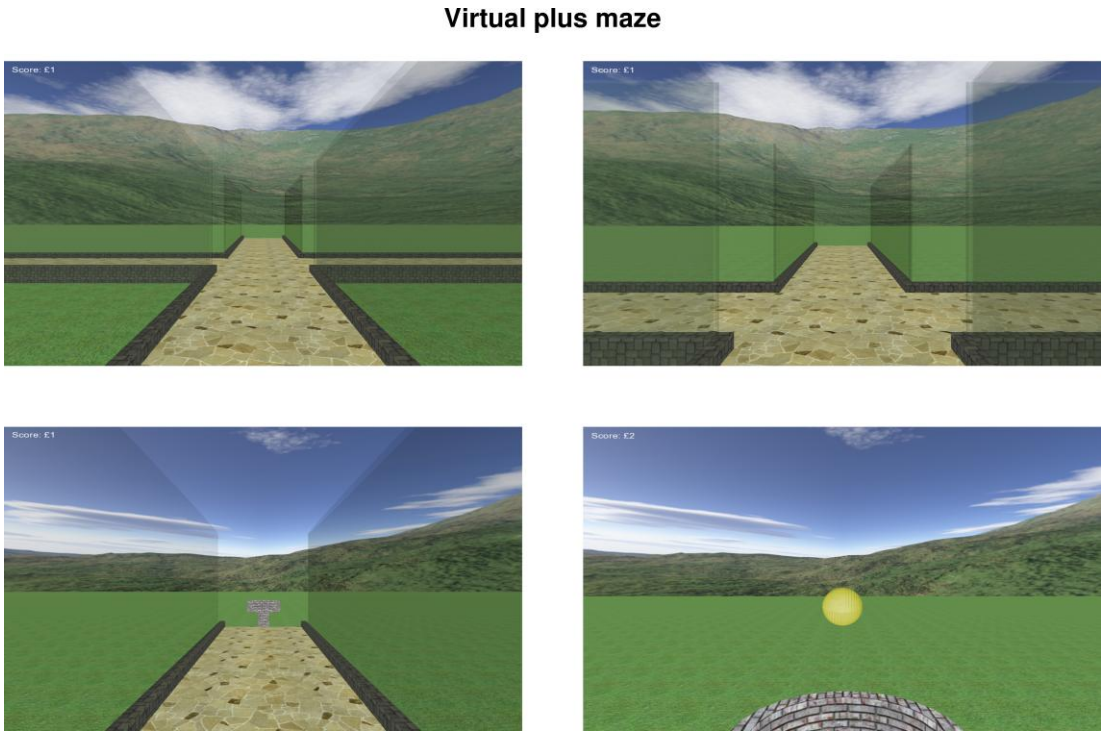

Figure 2.4 Virtual plus maze. Screen shots captured during the original version of the VPM at the start arm (*top left*), central junction (*top right*), entrance of the goal arm (*bottom left*) and goal arm reward well (*bottom right*).

same strategy, effectively producing some 40-trial blocks, which made strategy changes less predictable. The entire task involved a total of 320 trials in 16 blocks, with five switches and five reversals.

Trial length

The original VPM, as used in Studies 3 and 7, featured very long trials of up to 18s in length. This was due mainly to long and relatively slow periods of movement from each start arm to the central junction, and then from the central junction to a goal arm. I later drastically reduced, slightly accelerated and automated the start of these movement periods, reducing the maximum trial length to only 8s. Without changing the number of trials (as in Study 9, for example) this reduced the total task duration from almost an hour and a half to just over half an hour. I reduced the trial length just a little more for Study 5 by cutting half a second off the maximum decision time. The

VPM version used in Study 8, which I developed for use with fMRI, featured a fixed trial length (including decision time) of 6s (*figure 6.8*). In this version of the task, participants started each trial almost right at the central junction, and, following their response, only turned into the respective goal arm, so that very little time was devoted to movement. Variations in decision time and movement time (moving straight ahead took less time than turning) were compensated for by rest periods.

Rewarding the previous strategy

After using the VPM for a couple of studies, I noticed a problem with the design of the original plus maze task. As shown in *figure 2.3*, following a reversal, participants were never rewarded for using the previous strategy. However, following a switch, if participants continued to use the previous strategy, they were still rewarded on 50% of trials. In order to avoid this problem, I made two significant changes to the task; firstly, I allowed participants to proceed straight ahead at the central junction, giving them a three-way choice, and secondly, I used adjacent – rather than opposite – start arms. As shown in *figure 2.5*, this allowed me to ensure that participants were never rewarded for using the previous strategy following a switch.

Instructions and start arms

As above, I originally programmed the VPM to start participants from opposing start arms of the maze, either the north or south arm, as in the rodent plus maze task that it was based on. Later, in order to avoid rewarding the previous strategy, I began using adjacent start arms, for example south and west, or north and east. Still, the two start arms had to remain the same throughout trial blocks so that participants could use the same strategy on every trial. In fact they had to remain the same throughout the entire experiment, so that a change in start arms between trial blocks did not act as a cue that a change in strategy was required.

However, in some of the latest versions of the VPM, as used in Studies 5 and 8, I introduced instructions at the beginning of trial blocks, telling participants that they

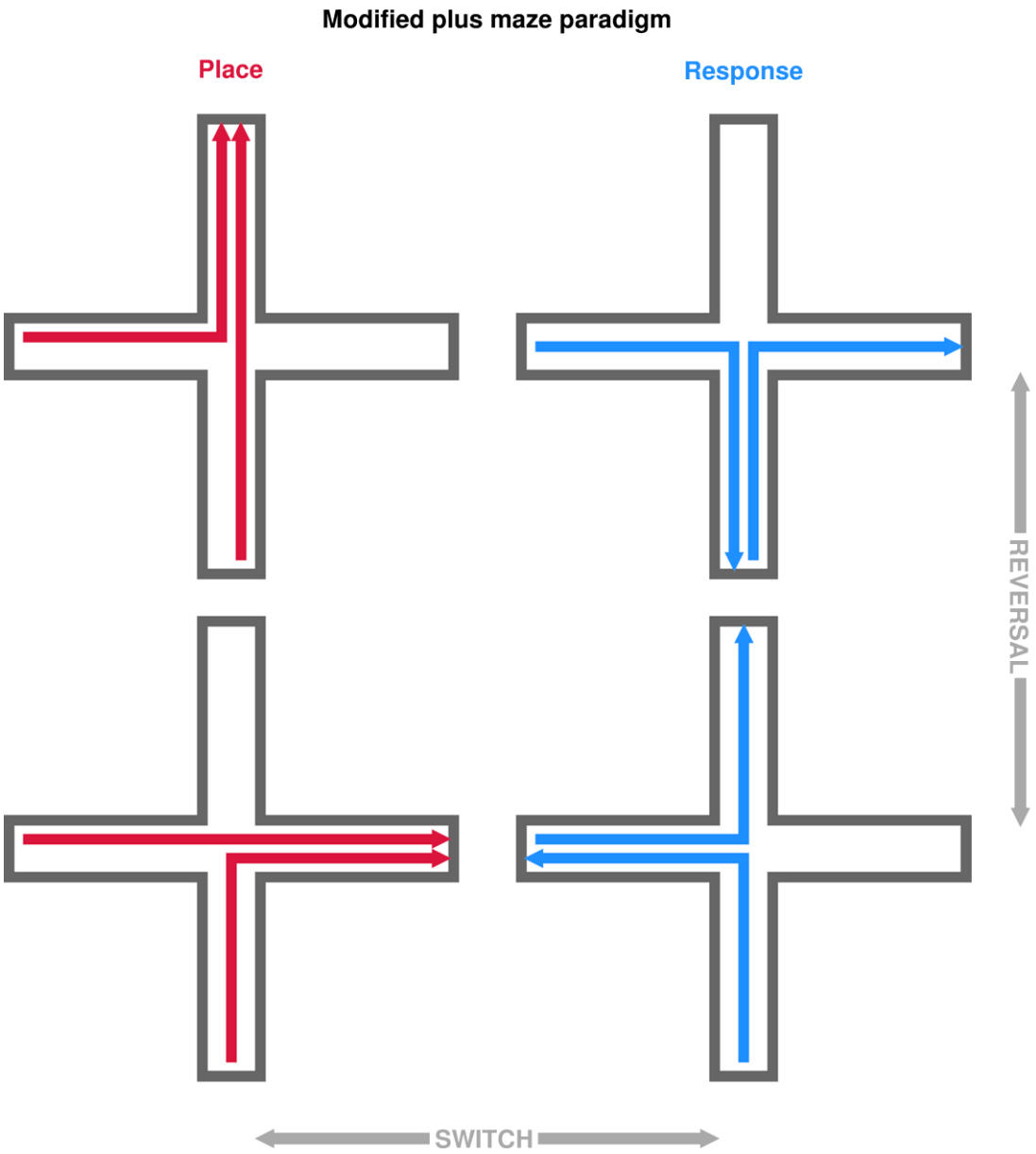

Figure 2.5 Modified plus maze paradigm. In later versions of the VPM, I used adjacent start arms (e.g. south and west) and a three-way choice (left/right/straight) to ensure that, following a switch, participants were never rewarded for using the previous strategy.

needed to adopt a new strategy, or even which strategy they needed to adopt. I had different reasons for doing so in each study, as discussed in Chapters Five (section 5.2.2) and Six (section 6.3.2). In each case, providing instructions meant that I no longer had to avoid cueing switches or reversals, and that I was free to vary the start arms. In these versions of the task, each new trial block used one of the start arms

that was used in the previous trial block (so that participants did not become completely disoriented) and one start arm that was not. This variation in start arms helped to ensure that participants did use an allocentric strategy when required to do so.

VE design

The original VPM featured a plus-shaped kerbed pathway, surrounded by transparent walls, in the centre of a large grass-texture plain, surrounded by mountain scenery. The east and west goal arms featured a reward well, out of which rose a yellow ball as a reward signal if participants responded in accordance with the current strategy. The plus-shaped pathway, grassy plain and mountain scenery were consistent aspects of all versions of the VPM. However, I soon decided that, as participants' movement was restricted to the pathway, the transparent walls were unnecessary, and these were removed from all but the earliest versions. At the same time I removed the reward wells, also feeling that they were unnecessary. Participants did not actually reach the well at the end of a trial, so it made no difference whether the reward signal appeared from out of the well, or just appeared. Also, after introducing the three-way choice, which arms were available as goals changed on each trial, so fixed reward wells were no longer appropriate. I also changed the colour of the ball that acted as a reward signal from yellow to green. Later, I changed the reward signal to a pile of three coins, being more consistent with the concept of a reward, and giving participants the motivation to collect as much virtual money as possible. I also removed the direction sign that appeared at the central junction, as this was not necessary when the same keys were used to make the same responses on every trial, as in all versions of the VPM except that used in Study 7.

As above, in Studies 5 and 8, I provided participants with instructions before each trial block, and varied the start arms, which meant that participants moved around the maze much more. In order to easily provide instructions on using an allocentric strategy, as well as to prevent participants from becoming disoriented, I added landmarks to the ends of the maze arms (*figure 2.6*). I was then able to provide

instructions such as “Go towards the log cabin”. Participants were also able to recognise the four maze arm locations much more easily, rather than having to rely on slight differences in the surrounding scenery. Additionally, I believe this may have facilitated the formation of an allocentric representation of the environment.

Trial and block numbers

While I dramatically reduced the total duration of the VPM by reducing the length of each trial, as above, in some studies I used the VPM as a secondary measure, or as one of several measures, and I needed the task to be shorter still. I achieved this by reducing the number of trials in each block and/or the number of trial blocks, so that there were fewer trials overall. The original version used blocks of 20 trials, but for one in every three potential change points, there was actually no change, so that there were effectively some blocks that were 40 trials long. This varied the block size in order to make strategy changes less predictable. However, in subsequent versions of the task I did this by varying the actual block size. For example, in Study 9, I used blocks of 20, 25 or 30 trials, which allowed me to include a strategy change between all blocks, thereby assessing more switches and reversals (12 rather than 10) with the same number of trials. In Study 6, I reduced the block lengths, reducing the overall duration of the task slightly without affecting the number of changes. In Studies 4 and 5, I used only nine blocks, producing shorter versions of the VPM, which still assessed eight strategy changes. In Study 5 in particular, as strategy changes were already cued by instructions, block length was fixed at 15 trials. Study 8 used a slightly different version of the VPM, with three sub-blocks of six trials per block, as described in further detail in Chapter Six (section 6.3.2). This version of the VPM also incorporated 20 trial blocks, slightly increasing the total number of trials and overall duration of the task.

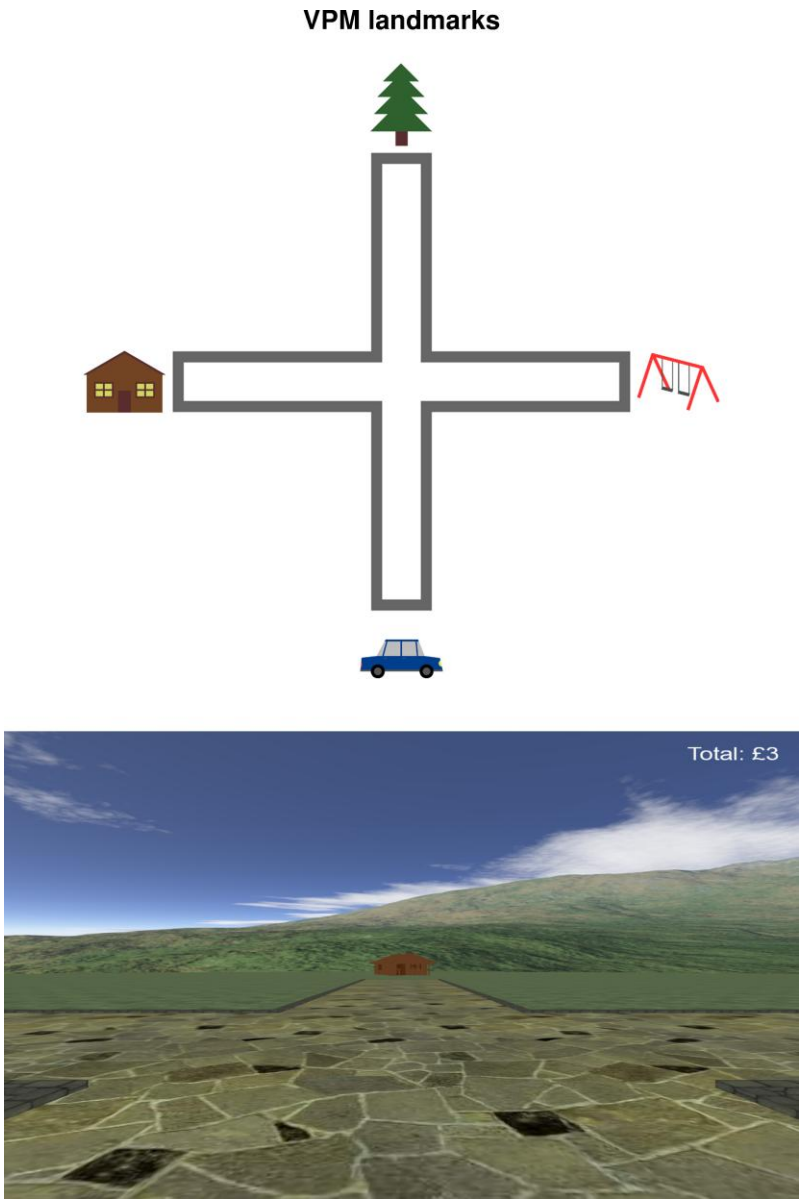

Figure 2.6 VPM landmarks. In the latest versions of the VPM, I included a copse, a playground, a car park and a cabin as landmarks at the end of each maze arm. *Top:* diagram of the VPM with landmarks. *Bottom:* screen shot of the VPM with landmarks.

Versions

I used one variation or another of the VPM in a total of seven of the experimental studies presented in the following chapters. Table 2.2 summarises the version of the VPM used in each study in terms of a number of key aspects of task and VE design.

VPM versions

Study	3	4	5a	5b
Trial time[1]	15s	5s	5s	5s
Decision time[2]	3s	3s	2.5s	2.5s
N trials	20 (/40)	15/20	15	15
N blocks	16 (11)	9	9	9
Total trials	320	155	135	135
Total time[3]	88min	17min	15min	15min
N switches	5	4	4	4
N reversals	5	4	4	4
Response choices	L/R	L/R	L/R/S	L/R/S
Start arms	N/S	N/S	varied	varied
First strategy	random	place	random	random
Previous rewarded[4]	50%	50%	0%	0%
Reward amount	£1	£1	$3	$3
Response keys	fixed	fixed	fixed	fixed
Instructions[5]	none	none	general	specific
Mountain scenery	yes	yes	yes	yes
Grass plain	yes	yes	yes	yes
Plus pathway	yes	yes	yes	yes
Transparent walls	yes	no	no	no
Reward wells	yes	no	no	no
Reward signal	yellow ball	green ball	3 coins	3 coins
Direction arrows	no	yes	yes	yes
Landmarks	no	no	yes	yes
Instructions[6]	yes	yes	yes	yes
Training	no	no	no	no
Practice	no	no	no	no

Table 2.2a VPM versions (3-5b). Summary of the VPM versions used in Studies 3-5 in terms of parameters relating to task length (red), task design (green), VE design (blue) and preparation (yellow). [1] Trial time excludes decision time, which varied. [2] Decision time represents the maximum time participants were allowed to decide which way to proceed at the central junction. [3] Total time is approximate, based on the mean possible decision time. [4] 'Previous rewarded' refers to how often the previous strategy was still rewarded following a strategy switch. [5] Here, 'instructions' relates to those that appeared on-screen between trial blocks. [6] Here, 'instructions' relates to those that participants received before beginning the task.

VPM versions

Study	6	7	8	9
Trial time[1]	5s	15s	4s	5s
Decision time[2]	3s	3s	2s	3s
N trials	17/20/23	20 (/40)	6+6+6	20/25/30
N blocks	13	16 (11)	20	13
Total trials	260	320	360	320
Total time[3]	28min	88min	42min	35min
N switches	6	5	8	6
N reversals	6	5	8	6
Response choices	L/R/S	L/R	L/R/S	L/R/S
Start arms	S/W	N/S	varied	N/E
First strategy	random	random	random	random
Previous rewarded[4]	0%	50%	0%	0%
Reward amount	$3	£1	$3	£0.02
Response keys	fixed	varied	fixed	fixed
Instructions[5]	none	none	stages	none
Mountain scenery	yes	yes	yes	yes
Grass plain	yes	yes	yes	yes
Plus pathway	yes	yes	yes	yes
Transparent walls	no	yes	no	no
Reward wells	no	yes	no	no
Reward signal	3 coins	yellow ball	3 coins	green ball
Direction arrows	yes	yes	no	yes
Landmarks	no	no	yes	no
Instructions[6]	yes	yes	yes	yes
Training	no	no	yes	yes
Practice	no	yes	yes	no

Table 2.2b VPM versions (6-9). Summary of the VPM versions used in Studies 6-9 in terms of parameters relating to task length (red), task design (green), VE design (blue) and preparation (yellow). [1] Trial time excludes decision time, which varied. [2] Decision time represents the maximum time participants were allowed to decide which way to proceed at the central junction. [3] Total time is approximate, based on the mean possible decision time. [4] 'Previous rewarded' refers to how often the previous strategy was still rewarded following a strategy switch. [5] Here, 'instructions' relates to those that appeared on-screen between trial blocks. [6] Here, 'instructions' relates to those that participants received before beginning the task.

2.3.4 Other tasks

Alternative approach task

The alternative approach task (AAT), used in Study 1, was developed in Vizard, primarily by Dr Jan Wiener at Bournemouth University, with whom I collaborated on this study. The task involved learning a route through six junctions of a grid-like brick wall maze, with two unique landmarks at diagonally opposite corners of each junction. Participants were then tested on rejoining the learned route from the original and two new directions. On specific test trials, participants' responses allowed us to discern whether they were using an egocentric beacon strategy, an egocentric associative cue strategy, or an allocentric configuration strategy. This task is described in more detail in Chapter Three (section 3.2.2) and illustrated in *figures 3.1* and *3.2*.

Route learning tasks

In Study 2, also conducted with collaborators at Bournemouth University, we used a route learning task (RLT), similar to the AAT in terms of VE design, featuring a grid-like brick wall maze, with two landmarks at each junction. However, participants were required to learn a much longer route, through 18 junctions, and were only tested by approaching each junction from the original direction. There were also two slightly different versions of the task; one featured two landmarks on opposite sides of each junction, intended to encourage use of the beacon strategy, while the other featured the landmarks one on top of the other in the centre of each junction, limiting participants to using the associative cue strategy. We used these tasks to assess age differences in ability to use each of the two strategies. In two shorter accompanying tasks, participants were presented with still images of each of the landmarks in turn. In the landmark direction test (LDT), participants had to indicate which way they had to turn when they saw the presented landmark. In the landmark position test (LPT), they simply had to indicate whether the landmark had appeared on the left or right, or at the top or bottom, of the junction. The RLT, LDT and LPT are also described in further detail in Chapter Three (section 3.3.2), and the RLT is shown in *figure 3.7*.

Shortcutting task

In Study 4, I assessed switching from an egocentric strategy to an allocentric strategy in a more realistic context than the VPM. The shortcutting task, which I developed in Vizard, featured two realistic virtual town environments, which I designed in 3ds Max. Participants were trained on four long routes through the VEs, as shown in *figure 4.6*, until they were able to follow each route without directions or errors, and to demonstrate having at least begun to form an allocentric representation of the VEs. During testing, participants were no longer restricted to the long training routes, and were instead instructed to find the shortest route to each goal location. This meant switching from an egocentric route following strategy to an allocentric wayfinding strategy in order to use the available shortcuts. The shortcutting task is described in more detail in Chapter Four (section 4.3.2).

Navigational gambling task

In Study 5, I used two variations of the VPM to assess the contribution of decision making abilities to navigational strategy switching performance. I compared performance at the standard and no-DM versions of the VPM to performance at a navigational adaptation of an established measure of decision making, the Iowa Gambling Task (IGT; Bechara et al., 1994). The navigational gambling task (NGT) involved visiting one of four landmark locations, each of which was associated with a consistent reward and a variable penalty. On average, two 'good' choices had a positive net value, while two 'bad' choices had a negative net value. Decision making was assessed in terms of the number of good choices. The NGT is described in further detail in Chapter Five (section 5.2.2) and depicted in *figure 5.1*.

Raven's Standard Progressive Matrices

In Study 6, I used Raven's Standard Progressive Matrices (RSPM; Raven, 1996; Raven et al., 1996) as a non-spatial measure of general fluid intelligence. The full RSPM consists of five sets of 12 items, each more difficult than the last. Each test

trial presents a two-dimensional pattern in a three-by-three grid, with the bottom right item missing. Beneath the pattern matrix are six (sets A & B) or eight (sets C-E) separate pieces that could fit in the bottom right space to complete the pattern (*figure 5.6*). Participants must determine which piece completes the pattern correctly. I used Vizard to create a computerised version of the RSPM, in which participants simply clicked on the piece that they thought completed the pattern. As I required a shorter test than the full RSPM, I used only the first four items from each set. Participants were allowed 10min to complete all 20 items, giving a score out of 20.

2.4 Physiological measures

2.4.1 Functional magnetic resonance imaging

Equipment

For Study 7, fMRI data were acquired at the UCSB Brain Imaging Center using a 3T Magnetom Trio Tim System (Siemens, Munich, Germany) with a 32-channel head coil. The VPM, running on a high performance laptop, was projected onto a screen behind the scanner, viewed by participants using a mirror angled at 45°. Participants provided input using an Inline four-button fibre optic response pad (Current Designs, Philadelphia, PA, USA).

Procedure

Soon after arrival, participants were screened for any metal implants or health conditions that may have prevented them from undergoing fMRI. They were asked to change their clothes and remove all jewellery, ensuring that they had no metal on their persons. Following instructions and a single practice session, participants performed the VPM over four sessions in the scanner, separated by several minutes' rest. During these four sessions, functional EPI volumes were acquired as 25 interleaved 2.5mm slices of 2.0x2.0mm voxels with 1.0mm gap (TR=2170ms,

TE=35ms, FA=70°), covering the entire brain. At the end of the experiment, participants remained in the scanner for acquisition of anatomical data, which followed a standard T_1-weighted sequence (TR=2300ms, TE=2.98ms, FA=9°, 1.0mm isotropic).

Data pre-processing

I used the Statistical Parametric Mapping (SPM) package for Matlab, version 8 (Wellcome Trust Centre for Neuroimaging, London, UK) to preprocess fMRI data, which involved slice timing correction, realignment and coregistration (without reslicing) of functional and anatomical images. I used the ArtRepair SPM toolbox (Mazaika et al., 2005) to check for bad volumes, and normalised and smoothed images with a 5mm FWHM kernel. I created region of interest (ROI) masks by segmenting structural images using FreeSurfer (Laboratory for Computational Neuroimaging, Boston, MA, USA), exporting and combining segments using FSL (FMRIB Analysis Group, Oxford, UK) and the built-in SPM ImCalc function, and splitting larger segments into smaller ROIs using the MarsBaR SPM toolbox (Brett et al., 2002).

2.4.2 Physiological correlates of LC-NA activity

Pupil size

In Study 7, pupil size was monitored throughout VPM performance using an EyeLink II eye-tracking system (SR Research, Mississauga, ON, Canada). At the beginning of the experiment, participants were fitted with a headset, supporting a small camera pointed at their left eye. The equipment was calibrated using the EyeLink software package, which required participants to visually track some dots presented on-screen. To ensure that PS was not affected by changes in environmental lighting, the experiment was conducted in an isolated and dimly lit room, and the colours used in the VPM were changed in order to minimise task-related changes in screen luminosity. As the VPM was run on a separate computer to the eye-tracking

software, the system times of the two machines were synchronised regularly. PS was measured in relative arbitrary units (related to the number of pixels within the camera image identified as being within the pupil) at 500Hz. Therefore, after preprocessing to remove and interpolate blink periods, PS data were z-scored by participant (subtracting each participant's mean PS from their data, then dividing it by the standard deviation) before making any group comparisons.

Heart rate

In the same study, HR was also monitored, using a Lifecard CF 3-channel holter monitor (Spacelabs Healthcare, Snoqualmie, WA, USA). For each participant, the holter monitor was fitted with a new battery, then synchronised with the system time of the computer running the VPM. Participants were instructed on how and where to fit the electrodes and the output of the monitor was checked before beginning the task. The monitor recorded the time of each detected heartbeat, from which HR data could be derived. These HR data were then interpolated and resampled at a constant rate of 10Hz, so that faster HRs were not over-represented. HR data were also z-scored by participant following initial group comparisons.

2.5 Data analysis

2.5.1 Software

I performed all of my data analysis in Matlab (The Mathworks, Natick, MA, USA), versions 2010a and 2011b, with the Matlab Statistics Toolbox. In addition to the standard functions included in Matlab and the Statistics Toolbox, I made use of the Mixed (Between/Within Subjects) ANOVA function, the NaN Suite toolbox and the Measures of Effect Size Toolbox, all downloaded from the Matlab Central File Exchange. I used SPM8 to analyse fMRI data in Matlab, after preprocessing the images and creating ROIs using SPM8, the ArtRepair SPM toolbox, FreeSurfer, FSL and the MarsBaR SPM toolbox, as described in section 2.4.1. I also applied multi-

voxel pattern analysis (MVPA) using the Princeton MVPA toolbox (Princeton Neuroscience Institute, Princeton, NJ, USA). The Bayesian learning analysis (Smith et al., 2004), described below in section 2.5.3, was run in WinBUGS (Lunn et al., 2000) through the Matbugs function for Matlab.

2.5.2 Data representation

Participant information

Participants' ages were measured in full years at the time of testing. Gender information was represented by a single figure (1=male, 2=female). Where relevant, task condition (1=associative cue, 2=beacon) and orienteering group (0=control, 1=orienteer) were recorded in the same way, while length of involvement in orienteering was measured in full years at testing, as for age. Computer experience measurements on the two nine-point scales were combined to produce a single score.

Behavioural data

Results of the MMSE, MoCA, Corsi blocks task, NART and RSPM were represented by a single score. As for computer experience, the CMT produced two measures, but these were combined as a corrected total score. The PME questionnaire also produced two measures, which were combined by calculating the strategy change-related increase in PME. Performance at the various VR tasks was usually recorded in terms of response and response time (or route length and shortcut use for the shortcutting task) for each trial, alongside the current settings of variable task parameters used on that particular trial. SWMT data were then reduced to three figures, representing scores for place recall, route recall and reward sensitivity. For each of the other VR tasks, I was then able to summarise performance over all trials or within various groups of trials. Further details on the analysis of data derived from VR tasks that I used in only one study (the AAT, RLT, LDT, LPT, shortcutting task and NGT) are discussed in more detail in the subsequent experimental chapters in which the respective studies are presented. Briefly, I generally assessed VPM data in

terms of the proportions of trials correct (TC), blocks learned (BL) and stable trials (ST) for each change type (switch-to-place, S-P; switch-to-response, S-R; reverse-place, R-P; reverse-response, R-R). Blocks learned and stable trials measures were derived from patterns of correct responses throughout trial blocks using the Bayesian Learning analysis, described below in section 2.5.3. Again, further information on analysis of VPM data is included in subsequent experimental chapters.

Physiological data

As described above in section 2.4.1, fMRI data were represented as a series of EPI volumes, comprising 25 interleaved 2.5mm slices of 2.0x2.0mm voxels with 1.0mm gap, along with an anatomical image of 1.0mm isotropic voxels. PS was measured in relative arbitrary units, relating to the number of pixels in the camera image identified as being within the pupil, at 500Hz. Cardiac activity was measured in terms of the times at which individual heart beats occurred, from which HR data could be calculated.

2.5.3 Data preprocessing

Outlier removal

For each study, data were checked for participants who performed very differently to the rest of their group. For this purpose, I used a general measure of performance of particular relevance to each study, for example, overall VPM trials correct. Outliers were defined as those whose performance, in terms of this measure, was either lower than 2.5 times the group standard deviation (SD) below the group mean, or higher than 2.5 SDs above the group mean. Identified outliers, detailed in subsequent experimental chapters, were excluded from all further analyses. Importantly, outlier removal was performed separately for young and old participant groups.

Bayesian learning analysis

I used a Bayesian learning analysis package, developed by Smith, Frank, Wirth et al. (2004), primarily to assess learning of each strategy throughout VPM trial blocks. I performed a separate analysis for each block, for each participant. Smith et al.'s main function received three inputs; the performance for each trial in the block, the maximum possible performance for each trial in the block, and the chance probability of responding correctly on any given trial. Maximum performance was always an array of ones with the same length as the trial block, for example, 20. For each study, chance probability was always the same too; either .5 or .333, depending on which version of the VPM I had used. The performance variable was also an array of the same length as the trial block, but represented the accuracy of responses throughout the block as a binary sequence.

From the pattern of correct responses, the Bayesian learning analysis used a state-space smoothing algorithm to estimate the probability of a correct response at each point throughout the block. This probability, as a function of trial number, represented a learning curve. Upper and lower confidence intervals of this learning estimation were also calculated, as plotted in the examples shown in *figure 2.7*. If the lower confidence interval rose above and stayed above the chance probability threshold, I inferred that the participant had learned the correct strategy for that block. Performing this analysis for every block thereby produced the blocks learned measure; the proportion of blocks for which the participant learned the correct strategy.

I also took the last point at which the lower confidence interval crossed the chance probability threshold as the point at which the participant learned the strategy for that block. After this point, even if they made a small number of errors, they were stably using the correct strategy. The stable trials measure represented the proportion of trials after this point. Importantly, if the lower confidence interval crossed the chance probability threshold, but then dropped back below it and stayed below it, the participant was not said to have learned the strategy for that block, or to have stably

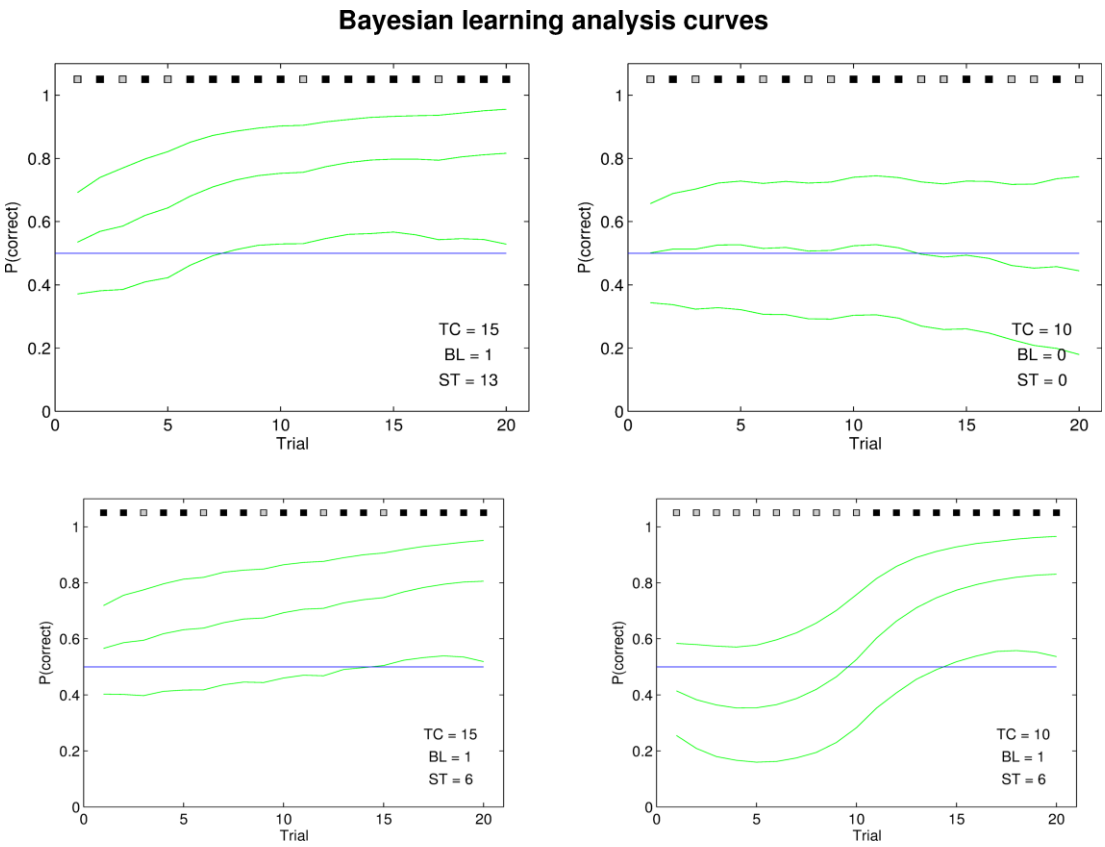

Figure 2.7 Bayesian learning analysis curves. Four examples of the curves output by the Bayesian learning analysis package, representing an estimation of learning, with 95% confidence intervals, throughout VPM blocks of 20 trials. Correct responses are marked as white squares at the top of each plot. These four examples illustrate the potential differences between trials correct (TC), blocks learned (BL) and stable trials (ST) measures of VPM performance.

used the correct strategy for any of the trials.

Physiological data

As described above in section 2.4.1, I used SPM to correct slice timings and to realign, coregister, normalise and smooth images, prior to analysis of fMRI data. For PS data, blink periods were removed and interpolated, and data were z-scored by participant. HR data were also interpolated, resampled at a constant rate of 10Hz, and then z-scored by participant.

2.5.4 Statistical analysis

Summary statistics

Data were generally assumed to derive from normal distributions, and were therefore summarised using parametric descriptive statistics. Group data were represented by their mean and SD. In most of the results figures in subsequent chapters, bars and plotted points represent group means, while error bars represent standard error of the mean (SEM). The mean was also used to summarise individual participants' data, across trials or blocks for example, in order to produce a single figure that could be used in group analyses.

Inferential statistics

Throughout my data analysis, I often assessed the effects of age and another factor, for example VPM change type, using a two-way mixed ANOVA. I followed these, and other ANOVAs, with post-hoc t-tests, correcting for multiple comparisons using the Holm-Bonferroni method, as described in the following section. I also commonly used stepwise regression analyses to identify which of a number of factors significantly predicted performance, and generalised linear models (GLMs) to assess the relative contributions of multiple factors or predictors. In some studies, I computed Pearson's product-moment correlation coefficient to assess the relationship between variables, used chi-squared tests to investigate differences between distributions, and computed cumulative distribution functions (CDFs) to assess deviation from chance performance. In Study 4, I applied the Bayesian learning analysis described above to data on use of shortcuts in order to assess whether participants stably switched to an allocentric wayfinding strategy. Further details on how I utilised these statistical procedures are included in the relevant experimental chapters.

Multiple comparison correction

I corrected for multiple comparisons based on the Holm-Bonferroni method (Holm, 1979). Considering an example of a set of six related p values, drawing inferences without correcting for multiple comparisons simply involves comparing each of the p values to the same α value, for example, .05. Using the Bonferroni method involves dividing the α value by the number of comparisons, so that each p value is instead compared to .0083. Each effect has to be much stronger in order to achieve significance, but this reduces the chance of making a type I error (identifying a false positive), thus compensating for the problem of multiple comparisons. However, the original Bonferroni method is quite conservative, and increases the probability of making a type II error (finding a false negative). Applying the Holm-Bonferroni method involves first ranking the set of p values. The smallest is then compared to α/n, as with the Bonferroni method. However, if this effect is significant, the next p value is compared to α/(n-1), or 0.01; the following to α/(n-2), or 0.0125, and so on, until the highest p value is simply compared to α, or .05, as without correcting for multiple comparisons. This method, in comparison to not correcting for multiple comparisons, still reduces the chance of making a type I error, but also, in comparison to the original Bonferroni method, reduces the chance of making a type II error.

While the Holm-Bonferroni method suggests that the α value to which p values are compared should be reduced by a variable factor (dependent on the p value's ranking), multiplying the p value by the same factor, without changing the α, is equivalent, and in each case leads to the same inference. However, using this variation of the Holm-Bonferroni method produces a corrected p value for each comparison, which may be useful to report. Throughout my data analyses, I corrected for multiple comparisons using this variation of the Holm-Bonferroni method so that, in subsequent chapters, I was able to report corrected p values, which I have denoted p_{HB}.

fMRI analysis

fMRI analysis methods are detailed in Chapter Six (section 6.2.2). Briefly, I performed first and second level general linear model (gLM) analyses in SPM, first modelling data with regressors defined in terms of trial phase, learning stage and either change type or strategy. I then performed F and t contrasts for each participant, and subsequently for the whole group, assessing activation differences between switch learning and stable strategy periods, and between place and response stable strategy periods. These analyses were restricted to ROIs by applying masks, and I used small volume correction (SVC) to correct for familywise error (FWE) within each ROI. I also tried to decode switching status, change type, strategy, future and past locations, and movement type from activity within ROIs using the Princeton MVPA toolbox. Data were high pass filtered, z-scored and averaged, and regressors were shifted by three TRs. I used ridge regression, following ANOVA-based feature selection, to classify data from the four sessions. Finally, I used the 'wavestrapper_results' function to check whether classification accuracies were significantly higher than chance.

Chapter Three

Use of Allocentric and Egocentric Navigational Strategies in Ageing

3.1 Chapter overview

The majority of my doctoral research focused on the ability of older people to switch between allocentric and egocentric strategies during navigation, as described in subsequent experimental chapters of this thesis. The ability to switch between various strategies is critical to everyday navigation, as, due to factors such as the inconsistent availability of different cues and the revision of navigational goals, the optimal navigational strategy can change frequently. A deficit in strategy switching may impair an individual's ability to use the most appropriate navigational strategy, which could have subtle or even severe consequences for navigational performance. Before addressing the issue of navigational strategy switching directly, this chapter introduces the concepts of allocentric and egocentric strategies, presenting two studies exploring their use by older people.

In section 3.2, I present Study 1, which assessed the use of an allocentric configuration strategy and egocentric associative cue and beacon strategies by young and older people. During training, participants learned a short route through four junctions in a virtual maze. During testing, they approached each of these junctions in a random order, either from the same direction or from one of two novel directions. On same direction test trials, accurate use of any of the three possible strategies produced a correct response, whereas on different direction test trials, the three strategies predicted different responses, and only the allocentric configuration strategy consistently led to a correct response. However, as allocentric navigation depends upon a representation learned through environmental experience, use of the appropriate configuration strategy likely required participants to switch to this strategy at some point throughout repeated training and testing cycles. This study aimed to assess age differences in spontaneous use of allocentric and egocentric

strategies, which may demonstrate the potential impact of navigational strategy switching deficits in ageing.

Study 2, reported in section 3.3, followed on from Study 1 by investigating age differences in ability to navigate using the egocentric associative cue and beacon strategies. Specifically, this study assessed whether older people are impaired at using the associative cue strategy. Young and old participants completed one of two versions of a route learning task; one of which limited them to using an associative cue strategy, while the other encouraged use of a beacon strategy. Participants also performed some secondary tasks, designed to further explore the nature of any deficits in use of the associative cue strategy.

Both studies were conducted in collaboration with Dr Jan Wiener and Olivier de Condappa at Bournemouth University, while several undergraduate students also assisted with data collection. However, I was directly involved in designing and running each study, I performed the data analysis reported here myself, and the content of this chapter is entirely my own work. Study 1 has been published in *The Journal of Neuroscience* (Wiener et al., 2013).

3.2 Study 1: Use of allocentric and egocentric navigational strategies in ageing

3.2.1 Introduction

Route navigation in ageing

While navigation is impaired in ageing, this applies mainly to allocentric navigation (Moffat & Resnick, 2002; Moffat et al., 2006; Antonova et al., 2009; Iaria et al., 2009), supported by the hippocampus (O'Keefe & Nadel, 1978; Morris et al., 1982; Hartley et al., 2003; Iaria et al., 2003), which shows substantial atrophy with ageing (Jack et al., 1997; Moffat et al., 2006; Du et al., 2006; Lister & Barnes, 2009). Some

egocentric aspects of navigation, such as route traversal, are less affected by ageing (Begega et al., 2001; Jansen et al., 2010), as they do not depend upon the hippocampus. Egocentric strategies are instead more reliant upon the caudate nucleus (Cook & Kesner, 1988; Packard & McGaugh, 1996; Hartley et al., 2003; Iaria et al., 2003), which is still prone to age-related neurodegeneration (Raz et al., 2005; Hasan et al., 2008), but less so than the hippocampus (Jernigan et al., 2001; Fjell et al., 2009; Raz et al., 2010). However, egocentric and allocentric representations interact hierarchically (Zaehle et al., 2007; Pellizer et al., 2009), and, while route navigation normally begins by encoding the route procedurally, the route is also subsequently (Hart & Moore, 1973; Siegel & White, 1975; Dabbs et al., 1998) or simultaneously (Montello, 1998; Ishikawa & Montello, 2006) encoded within a higher level allocentric representation of the surrounding environment. Consequently, allocentric processing abilities, as well as the ability to switch to an allocentric strategy, may also be important to route navigation. As ageing produces greater impairments in allocentric than egocentric navigation, as well as deficits in strategy switching (Moore et al., 2003; Ashendorf & McCaffrey, 2008; Young et al., 2010), older people may be less able to engage allocentric processes during route navigation, and may instead prefer to continue using egocentric strategies. Some studies have already demonstrated a greater preference for egocentric strategies among older people (Rodgers et al., 2012; Konishi et al., 2013).

Types of egocentric strategy

Egocentric navigation typically involves the encoding and use of procedural route knowledge, in the form of a series of associations between visual landmarks encountered along the route and body movements required at each landmark location; for example, “at the clock tower, turn right” (Siegel & White, 1975; Waller & Lippa, 2007). However, route navigation is also possible by a similar but even simpler strategy than this associative cue strategy. Visual cues can be used as beacons, in which case navigators do not need to encode a specific associated response, but can simply remember to move towards each beacon; for example, “go towards the clock tower” (Collett, 1996; Waller & Lippa, 2007; Redhead et al.,

2013). While still supported by the dorsomedial striatum (Devan & White, 1999), beacon navigation is less dependent upon dorsolateral striatal stimulus-response learning (Reading et al., 1991; Featherstone & McDonald, 2004). Therefore, just as hippocampal degeneration would predict a greater reliance on egocentric strategies among older people, greater dysfunction of dorsolateral striatum (Raz et al., 2003; Abedelahi et al., 2013) suggests that older people may be specifically inclined to favour a beacon strategy.

Current study

In this study we investigated age differences in navigational strategy preference using a novel virtual route navigation task. Participants learned a route through four junctions of a grid-like maze, and were tested on trials that involved rejoining the route at each junction, either from the same direction as in the original route or from a different direction. Participants could learn the route and accurately complete same direction test trials using an associative cue strategy, a beacon strategy or an allocentric configuration strategy. However, to perform well on different direction test trials they had to use the configuration strategy. Some different direction trials were also able to differentiate between responses derived from each of the three strategies, providing a measure of strategy preference. We predicted that older participants would perform significantly worse on different direction test trials, due to significantly less frequent use of the allocentric configuration strategy. As above, of the two alternative egocentric strategies, older participants could also be expected to show a specific preference for the beacon strategy. Finally, as using the egocentric strategies required less cognitive processing than the configuration strategy, we expected that older participants would respond significantly quicker on both same and different direction test trials.

3.2.2 Methods

Participants

Twenty-three (12 female) young (aged 18-23, M=20.7) and 24 (12 female) older (aged 65-86, M=74.3) participants were recruited from the School of Philosophy, Psychology and Language Sciences (PPLS) panel of psychological research volunteers and from the local student population. All had normal or corrected-to-normal vision, and no known neuropsychological impairments. Participants were reimbursed for their time at a rate of £6 per hour. One 86-year-old female was excluded based on her Montreal Cognitive Assessment (MoCA) score, which was below the criterion of 23 out of 30.

Procedure

Participants were fully informed about the study and provided written consent before participating. They then completed the MoCA on paper, as described in Chapter Two (section 2.3.1), followed by the spatial working memory task (SWMT), also described in Chapter Two (section 2.3.2), and the alternative approach task (AAT), described below. All tasks were completed on a desktop computer with a 24in widescreen monitor and a standard UK keyboard. Following completion of the AAT, participants were told a little more about the design of the task and the expected results. The experiment was approved by ethics committees at the University of Edinburgh and Bournemouth University, and conducted in accordance with the British Psychological Society's (BPS) code of ethics.

Alternative approach task

This task was set in a virtual environment (VE) comprising a labyrinth of brick-walled tunnels and four-way junctions, designed, programmed and run in Vizard. At each junction, two boxes situated on the ceiling in diagonally opposite corners featured unique pictures of animals, serving as landmarks (*figure 3.1*), and the view

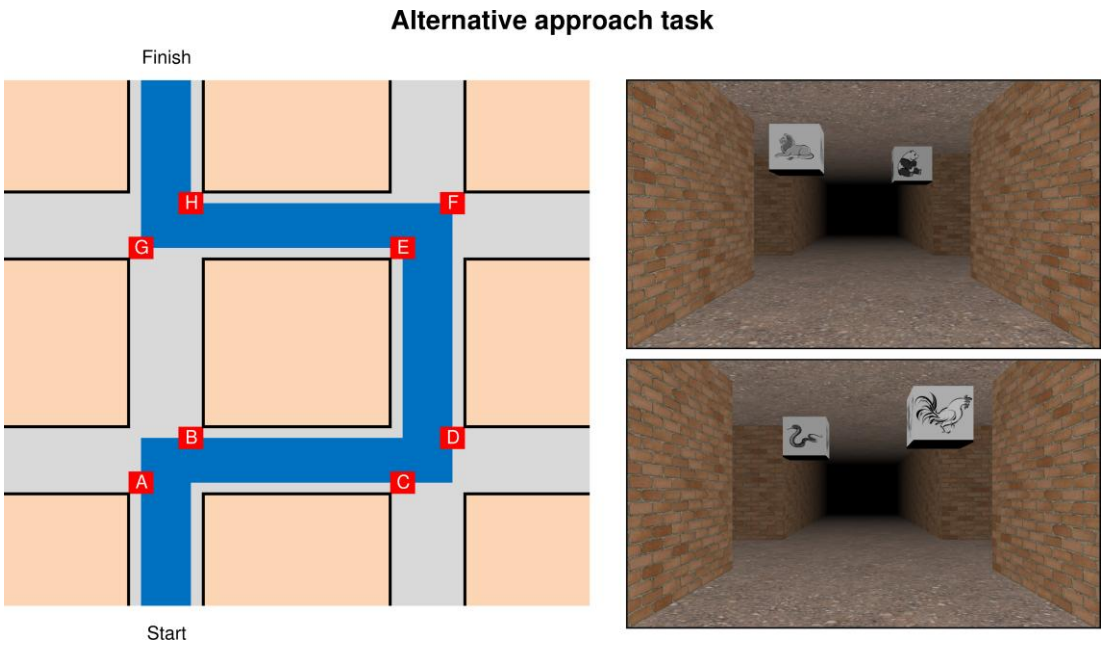

Figure 3.1 Alternative approach task. *Left:* Diagram of the training route through four junctions of the grid-like virtual maze, showing landmarks A to G placed at two diagonally opposite corners of each junction. *Right:* Screen images captured at two of the junctions during the task.

of other junctions was obscured by a fog. Participants were trained and tested on a route from one side of the maze to the other, passing through four junctions, viewing eight different landmarks. The training phase consisted of two passive traversals of the entire route, with participants having received instructions to memorise it. During the testing phase, participants approached each junction three times – from the same direction as in the original route and from two different directions – producing a total of 12 trials, presented in a pseudorandomised order. Participants were required to indicate which direction the route proceeded in from the junction featured in each trial by pressing the left, right or up arrow key on the keyboard. Responses and response times were recorded. This pattern of training and testing was repeated six times throughout the experiment.

Participants were free to memorise the route however they pleased, and three possible strategies would have led to successful route learning. Participants could have used an egocentric associative cue strategy, associating one of the landmark

cues at each junction with the response required at that junction, for example, "turn left at the lion". Alternatively, as the route always involved turning left or right at a junction, participants could have used a beacon strategy, also egocentric, which meant using the landmark on the same side of the junction as the turn as a beacon, for example, "turn towards the lion". Finally, participants could have used an allocentric configuration strategy, encoding the spatial layout of the VE and the route, as well as the configuration of the landmarks at each junction, and using this to orient themselves at each junction before determining the correct direction to proceed in. As shown in *figure 3.2*, on same direction test trials, accurate use of any of these strategies produced a correct response. On different direction test trials, the configuration strategy always produced a correct response, while one or the other of the two egocentric strategies sometimes also produced a correct response. Two of the eight different direction test trials included in each testing repetition were able to differentiate between the associative cue, beacon and configuration strategies, as, on these trials, each predicted a different response, with only the configuration strategy producing a correct response.

Data analysis

Data analysis was performed using Matlab. SWMT performance was assessed in terms of place recall and route recall. AAT performance was assessed in terms of the proportion of correct responses to both same direction and different direction test trials. I first checked for effects of independent and control variables on different direction trial performance using a stepwise regression analysis. Following this, I explored the effects of factors age and testing repetition on same direction and different direction test trial performance, using mixed model ANOVAs and post-hoc t-tests, with Holm-Bonferroni correction for multiple comparisons (corrected p values are denoted p_{HB}). By the same method I assessed use of the associative cue, beacon and configuration strategies in terms of the proportion of responses in accordance with each throughout differentiating test trials. Within the older group, I assessed differences in frequency of use between strategies using a within-subjects ANOVA, with strategy and repetition as factors, followed by post-hoc t-tests. Across

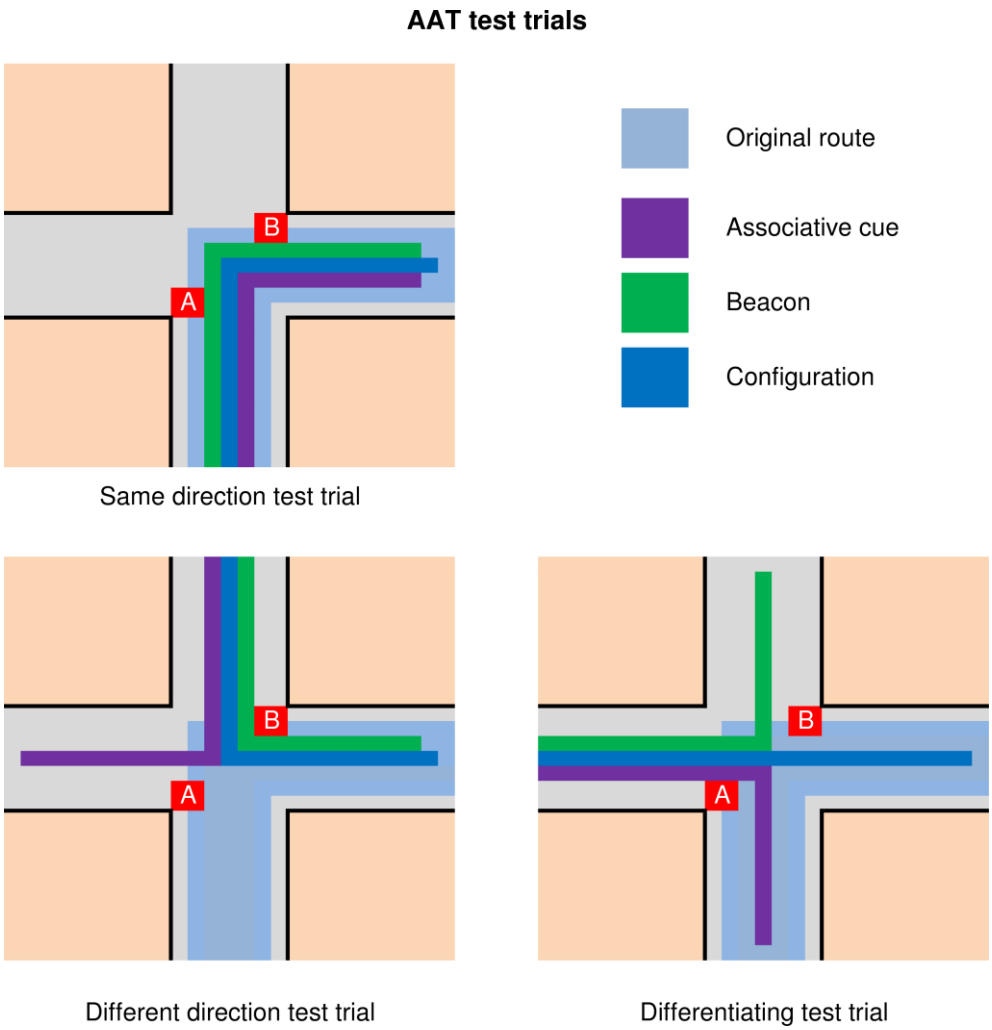

Figure 3.2 AAT test trials. *Top left:* On same direction test trials, accurate use of the associative cue (purple), beacon (green) or configuration (blue) strategy produced a correct response. *Bottom left:* On different direction test trials, use of the configuration strategy always produced a correct response, with use of one of the other strategies sometimes also producing a correct response. *Bottom right:* On specific different direction test trials, all three strategies predicted a different response, with only the configuration strategy predicting a correct response.

all participants, I assessed response times using a mixed ANOVA with trial type (same direction or different direction) as the within-subjects factor, also followed by post-hoc t-tests. I also computed a binomial cumulative distribution function (CDF) to assess deviation from chance performance for same direction trial responses in all participants, as well as for frequency of strategy use in older participants.

3.2.3 Results

Control variables

I first assessed the effects of age group and control variables gender, place recall and route recall on AAT different direction test trial performance using a stepwise regression analysis. As shown in *table 3.1*, only age was retained in the model as a significant predictor. Older participants performed worse than young on the SWMT in terms of both place recall (young: M=93.02, SD=5.12; old: M=61.75, SD=19.36) and route recall (young: M=92.92, SD=7.02; old: M=62.65, SD=8.65). However, as none of the control variables were identified as significant predictors of AAT performance, they were not considered in any of the subsequent analyses.

AAT performance stepwise regression results

Predictor	β	SE	In	p
Age group	-.294	.044	1	<.001
Gender	.006	.045	0	.890
Place recall	.431	.282	0	.133
Route recall	.146	.159	0	.366

Table 3.1 AAT performance stepwise regression results. A stepwise regression analysis assessed how well age, gender, place recall and route recall predicted AAT performance, in terms of correct responses, to different direction test trials. Factors retained in the model as significant predictors of performance are highlighted in blue.

Same direction test trials

Performance on same direction test trials served as a measure of route learning, irrespective of which strategy participants used. *Figure 3.3* represents the same direction trial performance of both young (red) and older (blue) participants across the six testing repetitions. This shows a general improvement throughout the experiment for both groups, indicating that participants were learning the route. The

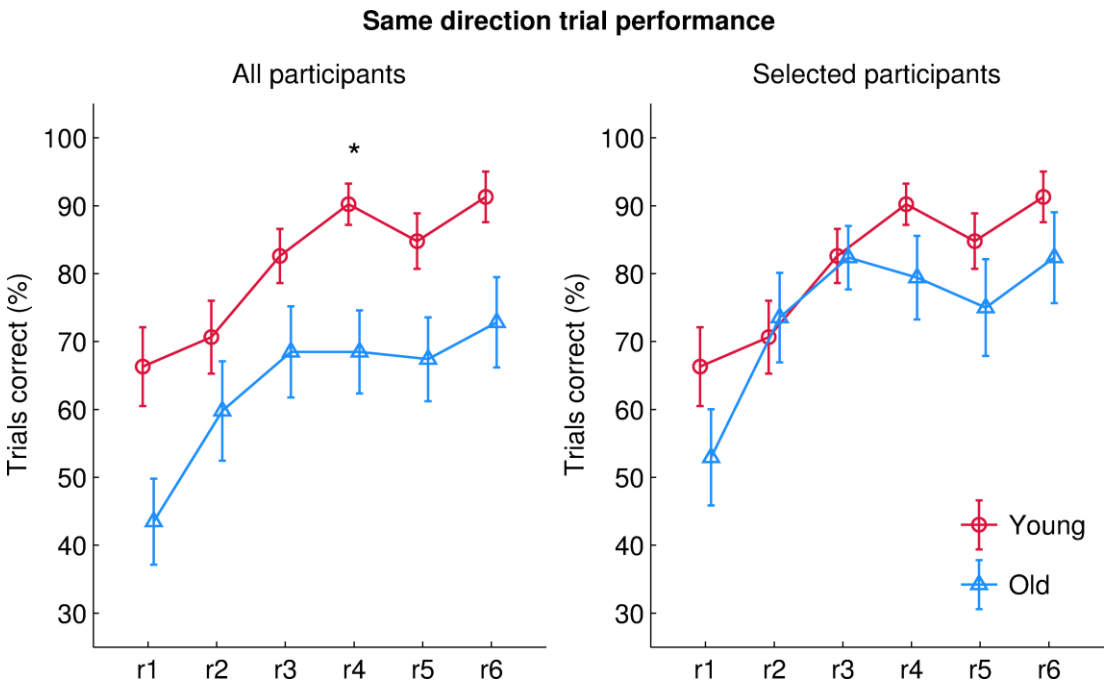

Figure 3.3 Same direction test trial performance. Proportion of same direction test trials, per repetition, on which all (*left*) and selected (*right*) young (red) and old (blue) participants responded correctly. Error bars represent standard error of the mean (SEM). * represents statistically significant age differences at $p_{HB}<.05$.

left panel represents these data for all participants, and shows an age difference in performance, with older participants achieving fewer trials correct throughout all testing repetitions. However, this was partly due to a sub-group of older participants who did not perform better than expected by chance. The right panel of the same figure summarises the same data after these participants were excluded, showing that the remaining older participants performed much more similarly to young participants.

I assessed same direction trial performance using a two-way ANOVA, with age group and testing repetition as factors. When all participants were included, there was a significant main effect of age ($F_{1,44}=9.90$, $p=.003$), as older participants responded correctly on fewer same direction test trials than young participants (*figure 3.3 left*). This difference was significant, or close to achieving significance, for most repetitions (R1: $t_{44}=2.72$, $p_{HB}=.047$; R2: $t_{44}=1.22$, $p_{HB}=.23$; R3: $t_{44}=1.85$, $p_{HB}=.142$; R4: $t_{44}=3.25$, $p_{HB}=.013$; R5: $t_{44}=2.40$, $p_{HB}=.062$; R6: $t_{44}=2.48$, $p_{HB}=.068$).

There was also a significant main effect of repetition ($F_{5,220}$=11.04, p<.001), as the performance of both groups improved from the first (young: M=66.30%, SD=27.81%; old: M=43.48%, SD=30.36%) to the last (young: M=91.30%, SD=17.85%; old: M=72.83%, SD=31.90%) repetition. There was no significant interactive effect ($F_{5,220}$=.54, p=.745), as, while age groups differed in performance, both showed similar patterns of improvement across repetitions.

As each test trial involved a three-way choice, the chance probability of responding correctly to a single trial was 33.33%, and participants could therefore be expected to respond correctly to eight of the total 24 by chance. By computing a binomial CDF, I determined that any number of correct same direction test trial responses greater than 11 was significantly better than chance. Three older male participants (aged 65, 74 and 77) and three older female participants (aged 65, 69 and 78) did not exceed this criterion, indicating that they were unable to learn the route, and were therefore excluded from all further analyses. The remaining 17 (eight female) older participants were aged 68-86 (M=74.7). Repeating the above analysis for only the remaining participants revealed that, while there was still a main effect of repetition ($F_{5,190}$=9.33, p<.001), there was no longer an effect of age ($F_{1,38}$=2.25, p=.142), confirming that the selected subset of older participants performed similarly to the young group in terms of route learning (*figure 3.3 right*).

Different direction test trials

While same direction trial performance did not depend on which strategy participants used, performance on different direction trials was affected by strategy use, largely depending upon use of the configuration strategy. *Figure 3.4* represents young and older participants' different direction trial performance across testing repetitions, as for same direction trial performance in *figure 3.3*. As illustrated, older participants performed relatively poorly on different direction test trials throughout the experiment. In contrast, young participants performed similarly at the beginning of the experiment, but they steadily improved throughout, so that by the final testing repetition their performance was much better than that of older participants.

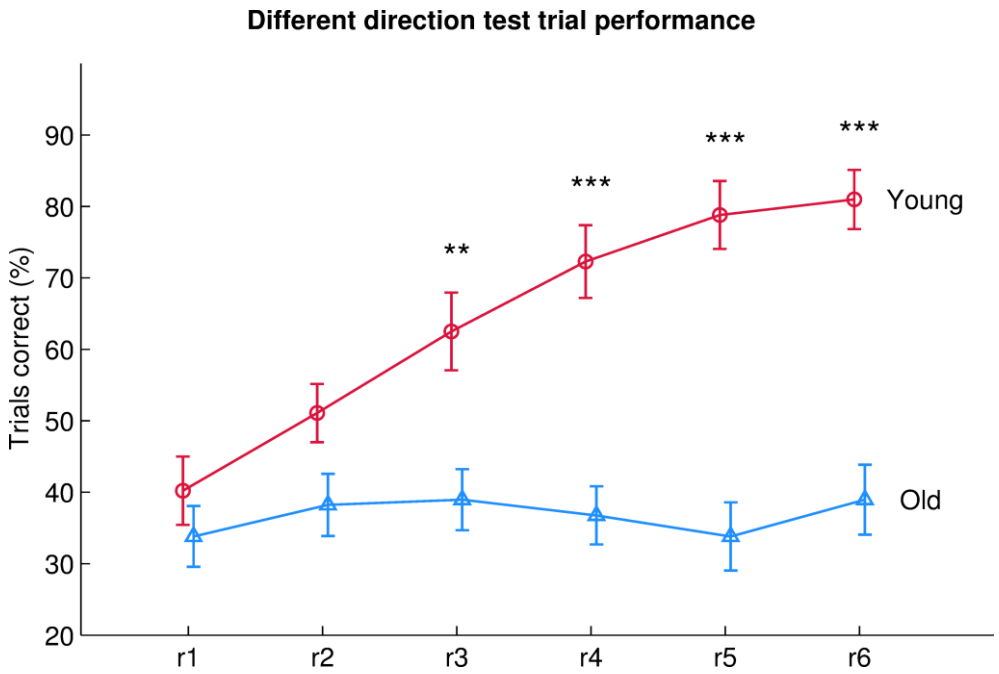

Figure 3.4 Different direction test trial performance. Proportion of different direction test trials, per repetition, on which young (red) and old (blue) participants responded correctly. Error bars represent SEM. ** and *** represent statistically significant age differences at $p_{HB}<.01$ and $p_{HB}<.001$.

The same analyses revealed significant main effects of both age ($F_{1,38}=29.87$, $p<.001$) and repetition ($F_{5,190}=12.06$, $p<.001$), as well as a significant interactive effect ($F_{5,190}=10.65$, $p<.001$). While the performance of young participants steadily increased from 40.22% (SD=22.91%) to 80.98% (SD=19.90%), accounting for the effect of repetition, that of older participants stayed between 33.82% (SD=17.55%) and 38.97% (SD=20.20%), explaining the effect of age and the interaction. The age difference in performance was significant, or close to achieving significance, for all but the first repetition (R1: $t_{38}=.98$, $p_{HB}=.331$; R2: $t_{38}=2.18$, $p_{HB}=.071$; R3: $t_{38}=3.29$, $p_{HB}=.007$; R4: $t_{38}=5.28$, $p_{HB}<.001$; R5: $t_{38}=6.71$, $p_{HB}<.001$; R6: $t_{38}=6.73$, $p_{HB}<.001$).

Differentiating test trials

Two trials in each testing phase were able to differentiate between all three navigational strategies that participants may have been using, as, on these trials, each strategy predicted a different response. *Figure 3.5* represents the proportion of

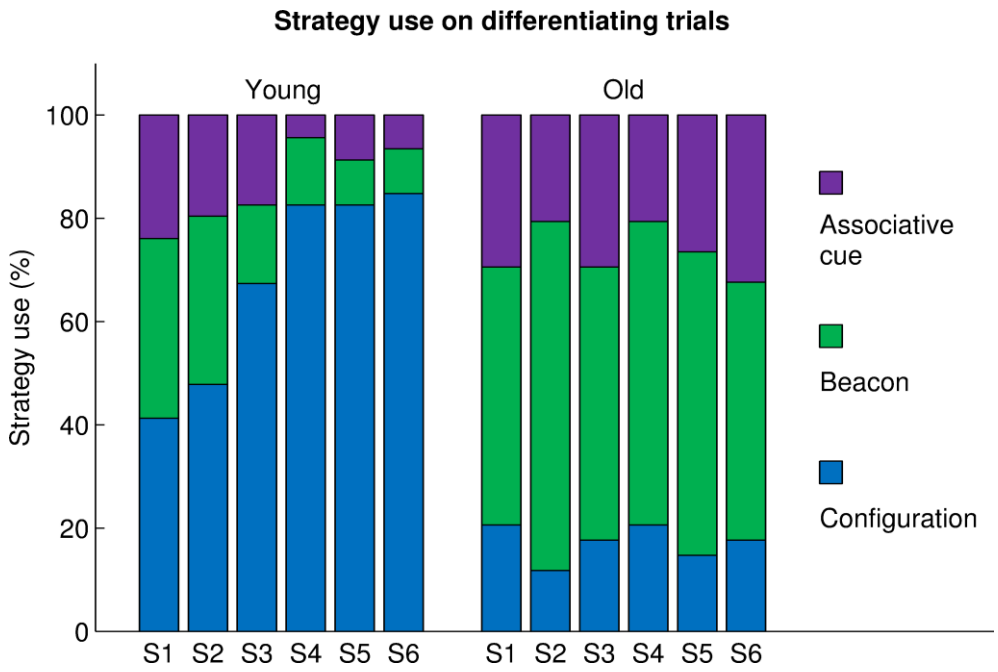

Figure 3.5 Strategy use on differentiating trials. Proportion of differentiating test trials, per repetition, on which young and old participants responded in accordance with the associative cue (purple), beacon (green) and configuration (blue) strategies.

differentiating trials on which young (left) and old (right) groups used the associative cue (purple), beacon (green) or configuration (blue) strategy. As shown, young participants used the appropriate configuration strategy on a minority of trials at first – although still more than either of the two egocentric strategies individually – but used this strategy increasingly frequently across subsequent testing repetitions. In contrast, strategy use within the older group changed very little across repetitions, and older participants used the associative cue strategy more often, the beacon strategy much more often and the configuration strategy much less often than young participants.

I assessed strategy use with a two-way mixed ANOVA for each strategy. Firstly, for the associative cue strategy, there was a significant main effect of age ($F_{1,38}$=6.01, p_{HB}=.019), as older participants used this strategy more than young participants, particularly in the last testing repetition (R1: t_{38}=.55, p_{HB}=1.176; R2: t_{38}=.110, p_{HB}=.913; R3: t_{38}=1.30, p_{HB}=.602; R4: t_{38}=2.29, p_{HB}=.140; R5: t_{38}=2.28, p_{HB}=.113; R6: t_{38}=2.90, p_{HB}=.037). Although use of the associative cue strategy tended to

decrease throughout-testing repetitions among the young group (R1: M=23.91%, SD=29.66%; R6: M=6.52%, SD=17.22%), the effect of repetition was not significant ($F_{5,190}$=1.49, p_{HB}=.195), and although there was no change in use of the associative cue strategy among the older group (R1: M=29.41%, SD=35.61%; R6: M=32.35%, SD=39.30%), there was also no significant interaction ($F_{5,190}$=1.25, p_{HB}=.288).

For the beacon strategy, there was a significant main effect of age ($F_{1,38}$=20.17, p<.001) and of repetition ($F_{5,190}$=2.98, p=.013), but only a tendency towards a significant interaction ($F_{5,190}$=1.99, p=.081). The effect of age was due to older participants using the beacon strategy significantly more frequently than young participants throughout all but the first-testing repetition (R1: t_{38}=1.39, p_{HB}=.174; R2: t_{38}=2.77, p_{HB}=.018; R3: t_{38}=3.36, p_{HB}=.005; R4: t_{38}=4.17, p_{HB}<.001; R5: t_{38}=5.01, p_{HB}<.001; R6: t_{38}=3.73, p_{HB}=.003). Older participants also consistently used the beacon strategy on between 50.00% (SD=39.53%) and 67.65% (SD=39.30%) of differentiating test trials, whereas use of the strategy by young participants fell from 34.78% (SD=31.75%) to 8.70% (SD=24.55%), accounting for the effect of repetition and the tendency towards a significant interaction.

On differentiating test trials, only use of the configuration strategy produced the correct response. There was a significant main effect of age ($F_{1,38}$=37.67, p<.001), with older participants using the configuration strategy consistently less frequently (R1: t_{38}=1.86, p_{HB}=.071; R2: t_{38}=3.35, p_{HB}=.003; R3: t_{38}=4.50, p_{HB}<.001; R4: t_{38}=6.27, p_{HB}<.001; R5: t_{38}=7.52, p_{HB}<.001; R6: t_{38}=6.92, p_{HB}<.001), which explains their poorer performance on different direction test trials. There was also a significant effect of repetition ($F_{5,190}$=7.53, p<.001), as well as a significant interaction ($F_{5,190}$=6.93, p<.001), as, while use of this strategy stayed at between 11.76% (SD=21.86%) and 20.59% (SD=35.61%) among older participants, it increased from 41.30% (SD=35.84%) to 84.78% (SD=27.94%) among young participants.

I assessed differences in strategy use across testing repetitions within the older group using a two-way within-subjects ANOVA with strategy and repetition as factors. The

analysis revealed a significant main effect of strategy on frequency of use ($F_{2,288}$=30.23, p<.001), suggesting the older participants did exhibit a strategy preference. There was no significant effect of testing repetition ($F_{5,288}$=.025, p=.999) and no significant interaction ($F_{5,288}$=.36, p=.964), indicating that this strategy preference did not change throughout the experiment. Post-hoc t-tests confirmed that older participants showed a preference for the beacon strategy, using it significantly more often than the associative cue (t_{16}=2.68, p_{HB}=.033) and configuration (t_{16}=3.02, p_{HB}=.025) strategies. There was no significant difference between use of these two other strategies (t_{16}=1.21, p_{HB}=.244). I also computed a binomial CDF, which suggested that during each testing repetition, older participants would have used each strategy between 20.59% and 47.06% of the time just by chance. Across all repetitions, use of the associative cue strategy remained within this range, use of the beacon strategy consistently exceeded the upper limit, and use of the configuration strategy was in each case less than or equal to the lower limit.

As an additional check that these results did not occur by chance, I explored the number of participants that responded in accordance with each strategy on all four differentiating trials of the final two testing repetitions. By the end of the experiment none of the young participants were consistently using either the associative cue or the beacon strategy, while 60.87% were consistently using the configuration strategy. Of the remainder, who used more than one strategy on the last four differentiating trials, a further 13.04% used the configuration strategy on both of the differentiating trials of the final repetition. On the other hand, only 5.88% of old participants were using the configuration strategy throughout the last four differentiating trials, with another 5.88% using the associative cue strategy, and 35.29% using the beacon strategy. Considering only the last two, these figures increased to 11.76%, 17.65% and 41.18%, respectively. Chi square tests confirmed that, in terms of distribution of consistent strategy use throughout the last differentiating trials, the young group significantly differed from chance ($\chi^2_{1,22}$=20.13, p<.001), and while the old group did not ($\chi^2_{1,17}$=2.66, p=.103), they did significantly differ from the young ($\chi^2_{2,39}$=51.04, p<.001).

Response times

I also assessed young and older participants' response times to same and different direction test trials, illustrated in *figure 3.6*. Generally, older people exhibit slower responses than young people (Cerella, 1985; Fozard et al., 1994; Ratcliff et al., 2001), but, as shown, our older participants responded quicker on same direction and particularly different direction test trials. The response times of both groups were also greater for different direction trials. I confirmed these results using a two-way ANOVA with age and trial type as factors. There was a significant main effect of age ($F_{1,38}$=14.81, p<.001), as older participants responded significantly quicker on both same direction (t_{38}=2.64 p_{HB}=.012) and different direction (t_{38}=4.27, p_{HB}<.001) trials. There was also a significant main effect of trial type ($F_{1,38}$=39.47, p<.001), as both young (t_{22}=6.56, p_{HB}<.001) and older (t_{16}=2.71, p_{HB}=.015) participants took significantly longer to respond on different direction test trials. Finally, there was a significant interaction ($F_{1,38}$=8.40, p=.006), which was due to a greater difference in response times between same and different direction test trials among young participants.

3.2.4 Discussion

Summary of findings

Performance on same direction test trials was significantly lower among older participants, but increased throughout the experiment in both age groups. However, six older participants did not perform significantly better than would be expected by chance, and were therefore excluded from further analyses. The remaining older participants did not perform significantly worse than the young group, suggesting that they were similarly able to learn the route. On different direction test trials, older participants not only performed worse than young participants, but also failed to show improvement throughout the experiment – in contrast to the steady improvement exhibited by young participants. Responses to differentiating trials indicated that young participants preferred to use the configuration strategy from the

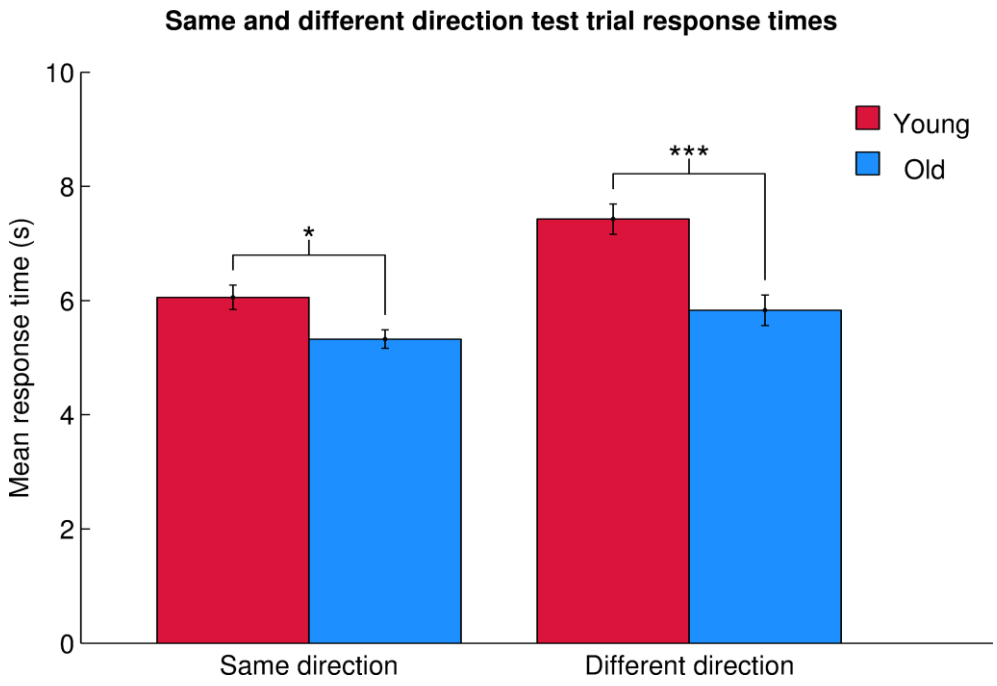

Figure 3.6 Same and different direction test trial response times. Mean response times for same direction and different direction test trials across all six repetitions for young (red) and old (blue) participants. Error bars represent SEM. * and *** represent statistically significant age differences at p_{HB}<.05 and p_{HB}<.001.

earliest testing repetitions, which strengthened throughout the experiment. Older participants, on the other hand, exhibited a preference for the beacon strategy throughout the experiment, using the other strategies, particularly the configuration strategy, much less frequently. Older participants were also quicker to respond to same direction and especially different direction test trials.

Interpretation of findings

Same direction test trial performance served as a measure of route learning, and the improvement throughout the experiment shown by older participants demonstrates that older people are still able to learn routes. In the original sample, there was still an age difference in same direction trial performance, suggesting that route learning is impaired to some extent in ageing. This is consistent with previous studies of route navigation (Begega et al., 2001; Jansen et al., 2010), and if older participants were relying upon egocentric strategies, the slight deficit in route learning may relate to

striatal neurodegeneration (Raz et al., 2005; Hasan et al., 2008; Raz et al., 2010). However, the age difference was caused by a small subset of older participants that did not perform significantly better than chance, which may have been due to severely impaired route learning, but could have resulted from a failure to understand the task. After excluding these participants, there was no age difference in same direction trial performance, suggesting that the age differences in other measures were present despite intact route learning abilities among the remaining older participants.

In everyday life, navigation sometimes involves repeatedly following the same route; but more often we navigate between numerous locations within our local environment, often deviating from known routes and rejoining them from unfamiliar directions. Whereas same direction trials assessed simple route learning ability, different direction trials assessed this more flexible – and perhaps more ecologically relevant – aspect of navigation. The poorer performance of older participants on different direction trials, and their failure to improve throughout the experiment, demonstrates why older people, even with intact route learning abilities, may still experience real-world navigational difficulties. These difficulties may be related to allocentric processing deficits (Moffat & Resnick, 2002; Moffat et al., 2006; Antonova et al., 2009; Iaria et al., 2009), which can account for poorer different direction test trial performance, as only use of an allocentric configuration strategy guaranteed a correct response on these trials. While, initially, routes may be learned in terms of egocentric responses, once available, an allocentric representation of the environment may be used to guide route navigation instead. Young participants progressed to this stage by adopting the allocentric configuration strategy after only very few route traversals, providing evidence for more recent models of spatial microgenesis, which suggest that survey information is encoded at the same time as route and landmark information (Montello, 1998; Ishikawa & Montello, 2006). However, older participants did not, which may reflect allocentric deficits, but could also be attributable to an inability to switch from an egocentric to an allocentric strategy, as ageing does also impair strategy switching (Moore et al., 2003; Ashendorf & McCaffrey, 2008; Young et al., 2010). This, however, is based on the

assumption that the poorer performance of older participants on different direction trials was due to the continued use of an egocentric strategy, as opposed to the ineffective use of an allocentric strategy.

Differentiating test trials made it possible to discern which strategy participants were using. During the first-testing repetition, both groups relied primarily upon egocentric strategies – although, of the three strategies, young participants did use the one allocentric strategy the most. But throughout the experiment, young participants progressed to a stage where they used the configuration strategy most of the time, whereas older participants continued to rely mainly upon the egocentric strategies. I suggest that, while the initial age difference in use of the configuration strategy likely reflects age-related allocentric impairments, the lack of increase in use of this strategy within the older group also reflects an inability to switch to an allocentric strategy. An alternative explanation is that older participants did switch to using the allocentric strategy, but were simply unable to use it effectively. In fact, because each trial involved a three-way choice, and each was associated with a different strategy on differentiating trials, errors could not be detected; i.e. responses attributed to associative cue or beacon strategy use could actually have been random errors resulting from allocentric deficits. However, older participants showed a significant preference specifically for the beacon strategy, using it significantly more than the other two strategies and than would be expected by chance, which confirms that they were persevering with an egocentric strategy. This preference for the beacon strategy over the associative cue strategy could be explained in terms of selective patterns of neurodegeneration within the striatum (Raz et al., 2003; Abedelahi et al., 2013). The fact that the majority of older participants responded in accordance with the same egocentric strategy on both differentiating trials of the final testing repetition also argues against the idea that they were ineffectively trying to use the configuration strategy.

Response times are typically greater in older people (Cerella, 1985; Fozard et al., 1994; Ratcliff et al., 2001), but we also anticipated a difference in response time between strategies. Before making a response, participants using an egocentric

strategy had only to recall which direction to turn in response to one of the landmarks, or simply which of the two landmarks to turn towards. Participants that used the allocentric configuration strategy, on the other hand, had to identify their position within their allocentric representation of the environment, recall which allocentric direction the route progressed in from that junction, orient themselves around the junction using the two-dimensional configuration of the landmarks, and then translate the recalled allocentric direction into an egocentric response. We therefore expected that use of the allocentric configuration strategy would increase response times, and that older participants, who we predicted would be less inclined to use the configuration strategy, may actually be quicker to respond than young participants. Our results confirmed this hypothesis, providing further evidence that older participants were deliberately using an egocentric strategy, rather than making errors while trying to use the configuration strategy. Both groups took longer to respond on different direction trials than same direction trials, which would be expected when using the configuration strategy. This difference was much smaller for the older group, also consistent with the older group using the configuration strategy on a much smaller proportion of trials.

Limitations

One clear limitation of this study was that the most impaired older participants – representing just over a quarter of the group – had to be excluded from the majority of analyses. Had it been possible to include these participants, they could have significantly altered the results, as they may, for example, have been unable to use the beacon strategy. On the other hand, the fact that age differences in different direction test trial performance, strategy use and response time were still detected in a sample representing the less impaired majority of the healthy older population may simply suggest that impairments in allocentric processing and navigational strategy switching among the entire population are even more severe than these results indicate. A related point is that the study design was unable to distinguish the relative contributions of allocentric processing and navigational strategy switching deficits to the older group's bias against using the allocentric configuration strategy. Another

obvious limitation that I have already mentioned was that, because each possible response on differentiating test trials was associated with a particular strategy, the strategy use assessment did not consider that some of the participants' responses could have been errors. In fact, around a quarter of participants responded in accordance with different strategies to the two final differentiating trials, suggesting that they were still making errors at the end of the experiment. However, the significant strategy preferences do at least confirm that participants made deliberate responses on the majority of trials. A related limitation is that the AAT did not indicate whether their preference for the beacon strategy was caused by an impaired ability to use the associative cue strategy.

Conclusion

This study demonstrated that older people are impaired at rejoining a known route from an unfamiliar direction, which is likely to contribute to navigational difficulties experienced in everyday life. This impairment was not due to deficient route learning, but to a tendency to persevere with using an egocentric strategy during route learning, where progressing to using an allocentric strategy was more appropriate, required for accurate completion of the rest of the task, and demonstrated by young participants. Whether this finding was due to an impaired ability to use the allocentric configuration strategy or an impaired ability to switch to it – or rather how much allocentric and strategy switching deficits contribute – is unclear, but it is likely that both contribute. This will be discussed further within the context of other studies presented in later chapters. More specifically, older participants showed a preference for the beacon strategy over both the allocentric configuration strategy and the other egocentric associative cue strategy. Again, it is unclear whether this was simply a preference or due to an impaired ability to use the associative cue strategy, but this limitation was addressed by the second study presented in this chapter.

3.3 Study 2: Associative cue and beacon navigation in ageing

3.3.1 Introduction

Recapitulation

Study 1 demonstrated that older people tend to navigate using egocentric strategies even when an allocentric strategy is required. Precisely how this finding relates to impairments in allocentric processing and switching between navigational strategies remains to be determined, although the remainder of this thesis will further explore the role of navigational strategy switching deficits. However, while the results seem to suggest that egocentric navigation is relatively preserved in older people, the previous study did not directly address age differences in egocentric ability. Furthermore, older participants exhibited a specific preference for the beacon strategy over the associative cue strategy, which could have been due to a decreased ability to use the associative cue strategy, or even an increased capacity for beacon navigation. I mentioned in section 3.2.1 that beacon navigation, being less dependent on stimulus-response learning, is also less dependent on the dorsolateral striatum (Reading et al., 1991; Featherstone & McDonald, 2004). Furthermore, as the striatum is not uniformly affected by age-related degradation (Raz et al., 2003; Abedelahi et al., 2013), use of the beacon strategy may remain less impaired, not only than use of an allocentric strategy, but also than use of the associative cue strategy. But again, the previous study did not directly assess age differences in use of the two strategies, or a difference between the strategies among older participants.

Current study

Following on from Study 1, Study 2 aimed to investigate whether older people were impaired at using the associative cue and beacon strategies. We used a route learning task (RLT), similar to the AAT, but with many more junctions along the route and only same direction test trials. Furthermore, we used two variations of the RLT – one

with two central landmarks, designed to enforce use of the associative cue strategy, the other with two lateral landmarks, to encourage use of the beacon strategy – and half of each age group were assigned to use each. I expected that older participants assigned to the beacon condition would perform as well as young participants, whereas those assigned to the associative cue condition would not. During the final testing repetition, the positions of the two landmarks at three of the junctions were switched, to check whether participants were actually using the strategy that they were supposed to be. Those assigned to the beacon condition were expected to turn towards the beacon landmark, now on the incorrect side of the junction, producing an incorrect response, whereas those tested on the associative cue variation of the task should have been unaffected by the change, and were therefore expected to perform just as on ordinary test trials. Participants were also tested on their memory of the response associated with each individual landmark, at which I expected the young associative cue group to perform better than the old, and both to perform better than the beacon groups. Finally, participants were tested on their memory of the positions of landmarks. Although this information was irrelevant to the use of either strategy, it may have been learned while simultaneously forming an allocentric representation of the environment, perhaps predicting poorer performance among older participants. I also expected that associative cue participants would perform better at this test, being able to infer the position of each landmark based on whether or not they had associated a response with it, assuming that they habitually focused on either the top or bottom landmark during encoding.

3.3.2 Methods

Participants

Forty-four (25 female) young participants (aged 18-28, M=20.2) were recruited from the local student populations in Bournemouth and Edinburgh, and 36 (19 female) older participants (aged 65-85, M=74.1) were recruited from the panel of research volunteers in Edinburgh. All participants had normal or corrected-to-normal vision, and no known neuropsychological impairments, and older participants had recently

been tested for MCI. Twenty-two young and 18 old participants were randomly assigned to the associative cue condition, and the remaining 22 young and 18 old were assigned to the beacon condition. One 80-year-old female assigned to the beacon condition chose to withdraw from the study before completion of the experiment, so her data was excluded from all analyses. Participants were reimbursed for their time at a rate of £7 per hour.

Procedure

After being fully informed about the nature of the study and providing written consent to take part in the study, participants indicated their level of experience with computers and computer games on two nine-point scales. They then completed three tasks, each described below, on a desktop computer with a 24in widescreen monitor and a standard UK keyboard. Participants completed the first six training and testing repetitions of the RLT, followed by a landmark direction test (LDT), then a seventh RLT testing repetition, followed by a landmark position test (LPT), after which they were debriefed. As described below, the seventh RLT testing repetition differed slightly from the preceding repetitions, but participants were not informed of this until after they had completed the experiment. The experiment was conducted in accordance with ethical guidelines provided by the University of Edinburgh, Bournemouth University and the BPS.

Route learning task

This task was programmed and run in Vizard, and set in a grid-like VE, very similar to that used in the AAT – featuring brick walls, a fog to limit visual range and two visual cues at each junction serving as landmarks – but with many more junctions (*figure 3.7*). As in the AAT, participants were passively moved along the route during a training phase, then tested on each junction in a random order during a subsequent testing phase, indicating which direction the route proceeded in from that junction using the left and right arrow keys. However, the trained route was much longer, passing through 18 junctions, and on test trials, participants always approached

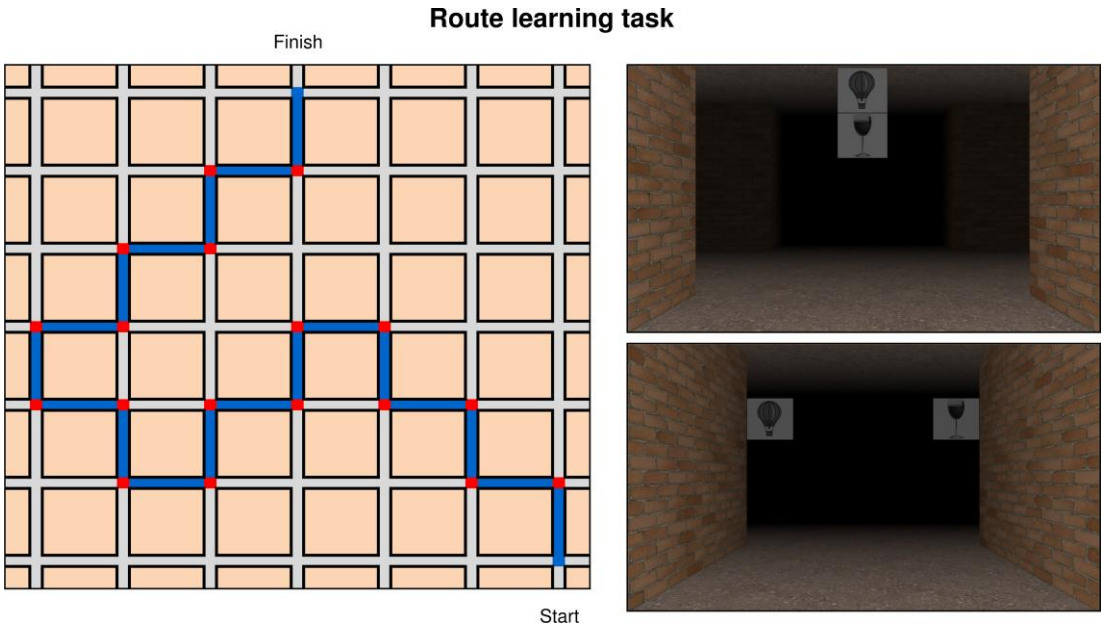

Figure 3.7 Route learning task. *Left:* Diagram of the training route through eighteen junctions of the grid-like virtual maze, each of which featured two landmarks either stacked on the ceiling at the centre of each junction or placed on opposite sides of each junction. *Right:* Screen images of two junctions captured during the associative cue *(top)* and beacon *(bottom)* variations of the task.

junctions from the same direction as in the original route. The arrangement of landmarks at junctions also differed from the AAT, as well as between the two conditions. Half of participants completed a variation of the task designed to limit participants to using an associative cue strategy by featuring the two landmarks in the centre of each junction, one above the other. The other half completed a variation designed to encourage use of the beacon strategy by featuring a landmark on either side of the junction, i.e. one for each possible turning direction. This task also consisted of six repetitions of the training and testing phases, but included an additional seventh testing repetition, during which the positions of the landmarks at three of the junctions were switched. As participants were not informed of this change, the three trials probed whether participants assigned to each condition were actually using the strategy they were intended to.

Landmark direction test and landmark position test

Participants were also tested on their memory of the 36 images used as visual landmarks throughout the RLT. In the LDT and LPT, each visual cue appeared as a still image on-screen in a random order. In the LDT, participants indicated, using the left and right arrow keys, which direction the route had proceeded in from the junction at which they saw that particular landmark. In the LPT, participants assigned to the associative cue condition used the up and down arrow keys to indicate whether each landmark had been positioned at the top or the bottom of the stack in the centre of the junction. Participants assigned to the beacon condition used the left and right arrow keys to indicate whether the landmark featured in each image had been on the left or right of the junction. The LPT was performed after the seventh RLT testing repetition, so the six landmarks that had switched positions in this repetition were not included in the LPT.

Data analysis

Scores on the computer and computer games scales were combined to produce a single measure of computer experience. Performance at each of the three tasks was assessed in terms of both performance accuracy, i.e. proportion of correct responses, and response time. Switched landmark trials from the seventh RLT testing repetition were excluded from analyses of RLT performance and analysed separately. For the RLT, I first assessed the contributions of condition, age group, gender and computer experience to performance using a stepwise regression analysis. Performance and response times were then analysed in terms of age and repetition using mixed model ANOVAs for each condition, and in terms of age and condition using between-groups ANOVAs across all repetitions; each followed by post-hoc t-tests with Holm-Bonferroni correction for multiple comparisons. The effects of age and condition on performance on switched landmark trials, and at the LDT and LPT were assessed in the same way. For the LDT and LPT, I also assessed the effect of landmark position (i.e. whether landmarks were positioned at the top or bottom of the stack at the centre of the junction) in the associative cue condition, and landmark pertinence (i.e.

whether or not landmarks were on the side of the junction that the route turned towards) in the beacon condition, each included as repeated-measures factors in mixed model ANOVAs.

3.3.3 Results

RLT

Young and old participants in both conditions performed similarly across testing repetitions. *Figure 3.8* summarises the performance (in terms of the percentage of correct responses) of young and old participants assigned to the associative cue (left) and beacon (right) conditions. As illustrated, accuracy gradually increased from around 50%, or slightly higher, in the first testing repetition to around 90% in the last. As above, this pattern of improvement was similar across age groups and strategy conditions. Performance was very slightly higher in the beacon condition, particularly for young participants, who appeared to outperform older participants on the first testing repetition only. Performance data were then collapsed over testing repetitions, as shown in the left panel of *figure 3.9*. This figure also illustrates that performance was similar across groups and conditions, with very slightly higher performance in the beacon condition, particularly for young participants. The right panel of *figure 3.9* summarises response time data, illustrating that older participants took longer to respond than young participants, but also that response times, and the age difference therein, were consistent across strategy conditions.

I explored these results more precisely using statistical tests. An initial stepwise regression analysis demonstrated no significant effects of condition, age group, gender or computer experience on overall RLT performance (*table 3.2*). Subsequently, although I continued to assess the effects of condition and age, being the primary independent variables, I did not explore the effects of gender or computer use any further. As mentioned above, RLT performance steadily increased throughout testing repetitions among both young and old participants from 48.99% (SD=10.66%) and 55.25% (SD=12.71%) to 86.67% (SD=21.18%) and 88.15%

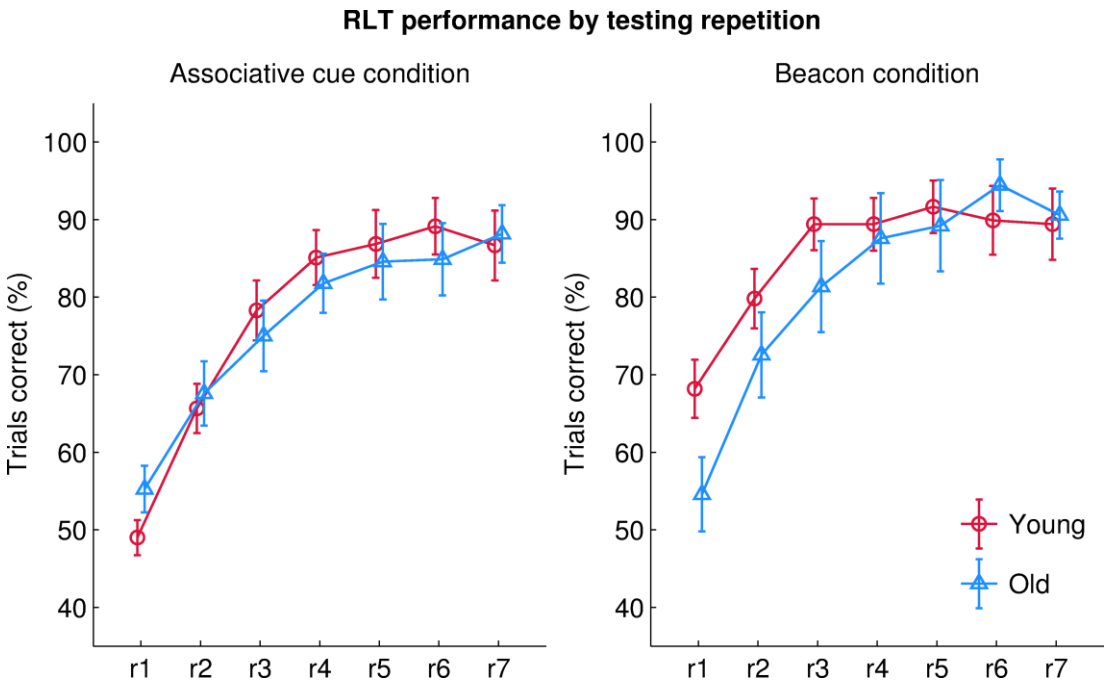

Figure 3.8 RLT performance by testing repetition. *Left:* Mean percentage of correct trials during each testing repetition for young (red) and old (blue) participants assigned to the associative cue task condition. *Right:* Mean percentage off correct trials by age group and testing repetition for participants assigned to the beacon condition. All trials from the first six testing repetitions are included. Only trials featuring landmarks in their original positions are included from the seventh repetition. Error bars represent SEM.

(SD=15.77%) in the associative cue condition and from 68.18% (SD=17.58%) and 54.58% (SD=19.76%) to 89.39% (SD=21.54%) and 90.59% (SD=12.49%) in the beacon condition (*figure 3.8*). Mixed model ANOVAs with age group and testing repetition as factors confirmed significant main effects of repetition in both the associative cue ($F_{6,228}$=71.64, p<.001) and beacon ($F_{6,222}$=46.84, p<.001) conditions, but no significant effects of age group (AC: $F_{1,38}$=.01, p=.917; Bcn: $F_{1,37}$=.52, p=.477). Although not in the associative cue condition ($F_{6,228}$=1.51, p=.177), there was a significant interaction in the beacon condition ($F_{6,222}$=3.59, p=.002). However, after correcting for multiple comparisons, the apparent age difference in performance during the first testing repetition was not significant (t_{37}=2.33, p_{HB}=.177), nor were there any other significant age differences in performance for other repetitions (R2: t_{37}=1.15, p_{HB}=1.292; R3: t_{37}=1.29, p_{HB}=1.230; R4: t_{37}=.29, p_{HB}=1.547; R5: t_{37}=.39, p_{HB}=2.093; R6: t_{37}=.80, p_{HB}=1.723; R7: t_{37}=.21, p_{HB}=.836), which explains why

RLT performance stepwise regression results

Predictor	β	SE	In	p
Condition	.051	.035	0	.149
Age group	-.022	.035	0	.537
Gender	-.026	.035	0	.457
Computer use	.008	.010	0	.441

Table 3.2 RLT performance stepwise regression results. A stepwise regression analysis assessed how well condition, age, gender, and computer experience predicted performance in terms of correct responses throughout the RLT. No factors were retained in the model as significant predictors.

there was no main effect of age. However, I performed a further t-test assessing age differences in the change in performance from the first to the last repetition, and this indicated that the interaction could be explained by significantly greater improvement among older participants (t_{37}=2.20, p=.034).

Despite the slightly greater improvement of older participants in the beacon condition, both groups showed very similar patterns of performance across testing repetitions in each condition. In subsequent analyses I assessed performance in terms of mean performance across the seven repetitions. A two-way between-subjects ANOVA with age group and condition as factors revealed no significant main effect of age group ($F_{1,75}$=.38, p=.542), nor a significant interaction ($F_{1,75}$=.23, p=.637), but a tendency towards a main effect of condition ($F_{1,75}$=3.20, p=.078), as performance was slightly higher in the beacon condition (*figure 3.9 left*). However, post-hoc t-tests showed no significant performance differences between conditions within either the young (t_{42}=1.89, p_{HB}=.132) or old (t_{42}=.83, p_{HB}=.413) groups.

I performed the same analysis on response time data, which revealed a significant main effect of age ($F_{1,75}$=34.74, p<.001), but not of condition ($F_{1,75}$=.83, p=.366), nor a significant interaction ($F_{1,75}$=.36, p=.550). The effect of age seemed to relate to increased response times among older participants (*figure 3.9 right*), and post-hoc t-tests confirmed that this age difference was significant within both the associative

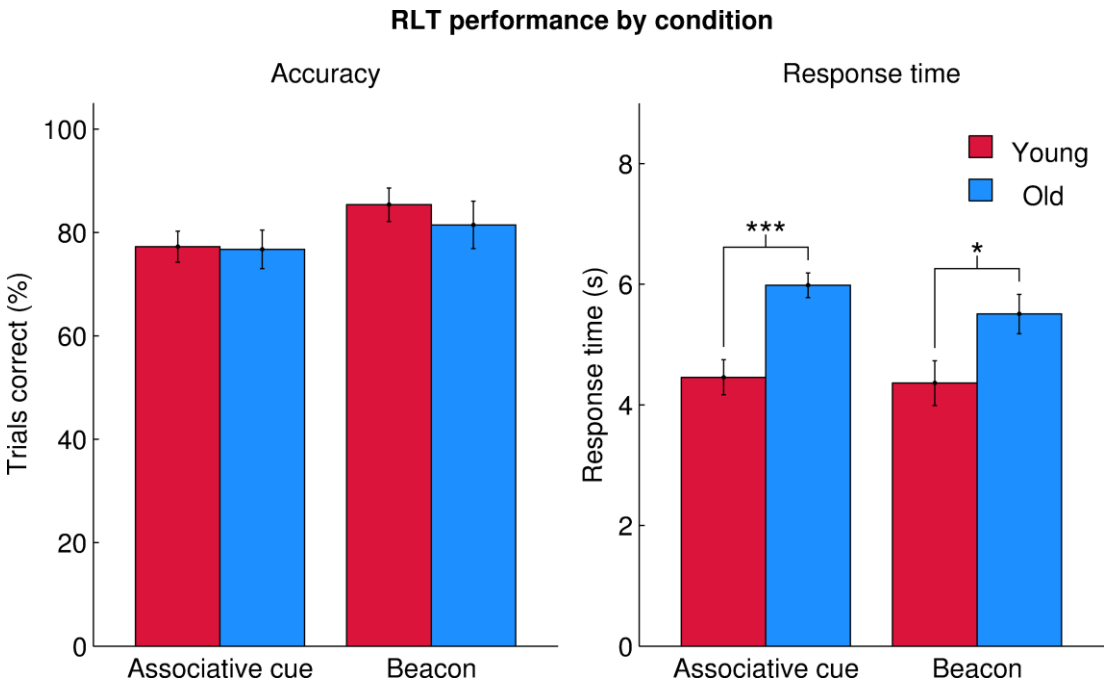

Figure 3.9 RLT performance by condition. *Left:* Mean percentage of correct trials for young (red) and old (red) participants in each task condition. *Right:* Mean response times by age group and condition. All trials from the first six testing repetitions are included, as well as trials from the seventh repetition featuring landmarks in their original positions. Error bars represent SEM. * and *** represent statistically significant differences at $p_{HB}<.05$ and $p_{HB}<.001$.

cue ($t_{38}=4.21$, $p_{HB}<.001$) and beacon ($t_{38}=2.29$, $p_{HB}=.028$) conditions. However, for each of the four participant groups, there was no correlation between response time and performance accuracy (young AC: r=.188, p=.402; Bcn: r=.147, p=.513; old AC: r=.133, p=.599; Bcn: r=.268, p=.298).

Switched landmark trials

During the final repetition of the RLT, the positions of the two landmarks at three of the junctions were switched. Switched landmark trials were of course excluded from the above analysis of RLT performance, but then analysed separately by the same procedure. *Figure 3.10* summarises accuracy (left) and response time (right) data for switched landmark trials, as in *figure 3.9* for all other trials. Again, both performance and response times were similar across conditions, and older participants still took longer to respond than young. However, whereas performance in the associative cue

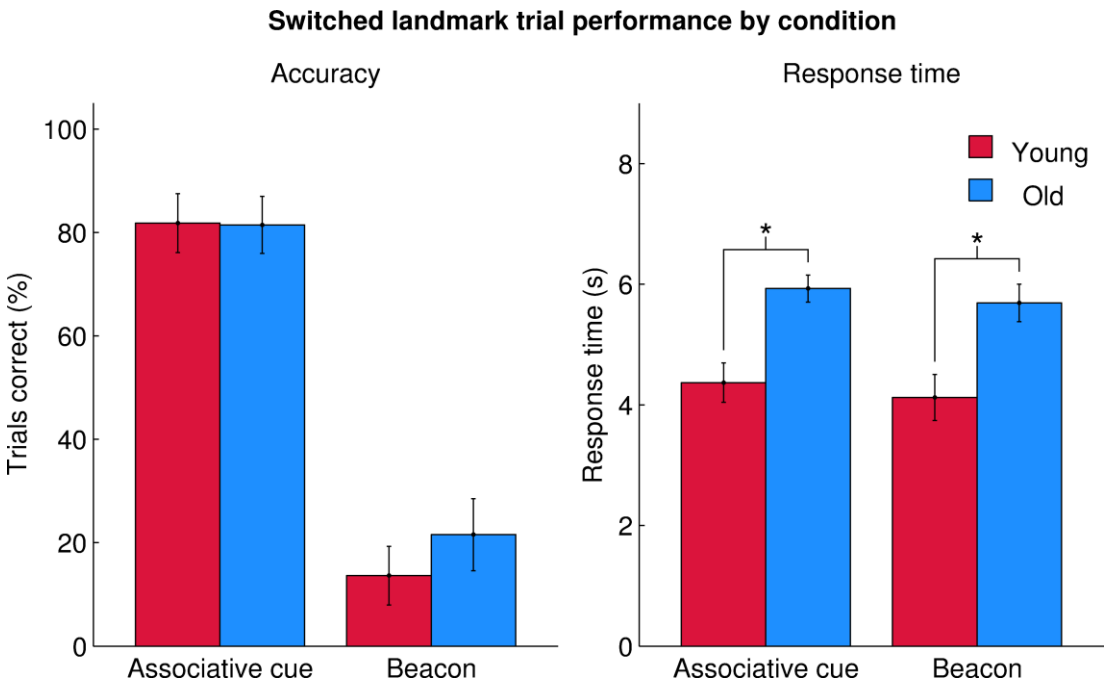

Figure 3.10 Switched landmark trial performance. *Left:* Mean percentage of correct trials for young (red) and old (blue) participants completing the associative cue and beacon variants of the task. *Right:* Mean response times by age group and condition. Error bars represent SEM. * represents statistically significant differences at $p_{HB}<.05$.

condition was unaffected by the change in the position of the landmarks, performance in the beacon condition was much worse. This could be expected if participants continued to turn towards the beacon landmark even when it was on the wrong side of the junction. In terms of responses consistent with the appropriate strategy (the inverse of correct responses in the beacon condition), performance was still similar across conditions.

Statistical analyses supported that, in terms of performance accuracy, there was a significant main effect of condition ($F_{1,75}=115.55$, $p<.001$), but no effect of age ($F_{1,75}=.40$, $p=.528$) and no significant interaction ($F_{1,75}=.48$, $p=.492$). Post-hoc tests confirmed that there was a large difference between conditions for both young ($t_{42}=8.70$, $p_{HB}<.001$) and old ($t_{33}=6.98$, $p_{HB}<.001$) groups, because, as expected, performance accuracy was much lower in the beacon condition (*figure 3.10 left*). When responses consistent with the appropriate strategy were considered correct,

there was no significant main effect of condition ($F_{1,75}$=.02, p=.901), suggesting that, even though use of the beacon strategy produced incorrect responses, participants in the beacon condition still used the appropriate strategy as accurately as those in the associative cue condition. For response times, there was a significant main effect of age ($F_{1,75}$=22.52, p<.001), but no significant effect of condition ($F_{1,75}$=.55, p=.462) and no significant interaction ($F_{1,75}$<.01, p=.991). Post-hoc tests showed a significant age difference in both conditions (AC: t_{21}=2.70, p_{HB}=.027; Bcn: t_{21}=2.18, p_{HB}=.041), again confirming that older participants took longer to respond than young (*figure 3.10 right*). However, as with normal trials throughout the rest of the task, there were no significant correlations between response time and accuracy (young AC: r=.268, p=.227; Bcn: r=.382, p=.080; old AC: r=.067, p=.791; Bcn: r=.035, p=.895).

LDT

LDT performance was also assessed in terms of correct responses and response times, as shown in the top two panels of *figure 3.11*. Again, performance was similar across age groups and strategy conditions, although performance was slightly higher in the young group and in the associative cue condition. As for the RLT, older participants took longer to respond, but response times were similar across conditions. However, I also assessed performance in relation to landmark position. The bottom left panel of *figure 3.11* depicts performance in the associative cue condition, separated by each landmark's absolute vertical position in the stack at the centre of the respective junction. As shown, both young and old participants were able to recall the direction they had turned in response to landmarks presented at the bottom better than for those presented at the top. Young participants also appeared to perform slightly better than old for both top and bottom landmarks. The bottom right panel depicts performance in the beacon condition, divided according to the route-relevant horizontal position – or pertinence – of each landmark (i.e. whether it was presented on the side of the junction towards which participants turned when following the route). Performance was similar across age groups, but, as expected, higher for pertinent landmarks than for impertinent.

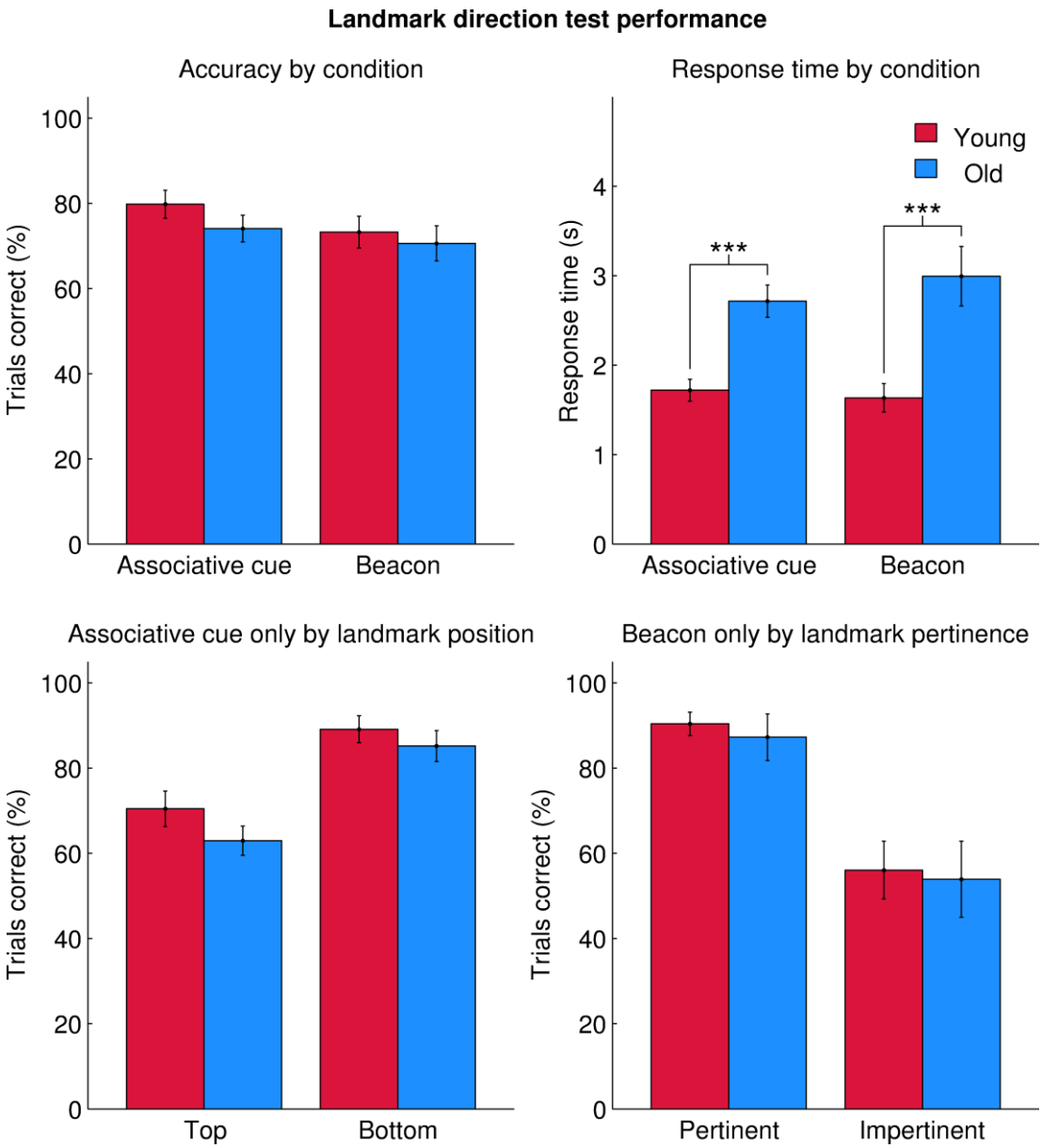

Figure 3.11 LDT performance. *Top left:* Accuracy in terms of mean percentage of correct trials for young (red) and old (blue) participants assigned to the associative cue and beacon conditions. *Top right:* Mean response times by age group and condition. *Bottom left:* Accuracy by age group and landmark position for participants assigned to the associative cue condition only. *Bottom right:* Accuracy by age group and landmark pertinence for participants assigned to the beacon condition only. Error bars represent SEM. *** represents statistically significant age differences at $p_{HB}<.001$.

Although some very slight differences in overall performance were observed (*figure 3.11 top left*), a two-way between-groups ANOVA revealed no significant main effect of age ($F_{1,75}=1.35$, $p=.250$) or condition ($F_{1,75}=1.94$, $p=.168$), and no significant

interaction between the two ($F_{1,75}$=.18, p=.671). As for the RLT, the large effect of age on response time (*figure 3.11 top right*) was confirmed by the same statistical analysis ($F_{1,75}$=34.53, p<.001), as older participants took significantly longer to respond in both conditions (AC: t_{38}=4.71, p_{HB}<.001; Bcn: t_{37}=3.96, p_{HB}<.001). There was no significant effect of condition ($F_{1,75}$=.24, p=.629), nor a significant interaction ($F_{1,75}$=.83, p=.366).

We expected that participants' memory of landmarks would be affected by their position. For the associative cue condition, a two-way mixed model ANOVA revealed a significant main effect of landmark position ($F_{1,75}$=75.25, p<.001), but no significant main effect of age ($F_{1,75}$=1.54, p=.223) and no significant interaction ($F_{1,75}$=.56, p=.458). The effect of landmark position was due to both young (t_{21}=5.59, p_{HB}<.001) and old (t_{21}=6.86, p_{HB}<.001) participants remembering the direction associated with landmarks that had been situated at the bottom significantly better than those that had been at the top (*figure 3.11 bottom left*). In the beacon condition, there was a significant main effect of landmark pertinence ($F_{1,75}$=24.94, p<.001), but not of age ($F_{1,75}$=.23, p=.637), nor a significant interaction ($F_{1,75}$=.01, p=.941). The landmark pertinence effect was due to both young (t_{21}=4.78, p_{HB}<.001) and old (t_{21}=2.71, p_{HB}=.02) participants having a significantly better memory for landmarks that had served as beacons than for those that had not (*figure 3.11 bottom right*).

LPT

The LPT differed from the LDT in that participants had to recall the position of landmarks featured in the RLT, rather than the directions associated with them, and in that the landmarks that changed position during the final testing repetition were not included. Otherwise, the task was the same, and the data it produced were analysed in the same way, firstly by assessing the effects of age and condition on accuracy and response time, and then separating performance data by landmark position. *Figure 3.12* shows that young and older participants performed similarly in both conditions for all landmarks, although young participants performed very slightly better in the associative cue condition for both top and bottom landmarks. Again, older

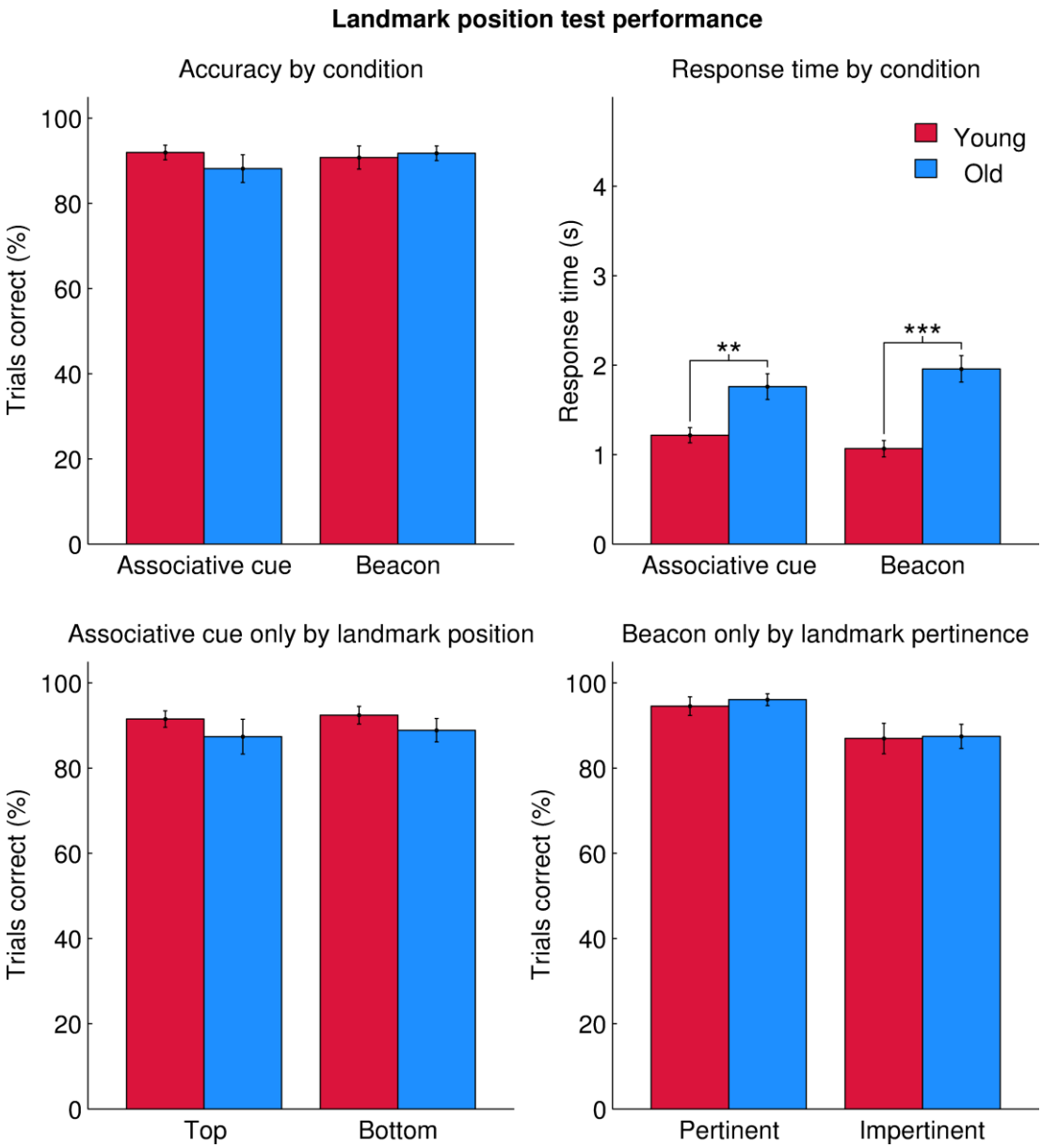

Figure 3.12 LPT performance. *Top left:* Accuracy in terms of mean percentage of correct trials for young (red) and old (blue) participants assigned to the associative cue and beacon conditions. *Top right:* Mean response times by age group and condition. *Bottom left:* Accuracy by age group and landmark position for participants assigned to the associative cue condition only. *Bottom right:* Accuracy by age group and landmark pertinence for participants assigned to the beacon condition only. Error bars represent SEM. ** and *** represent statistically significant age differences at p_{HB}<.01 and p_{HB}<.001.

participants took longer to respond than young. Overall performance and response times were similar across conditions, and, in the associative cue condition, performance was very similar for top and bottom landmarks. However, in the beacon

condition, both young and older participants better remembered the position of landmarks that had served as beacons.

Inferential statistics confirmed that there was no significant main effect of age ($F_{1,75}$=.33, p=.537), no effect of condition ($F_{1,75}$=.24, p=.625) and no interactive effect ($F_{1,75}$=.97, p=.327) on performance accuracy (*figure 3.12 top left*). Consistent with the other tasks, there was a large effect of age on response time ($F_{1,75}$=38.69, p<.001), but no significant effect of condition ($F_{1,75}$=.04, p=.847), nor a significant interaction ($F_{1,75}$=2.27, p=.136). Post-hoc tests confirmed that older participants took significantly longer to respond in both conditions (AC: t_{38}=3.40, p_{HB}=.002; Bcn: t_{37}=5.36, p_{HB}<.001; *figure 3.12 top right*).

Within the associative cue condition, there was no significant main effect of age ($F_{1,75}$=1.20, p=.280) or landmark position ($F_{1,75}$=.54, p=.467), nor a significant interactive effect ($F_{1,75}$=.03, p=.861) on performance accuracy (*figure 3.12 bottom left*). In the beacon condition, there was a significant effect of landmark pertinence ($F_{1,75}$=18.69, p<.001), but no effect of age ($F_{1,75}$=.09, p=.771) and no significant interaction ($F_{1,75}$=.08, p=.781). Again, the effect of landmark pertinence was due to both young (t_{21}=3.14, p_{HB}=.010) and old (t_{21}=2.97, p_{HB}=.009) participants remembering the position of landmarks that had served as beacons significantly better than for those that had not (*figure 3.12 bottom right*).

3.3.4 Discussion

Summary of findings

The main task used in this study assessed route learning ability, demonstrating a similarity between age groups and conditions. RLT performance increased similarly throughout testing repetitions in all four participant groups, although performance was slightly higher in the beacon condition, and older participants showed a little more improvement than young in this condition. We switched the positions of the two landmarks at three of the junctions during the final testing repetition, which

produced a large effect of condition on performance. There was, however, no such effect when strategy-concordant responses were considered correct. LDT performance was comparable across the four groups, showing no clear effects of age or condition. However, participants in the associative cue condition better remembered directions associated with lower landmarks, i.e. those positioned at the bottom of the central stack of landmarks, while participants in the beacon condition better remembered directions associated with pertinent landmarks, i.e. those on the side of the junction that allowed them to serve as beacons. There was a similar pattern of performance for the LPT, with no general age or condition differences, and with pertinent landmarks remembered better in the beacon condition. However, there was no effect of landmark position within the associative cue condition. Performance was also generally higher than in the LDT, and response times were lower. In all tasks, older participants took longer to respond than young participants, but response time was not related to performance.

Interpretation of findings

This study was based around the hypothesis that older people are impaired at using the associative cue strategy, explaining their preference for the beacon strategy in Study 1. I therefore expected that, on the main task, older participants in the beacon condition would perform as well as young participants, whereas those in the associative cue condition would not. The results contradicted this hypothesis, as there were no age differences in RLT performance in either condition. This finding is consistent with previous studies demonstrating that egocentric navigation remains relatively intact in ageing (Begega et al., 2001; Jansen et al., 2010). Older participants, in comparison to young, did seem to show marginally greater improvement throughout the task in the beacon condition, but this does not support the notion that their preference for the beacon strategy over the associative cue strategy is related to greater degradation in the dorsolateral striatum (Reading et al., 1991; Raz et al., 2003; Featherstone & McDonald, 2004; Abedelahi et al., 2013). The fact that performance was slightly higher in the beacon condition for both groups suggests that the beacon strategy may be a little easier, which can account for the

preference even in the absence of an associative cue strategy deficit.

While the associative cue version of the RLT was designed to restrict participants to using this strategy, and they were certainly unable to use a beacon strategy, they were still able to encode the route in terms of the vertical configuration of the two landmarks in the centre of each junction. The beacon version of the task, although it encouraged use of the beacon strategy, did not prevent participants from using the beacons – or opposing landmarks – as associative cues, or from encoding the configuration of the landmarks. The switched landmark trials in the last testing repetition were designed to probe whether or not participants were using the strategies they were supposed to be using. Performance in the associative cue condition was no different from performance on other trials, suggesting that landmark configuration was not important to participants, and therefore that they were simply using an associative cue strategy. Performance in the beacon condition was drastically reduced, as expected, because changing the position of the beacons meant that continuing to use the beacon strategy led to an incorrect response. In terms of strategy-concordant responses, performance was the same as on normal trials, with no difference between conditions, demonstrating that participants were using the beacon strategy. This simply confirms that my findings do relate to use of the associative cue and beacon strategies.

As use of the beacon strategy does not require encoding of direction, I expected participants assigned to the associative cue condition to perform much better at the LDT. Based on the hypothesis that older people are impaired at associative cue use, I also expected young participants in this condition to perform better than old. In contrast, there were actually no effects of age or condition. It seems that participants using the beacon strategy still encoded direction information associated with landmarks, even though they did not use it, as demonstrated by their performance on switched landmark trials. This encoding of superfluous information may reflect the simultaneous acquisition of survey knowledge (discussed further below), so it is surprising that there was no age difference, considering that older people experience difficulties with allocentric navigation (Moffat & Resnick, 2002; Moffat et al., 2006;

Antonova et al., 2009; Iaria et al., 2009). The LDT also revealed that associative cue participants had a better memory for landmarks at the bottom, which is understandable considering that these were nearer to eye level and visible for longer; and that beacon participants remembered landmarks serving as beacons better than those opposite, confirming that they were attending to the correct landmarks.

Landmark position was not relevant to either strategy, so I expected participants to perform worse on the LPT than on the LDT. However, participants may have encoded this information as part of an allocentric representation of the environment, which is formed at the same time that a route is learned (Montello, 1998; Ishikawa & Montello, 2006). As older people do not form allocentric representations as easily (Moffat & Resnick, 2002; Iaria et al., 2009; Liu et al., 2011), I therefore predicted poorer performance within the older group. I also anticipated that participants assigned to the associative cue condition would be more likely to learn position information incidentally, as I expected them to consistently use either the top or bottom landmark as the associative cue, which would allow them to infer the position of each landmark based on whether or not they had associated a response with it. Beacons appeared on both sides of the junction, so beacon participants would not have been able to do this. The results supported none of these hypotheses, as all four participant groups performed similarly, as well as slightly better than at the LDT. This suggests that both young and old encode additional information about an environment during navigation, even though not relevant to the current task. As above, this may reflect the acquisition of superfluous survey knowledge alongside task-relevant route knowledge, but does not definitively demonstrate allocentric processing, so the similar performance of both age groups does not necessarily provide evidence for intact allocentric processing among the older participants. In the beacon condition, there was again an effect of landmark pertinence, as expected, providing further evidence that participants were using the intended strategy. However, in contrast to the results of the LDT, there was no effect of position on LPT performance in the associative cue condition. As above, this may reflect a consistent reliance upon the bottom landmark, as, when presented with an unfamiliar top landmark, participants may have been unable to recall the associated direction, but

could easily have inferred that the landmark was in the position that they attended to less.

The fact that there were almost no age differences in performance across all tasks calls into question how representative the older group were of the elderly population. However, older participants took consistently longer to respond to all tasks, demonstrating a clear effect of ageing on cognition, consistent with numerous previous studies (Cerella, 1985; Fozard et al., 1994; Ratcliff et al., 2001). This suggests that the performance results are not simply a product of unrepresentative sampling, and can be taken at face value. The findings of this study therefore provide evidence that older people – despite showing a bias against allocentric strategies, most likely due to both allocentric processing and strategy switching deficits – are equally able to use the egocentric associative cue and beacon strategies tested in this study. Again, this indicates that the beacon strategy preference discovered in Study 1 was not due to a deficit in using the associative cue strategy, but instead attributable simply to the beacon strategy being slightly easier.

Limitations

This study successfully addressed some of the limitations of Study 1 by directly assessing associative cue and beacon navigation performance. However, in doing so, the design of this study became quite different from the previous one, and one consequent limitation was that the results of the two studies could not be directly compared. Different samples of the elderly population participated in the two studies, and it is assumed that they both represent a population that shows a bias towards a beacon navigation strategy as well as an unimpaired ability to use an associative cue strategy. However, as this study did not assess strategy preference, I cannot state this conclusively. Also, while older participants performed as well as young, they may have found use of the associative cue strategy – and perhaps also the beacon strategy – more cognitively demanding. This study did not assess differences in strategy-related neural activation, particularly in the dorsolateral striatum, which may still be worthwhile. Another limitation of this study is that, while it demonstrated that older

people are able to use both associative cue and beacon strategies as well as young, it did not assess switching between the two, which may be just as important to everyday navigation.

Conclusion

The aim of this study was to investigate whether the specific beacon strategy preference exhibited by older participants in Study 1 was due to a deficit in associative cue strategy use, possibly due to greater dependence on a dysfunctional dorsolateral striatum. Contrary to expectations, there were no age differences in performance within either condition, suggesting that older people are not impaired at using either egocentric strategy. Performance was slightly better in the beacon condition for both young and old participants, suggesting that this strategy is easier, which may account for the preference observed in the previous study. Whether or not age-related deterioration of dorsolateral striatum affects the neural mechanisms underlying performance of either egocentric strategy remains to be explored, perhaps using neuroimaging or animal models. Also contrary to expectations, both young and old demonstrated a surprisingly good memory of the directions and positions associated with individual landmarks encountered along the route (even in the beacon condition), showing that, even while navigating a route using a strategy that does not require such information, it is still acquired, possibly for the formation of allocentric representations. In conclusion, older people do not seem to be impaired at using an associative cue strategy, and may prefer to use a beacon strategy simply because it is less cognitively demanding.

3.4 Chapter conclusion

In this chapter I presented a study that used the AAT to assess the use of allocentric and egocentric strategies in young and older people. The results indicated that older participants were impaired at rejoining a known route from an unfamiliar direction, and that this impairment was due to their continued use of an egocentric strategy,

where an allocentric strategy, as used by young participants, was required for accurate completion of the task. Age-related decline in allocentric processing abilities likely contribute to this age difference, but it is probably also partly attributable to an impaired ability to switch to the allocentric strategy. Older participants' continued use of an egocentric strategy therefore demonstrates how a navigational strategy switching deficit may prevent use of the optimal strategy. Furthermore, as real-world navigation can often involve rejoining a familiar route from a novel direction, their poorer overall performance at this task highlights how much of a negative effect navigational strategy switching deficits – and consequent use of sub-optimal strategies – could have on navigational performance in everyday life. Older participants also showed a specific preference for the beacon strategy over the associative cue strategy, which could have been caused by an impairment in their ability to use the associative cue strategy.

This final point was addressed by a follow-up study, also reported in this chapter. In the second study, young and old participants completed one of two versions of an RLT, testing their ability to use either an associative cue strategy or a beacon strategy. Although I expected that older participants might be impaired at use of the associative cue strategy, the results did not confirm this. In each condition, both age groups performed similarly, demonstrating that older people are unimpaired at use of the two egocentric strategies. However, within both age groups, participants assigned to the beacon condition performed very slightly better than those assigned to the associative cue condition, suggesting that older participants in the first study may have shown a preference for the beacon strategy simply because it is easier. Secondary measures confirmed that participants were using the strategies they were supposed to on each variant of the task, but also demonstrated that both young and old participants in both conditions retained information that was superfluous to use of either strategy. This may reflect processes involved in the acquisition of survey knowledge, which is thought to occur automatically during route navigation. However, the finding that older participants performed as well as young on these measures, does not necessarily suggest that they are equally capable of forming allocentric representations, and therefore does not resolve the problem that deficits in

both allocentric processing and strategy switching could be responsible for a preference for egocentric strategies among older people, as observed in the preceding study.

In summary, Study 1 demonstrated that older people are less inclined to use an allocentric navigational strategy, and instead specifically prefer to use a beacon strategy. Study 2 demonstrated that this preference was not related to any impairment in use of the associative cue strategy. The overall performance of older participants in Study 1 highlights how a bias towards egocentric strategies can impair navigational performance. While this bias could be influenced by deficits in allocentric processing, impaired navigational strategy switching also likely contributes. Throughout the remainder of this thesis, within the context of studies presented in subsequent chapters, I will further explore the role of navigational strategy switching impairments.

Chapter Four

Navigational Strategy Switching Deficits in Ageing

4.1 Chapter overview

In the previous chapter, I reported two studies of navigational strategy use by older people, demonstrating that they show a preference for egocentric strategies – specifically for a beacon strategy – which could be related to an impaired ability to switch to an allocentric strategy. Study 1 in particular illustrated the importance of being able to switch between various strategies when rejoining a familiar route from a novel direction; just as when integrating spatial information on different scales, dealing with changes in the availability of cues, and making revisions to navigational goals. Navigational performance could be profoundly affected by an impaired ability to switch to the most appropriate strategy. Throughout the remainder of this thesis I will focus on navigational strategy switching in ageing, and I start by presenting two studies exploring age-related deficits in this chapter.

In section 4.2, I present Study 3, which assessed navigational strategy switching in young and older participants using a virtual plus maze (VPM), based on a task used to study strategy switching in rodents. Participants were required to find rewards using either an allocentric place strategy or an egocentric response strategy, periodically switching or reversing strategy. The task can therefore be used to assess age differences in use of allocentric and egocentric strategies, as well as in performance of strategy switches and reversals. Furthermore, I assessed age differences in switching to or reversing specifically one strategy or the other. Results are discussed in terms of a network hypothetically responsible for switching behaviour, incorporating the locus coeruleus (LC) and regions of prefrontal cortex (PFC), as well as connectivity between this network and the hippocampus, responsible for allocentric processing.

Study 4, reported in section 4.3, addressed a limitation of Study 3, related to the simple and abstract nature of the VPM as a navigational task. The study used a novel

shortcutting task set in more realistic town-like virtual environments (VEs). Participants were repeatedly trained on indirect routes through the two VEs, and then asked to take the direct route to goal locations during training. This was intended to explore age differences in switching from an egocentric to an allocentric navigational strategy within a more ecologically relevant context. Participants also completed a short version of the VPM, in order to confirm the contribution of strategy switching to performance at the shortcutting task, as well as a brief test of cognitive mapping, in order to assess the contribution of allocentric processing. Results are considered within the context of the same neurophysiological model of navigational strategy switching.

Study 3 was again conducted in collaboration with Dr Jan Wiener at Bournemouth University, and several undergraduate students assisted with collecting data for both studies. However, I played a leading role in designing and running each study, I performed the data analysis reported here myself, and the content of this chapter is entirely my own work. Study 3 has been published in *Frontiers in Aging Neuroscience* (Harris et al., 2012) and Study 4 has been published in *Neurobiology of Aging* (Harris & Wolbers, 2014).

4.2 Study 3: An age-related deficit in switching to an allocentric place strategy

4.2.1 Introduction

Navigation in ageing

While many cognitive faculties deteriorate in ageing, navigation abilities may be among those most severely affected. With advancing age, brain areas associated with navigation, including the hippocampus and entorhinal cortex, show extensive degradation (Jack et al., 1997; Driscoll et al., 2003; Du et al., 2003, 2006), and the integrity and activity of hippocampus in particular have been directly associated with

navigational performance (Moffat et al., 2006; Nedelska et al., 2012). Other research has also confirmed that ageing impairs navigational processes specifically dependent on these areas, such as allocentric processing (Moffat & Resnick, 2002; Antonova et al., 2009; Iaria et al., 2009) and path integration (Allen et al., 2004; Mahmood et al., 2009; Harris & Wolbers, 2012). The caudate nucleus is also susceptible to the effects of ageing (Raz et al., 2005; Hasan et al., 2008), although less so than the hippocampus (Jernigan et al., 2001; Fjell et al., 2009; Raz et al., 2010), meaning that egocentric navigation is less impaired than allocentric (Begega et al., 2001; Jansen et al., 2010). As shown in Study 1 (section 3.2), and by other previous research (Nicolle et al., 2003; Rodgers et al., 2012; Konishi et al., 2013), older individuals consequently tend to rely more upon egocentric strategies during navigation. In the real world, however, optimal navigation cannot usually rely entirely upon one particular strategy, but depends upon the ability to use various strategies, as well as the ability to flexibly switch between them as and when required.

Strategy switching in ageing

Impairments in the ability to switch between strategies have been demonstrated in older animals and humans. In rodents, strategy switching has been studied using an attentional set-shifting task, which involves locating a reward in one of two wells, each filled with a different substrate and scented with a different odour. The animals locate the reward based either on substrate or odour, but every so often the rewarded substrate/odour is reversed, or the rewarded cue is switched. Older animals are able to perform reversals as well as young controls, but show a deficit in switching from one cue-based strategy to the other (Young et al., 2010; Tanaka et al., 2011). Similar results have been found in non-human primates using a conceptual set-shifting task, involving switching between responding to colours and responding to shapes (Moore et al., 2003; Hara et al., 2011). A form of conceptual set-shifting task, the Wisconsin Card Sorting Task (WCST; Berg, 1948), has been used extensively to examine executive functioning in older people, and their performance is also indicative of a strategy switching deficit (Ashendorf & McCaffrey, 2008; Gamboz et al., 2009).

The noradrenaline (NA) hypothesis (Aston-Jones & Cohen, 2005) suggests that strategy switching is coordinated by regions of PFC and the LC-NA system. In response to changes in reward, OFC and ACC signal to LC, which, through changing its mode of NA output, prompts PFC to coordinate a switch to a new behavioural strategy. Bouret and Sara (2005) have also described a role for NA in reorganising functional networks during switching behaviour. As both PFC (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011) and the LC-NA system (Manaye et al., 1995; Grudzien et al., 2007) exhibit age-related dysfunction, the NA hypothesis can account for the impairments in strategy switching observed in ageing. Animal research has provided some support for the hypothesis by demonstrating that the effects of prefrontal NA depletion on strategy switching performance are similar to those of ageing (Tait et al., 2007; McGaughy et al., 2008; Caetano et al., 2013).

Navigational strategy switching

Navigation operates on smaller and larger scales and utilises a range of cues, many of which are not consistently available while moving around. It can therefore involve numerous navigational strategies, which can be discriminated by reference frame, with some operating in relation to the body's changing orientation (egocentric), and others in relation to a static external coordinate system (allocentric). For example, using environmental cues to work out a novel route to a familiar location relies on allocentric processing, while following a known route encoded as a series of turns depends on egocentric processing. Allocentric and egocentric strategies are dependent upon the hippocampus and caudate nucleus, respectively (Packard & McGaugh, 1996; Hartley et al., 2003; Iaria et al., 2003), supposedly operating in parallel (Bohbot et al., 2007; Iglói et al., 2009). PFC determines which actually guides behaviour by re-weighting inputs from each system accordingly (Doeller et al., 2008), when, for example, a strategy switch is required.

Use of allocentric and egocentric strategies has been studied in rats using the plus maze task (e.g. Ragozzino, 2007; Rich & Shapiro, 2007). The task involves starting from one of two opposing arms of a plus-shaped maze, and locating a reward at one

of the two adjacent arms. Which arm is rewarded depends upon the current strategy. Sometimes the subject is rewarded for finishing in a specific place, i.e. the east or west arm of the maze; at other times simply for a particular response, i.e. turning left or turning right. The task can therefore be used to study switches and reversals, much like the attentional set-shifting task, but within a navigational context. Several studies (Ragozzino et al., 1999; Rich & Shapiro, 2007; Young & Shapiro, 2009) have demonstrated impaired strategy switching, but unaffected reversals, following inactivation of regions of mPFC, which is comparable to findings of studies using the attentional set shifting task and consistent with the NA hypothesis.

Current study

This study was the first to investigate the effects of ageing on navigational strategy switching, and the first to assess navigational strategy switching in human participants. We did so using a virtual adaptation of the plus maze task, which, as with the rodent task, required that participants use and switch between an allocentric place strategy and an egocentric response strategy. Unlike the rodent task, the VPM was run on a computer in a VE, with only a visual signal and an increasing score serving as reward for correct trials. Young and old participants completed the VPM, as well as a spatial working memory task (SWMT) and a questionnaire measuring computing experience. I hypothesised that older people would perform worse at the VPM due to an impaired ability to perform strategy switches, but not reversals. I also expected that this specific deficit could not be accounted for by age differences in computing experience, spatial working memory, reward sensitivity (also assessed by the SWMT) or the ability to use either strategy.

4.2.2 Methods

Participants

Eighteen (10 female) young (aged 20-29, M=22.2) and 20 (11 female) older (aged 60-84, M=68.6) participants were recruited from existing databases of research

volunteers local to Edinburgh and Bournemouth. Most therefore had previous experience of participating in research. All had normal or corrected-to-normal vision, and no known neuropsychological impairments. Participants were reimbursed for their time at a rate of £6 per hour. One 20-year-old female participant was excluded based on her overall VPM performance, which was more than 2.5 SDs below the young group's mean.

Procedure

Participants provided informed consent before participating, and then began by rating their experience with computers and computer games on a nine-point scale. They then completed the SWMT, described in Chapter Two (section 2.3.1), and the VPM, as described below, on a desktop computer with a 24in widescreen monitor and a standard UK keyboard. Participants were debriefed following completion of the VPM. The experiment was approved by ethics committees at the University of Edinburgh and Bournemouth University, and conducted in accordance with the BPS code of ethics.

Virtual plus maze

As described in Chapter Two (section 2.3.3), the VPM was set in a VE comprising a grass-textured plain and surrounding mountain scenery (also used for the SWMT), a plus-shaped pathway and, in this version, transparent walls at the sides of the pathway and reward wells at the end of the east and west goal arms (*figure 2.5*). On each trial, participants were positioned at either the north arm or the south arm of the maze, and then automatically moved towards the central junction. Stopping just before the central junction, participants were allowed 3s within which to press either the left or right arrow key on the keyboard to indicate which direction they wanted to proceed in. Automatic movement then continued through the central junction in their chosen direction and towards the reward well at the end of either the east or west maze arm. A reward signal appeared if participants had made the correct choice, which also increased a running total, displayed in the top corner of the screen. Each

trial lasted around 16-19s, depending upon how long participants took to respond. Sometimes participants were rewarded for visiting the same place on each trial, i.e. the east or west reward well, regardless of which direction they had to turn to get there. At other times participants were rewarded for making the same response on each trial, i.e. turning left or right, regardless of which reward well this led them to. Participants used the same place or response strategy throughout blocks of 20 trials, between which either a strategy switch, a reversal or no change occurred. Participants completed a total of 320 trials, incorporating five switches and five reversals.

Data analysis

Data were analysed in Matlab. Computer experience information was combined to produce a single score. The SWMT produced scores for place recall (proportion of correct places visited), route recall (proportion of correct turns made) and reward sensitivity (proportion of rewards remembered). VPM performance was assessed primarily in terms of the proportion of trials to which participants responded correctly. I also used the Bayesian learning analysis described in Chapter Two (section 2.5.3) to identify if and when participants stably acquired the correct strategy for each block, producing two further measures of VPM performance; proportion of blocks learned and proportion of stable trials, related to learning speed. I first assessed age differences in all measures using independent t-tests, and the relationship between VPM performance and all other variables using stepwise regression analyses. Using mixed model ANOVAs and t-tests, with Holm-Bonferroni correction for multiple comparisons, I then assessed the effects of age group, strategy, change type and block type (incorporating both strategy and change type) on all three measures of VPM performance. Where behavioural data were divided by change type, blocks following unlearned blocks had to be excluded, as participants could not be said to have switched or reversed from the previous strategy if they had not necessarily been using that strategy. I also reviewed the proportions of unlearned blocks during which older participants used an incorrect strategy, as well as how often these errors were perseverative or regressive.

4.2.3 Results

Overall VPM performance and control measures

I first assessed VPM performance throughout all trials, in terms of the percentage of trials to which participants responded correctly, the percentage of trial blocks during which they successfully learned the correct strategy, and the percentage of trials for which participants stably used the correct strategy. *Figure 4.1* presents mean trials correct, blocks learned and stable trials for young (orange) and older (green) participants. As shown, older participants performed worse than young on all three measures. Before assessing the effects of strategy or change type, I also assessed the influence of other factors. There were age differences in most of the control variables, as reported below. However, *tables 4.1-4.3*, which summarise the results of a series of stepwise regression analyses, suggest that age predicted VPM performance better alone than in combination with any of these control variables.

Independent t-tests confirmed that older participants performed significantly worse at the VPM in terms of overall trials correct (t_{35}=3.14, p=.002), blocks learned (t_{35}=3.39, p<.001) and stable trials (t_{35}=3.19, p=.002; *figure 4.1*). They also took significantly longer to respond (t_{35}=3.24, p=.003). At the SWMT, they scored worse on place recall (young: M=83.33, SD=13.48; old: M=62.67, SD=15.01; t_{35}=4.70, p<.001) and reward sensitivity (young: M=83.75, SD=6.87; old: M=69.58, SD=13.88; t_{35}=3.60, p<.001), but not route recall (young: M=84.81, SD=4.27; old: M=83.17, SD=14.00; t_{35}=0.38, p=0.33). Older participants also reported a significantly lower level of computer experience (young: M=6.00, SD=3.14; old: M=2.18, SD=2.18; t_{33}=3.71, p<.001). However, as above, the stepwise regression analyses suggested that age group predicted VPM trials correct (β=-.097, p=.004), blocks learned (β=-.222, p=.002), and stable trials (β=-.183, p=.003), better alone than in combination with potential control variables. Gender, computer use, place recall, route recall, and reward sensitivity were not retained in any of the models as significant predictors of VPM performance (*tables 4.1-4.3*). Further stepwise regression analyses for each age group separately (excluding age as a predictor)

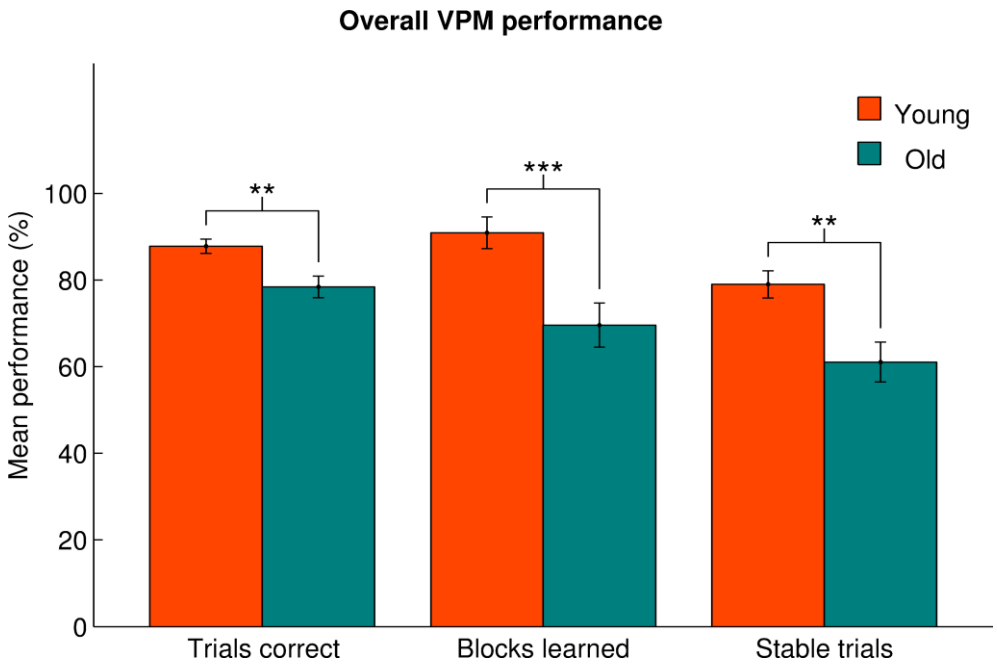

Figure 4.1 Overall VPM performance. Mean performance in terms of percentage of trials correct, blocks learned and stable trials throughout all trial blocks for young (orange) and old (green) participants. Error bars represent standard error of the mean (SEM). ** and *** represent significant age differences at p<.01 and p<.001.

maintained that none of the potential control variables were significant predictors for any measure of VPM performance. These variables were therefore not considered in further analyses.

Overall VPM trials correct stepwise regression results

Predictor	β	SE	In	p
Age group	-.097	.031	1	.004
Gender	.039	.031	0	.219
Computer use	-.035	.067	0	.602
Place recall	-.003	.115	0	.981
Route recall	.215	.144	0	.144
Reward sensitivity	.229	.136	0	.100

Table 4.1 Overall VPM trials correct stepwise regression results. An initial stepwise regression analysis assessed how well age and potential control variables predicted VPM performance in terms of overall trials correct. Variables that were retained in the model as significant predictors of performance are highlighted in blue.

Overall VPM blocks learned stepwise regression results

Predictor	β	SE	In	p
Age group	-.222	.065	1	.002
Gender	.075	.066	0	.269
Computer use	-.105	.014	0	.460
Place recall	-.157	.242	0	.521
Route recall	.481	.302	0	.121
Reward sensitivity	.403	.290	0	.174

Table 4.2 Overall VPM blocks learned stepwise regression results. A second stepwise regression analysis assessed how well age and potential control variables predicted VPM performance in terms of overall blocks learned. Variables that were retained in the model as significant predictors of performance are highlighted in blue.

Overall VPM stable trials stepwise regression results

Predictor	β	SE	In	p
Age group	-.183	.057	1	.003
Gender	.070	.058	0	.235
Computer use	-.050	.124	0	.689
Place recall	-.072	.214	0	.738
Route recall	.439	.265	0	.107
Reward sensitivity	.441	.251	0	.088

Table 4.3 Overall VPM stable trials stepwise regression results. A third stepwise regression analysis assessed how well age and potential control variables predicted VPM performance in terms of stable trials. Variables that were retained in the model as significant predictors of performance are highlighted in blue.

VPM performance by strategy

In order to better understand the age difference in VPM performance, I divided the data, firstly by strategy. *Figure 4.2* represents the performance of young and older participants – in terms of trials correct (top), blocks learned (centre) and stable trials (bottom) – throughout all place strategy trial blocks and all response strategy trial blocks. All three charts show that young and older participants performed similarly

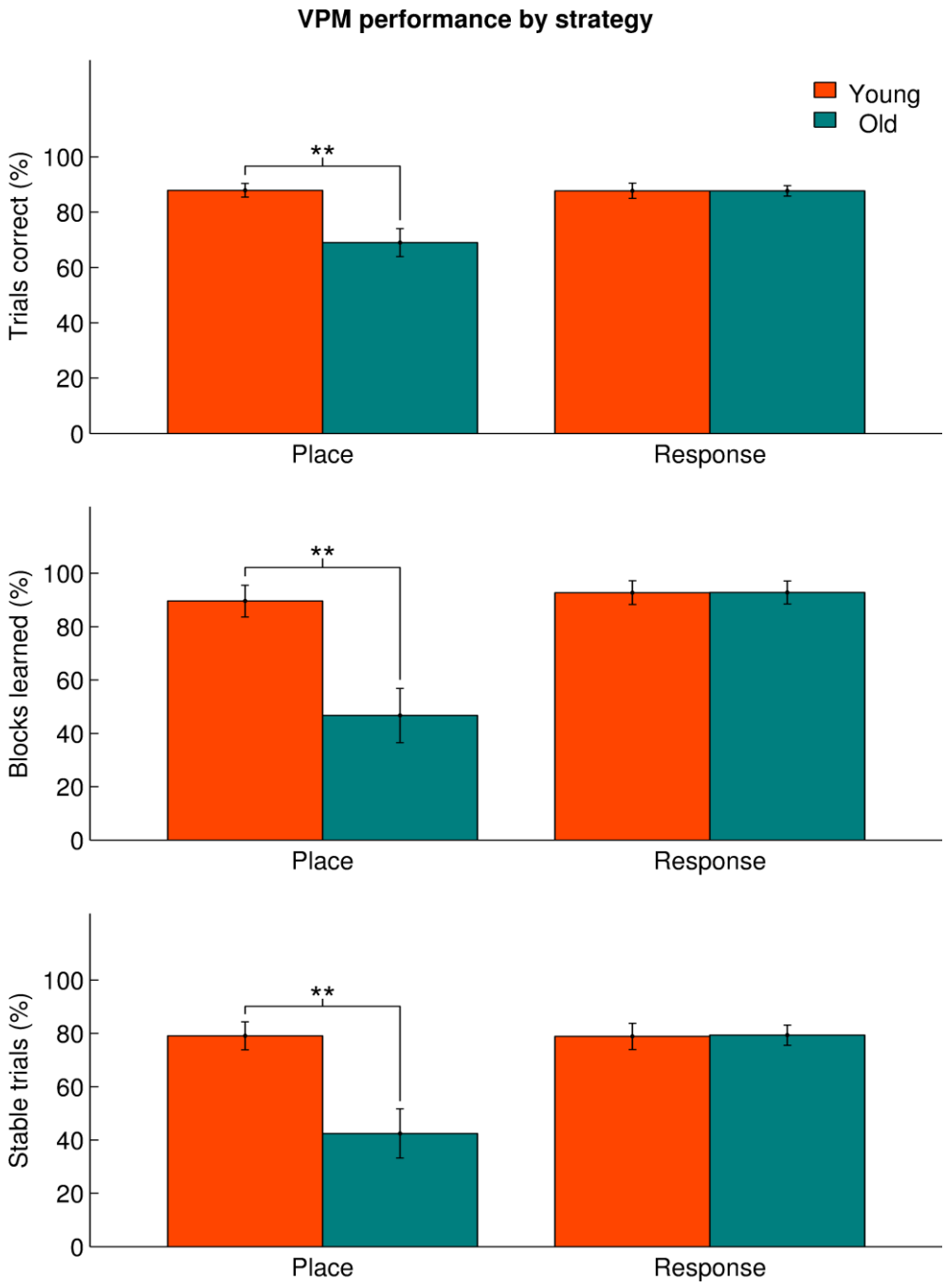

Figure 4.2 VPM performance by strategy. Mean performance in terms of percentage of trials correct (*top*), blocks learned (*centre*) and stable trials (*bottom*) throughout place and response blocks for young (orange) and old (green) participants. Error bars represent SEM. ** represents significant age differences at p<.01.

during response blocks, but worse throughout place blocks. These results seem to reflect an age-related impairment in allocentric navigation.

In support of this finding, two-way mixed ANOVAs, with age and strategy as factors, revealed significant main effects of age on trials correct (TC; $F_{1,35}$=9.36, p=.004), blocks learned (BL; $F_{1,35}$=11.93, p=.002) and stable trials (ST; $F_{1,35}$=9.69, p=.004), as well as, for each measure, significant effects of strategy (TC: $F_{1,35}$=6.45, p=.016; BL: $F_{1,35}$=10.68, p=.002; ST: $F_{1,35}$=7.15, p=.011) and significant age by strategy interactive effects (TC: $F_{1,35}$=6.71, p=.014; BL: $F_{1,35}$=8.13, p=.007; ST: $F_{1,35}$=7.29, p=.011). Post-hoc t-tests for each measure confirmed that old participants performed significantly worse during place blocks (TC: t35=3.27, pHB=.002; BL: t_{35}=3.58, p_{HB}=.001; ST: t_{35}=3.38, p_{HB}=.002), but not response blocks (TC: t_{35}=.01, p_{HB}=.498; BL: t_{35}=.02, p_{HB}=.506; ST: t_{35}=.08, p_{HB}=.531).

VPM performance by change type

I then split the data by change type, separating trial blocks following a strategy switch from those following a reversal. Blocks were only included if participants had stably acquired the correct strategy during the preceding block, as they could not otherwise be said to have actually performed a switch or reversal. *Figure 4.3* summarises trials correct (top), blocks learned (centre) and stable trials (bottom) data throughout blocks following switches and reversals. The two age groups performed similarly following reversals, but older participants performed much worse after strategy switches. These results seem to indicate that ageing does impair the ability to switch between navigational strategies, as hypothesised.

Again, these findings were supported by two-way ANOVAs, which revealed significant main effects of age (TC: $F_{1,35}$=8.08, p=.007; BL: $F_{1,35}$=9.79, p=.004; ST: $F_{1,35}$=8.44, p=.006) and change type (TC: $F_{1,35}$=23.11, p<.001; BL: $F_{1,35}$=20.98, p<.001; ST: $F_{1,35}$=26.92, p<.001) as well as significant interactions between the two (TC: $F_{1,35}$=5.07, p=.031; BL: $F_{1,35}$=7.28, p=.011; ST: $F_{1,35}$=6.64, p=.014), for all measures of performance. Post-hoc t-tests confirmed that these effects were due to significant age differences in performance after switches (TC: t_{35}=2.74, p_{HB}=.010; BL: t_{35}=3.13, p_{HB}=.004; ST: t_{35}=2.96, p_{HB}=.006) but not after reversals (TC: t_{35}=1.13, p_{HB}=.134; BL: t_{35}=1.18, p_{HB}=.123; ST: t_{35}=.82, p_{HB}=.208).

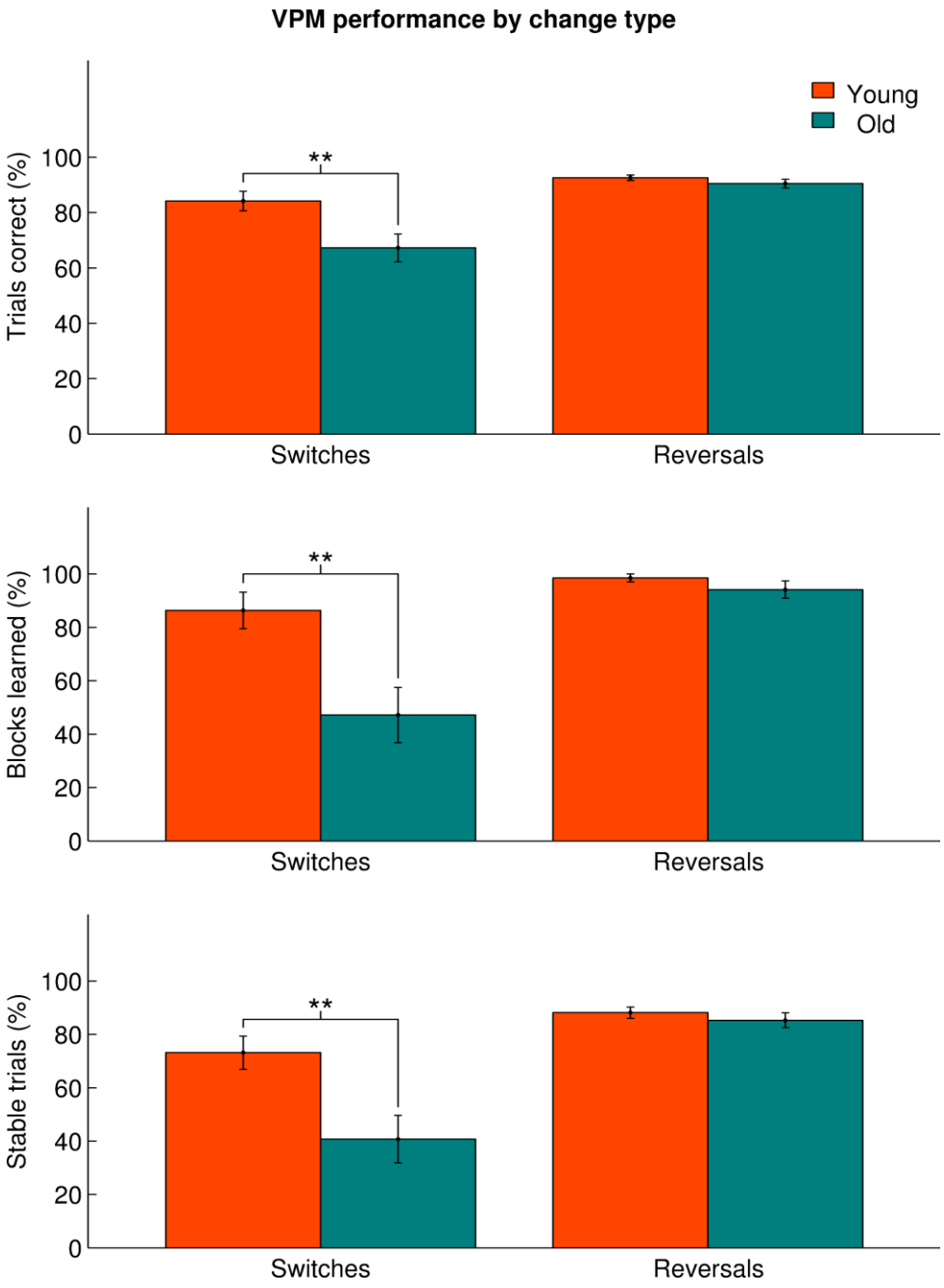

Figure 4.3 VPM performance by change type. Mean performance in terms of percentage of trials correct (*top*), blocks learned (*centre*) and stable trials (*bottom*) throughout blocks following switches and reversals for young (orange) and old (green) participants. Error bars represent SEM. ** represents significant age differences at p<.01.

VPM performance by strategy and change type

In order to investigate how these apparent allocentric processing and navigational strategy switching deficits related to one another, I performed further analyses separating the data by both strategy and change type. This produced four block types; those following a switch to either the place strategy (S-P) or the response strategy (S-R), and those following a reversal of either the place (R-P) or the response (R-R) strategy. *Figure 4.4* summarises the performance of young and old participants throughout each of these four block types, illustrating a more specific deficit than hypothesised. Older participants performed worse only during place blocks following a switch, indicating a specific impairment in switching to an allocentric strategy. As described below, this did not relate to differences in response time.

The same analyses revealed a significant main effect of age (TC: $F_{1,35}$=8.95, p=.005; BL: $F_{1,35}$=9.49, p=.004; ST: $F_{1,35}$=8.18, p=.007) and of block type (TC: $F_{3,105}$=9.76, p<.001; BL: $F_{3,105}$=9.93, p<.001; ST: $F_{3,105}$=9.76, p<.001), as well as a significant interactive effect (TC: $F_{3,105}$=5.70, p=.001; BL: $F_{3,105}$=6.77, p<.001; ST: $F_{3,105}$=5.57, p=.001), for each measure of VPM performance. Post-hoc tests confirmed that the specific age difference in performance during switch-to-place blocks was significant for trials correct (t_{35}=2.98, p_{HB}=.011), blocks learned (t_{35}=3.74, p_{HB}=.001) and stable trials (t_{35}=3.28, p_{HB}=.005), while there were no age differences in performance on switch-to-response (TC: t_{35}=.04, p_{HB}=.517; BL: t_{35}=.43, p_{HB}=.663; ST: t_{35}=.18, p_{HB}=.572), reverse-place (TC: t_{35}=1.78, p_{HB}=.133; BL: t_{35}=1.35, p_{HB}=.284; ST: t_{35}=1.37, p_{HB}=.275) or reverse-response (TC: t_{35}=.06, p_{HB}=.954; BL: t_{35}=.21, p_{HB}=.837; ST: t_{35}=.03, p_{HB}=.1.023) blocks.

At this point I also re-assessed group differences in response time. A two-way ANOVA with age and block type as factors, as performed for the three primary dependent variables, revealed a significant effect of age ($F_{1,35}$=12.13, p=.001), but not of block type ($F_{3,105}$=.59, p=.626), nor a significant interaction ($F_{3,105}$=.96, p=.416). Post-hoc t-tests confirmed that older participants took significantly longer to respond during all block types (S-P: t_{35}=2.90, p_{HB}=.013; S-R: t_{35}=3.56, p_{HB}=.006;

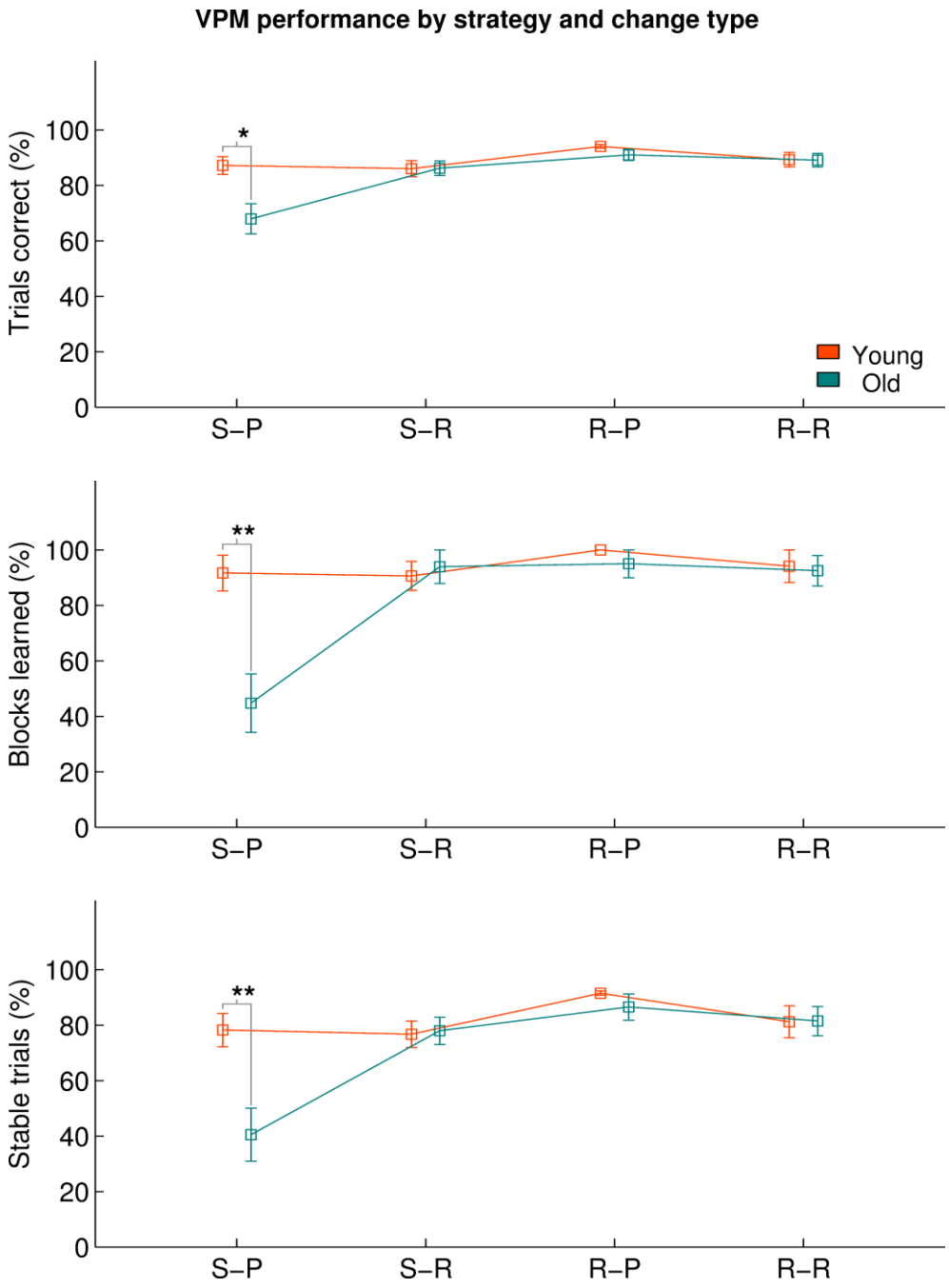

Figure 4.4 VPM performance by strategy and change type. Mean performance in terms of percentage of trials correct (*top*), blocks learned (*centre*) and stable trials (*bottom*) throughout switch-to-place (S-P), switch-to-response (S-R), reverse place (R-P) and reverse-response (R-R) blocks for young (orange) and old (green) participants. Error bars represent SEM. * and ** represent significant age differences at p<.05 and p<.01.

R-P: t_{35}=3.21, p_{HB}=.011; R-R: t_{35}=2.58, p_{HB}=.014), suggesting that the age

differences in performance and response time were unrelated. As participants were allowed a maximum of 3s to respond on each trial, greater response time could have affected performance by increasing the number of trials to which participants did not respond in time. However, there was no such age difference in the number of aborted trials (t_{35}=.92, p=.364).

Older participants' performance during unlearned blocks

In an effort to understand why older participants performed worse during switch-to-place blocks, I explored their use of alternative strategies during unlearned blocks. I associated each block with a particular strategy if the participant responded in accordance with this strategy significantly more than expected by chance (p<.001). As shown in *figure 4.5*, while, on many trials (39.39%), older participants simply did not acquire any strategy, they usually employed an incorrect strategy. Interestingly, older participants used an incorrect place strategy (28.79%) approximately as often as an incorrect response strategy (31.82%), suggesting that, despite the observed deficit in switching to a place strategy, they were able to use one. Considering only blocks where older participants did use an incorrect strategy, their strategy use was deemed perseverative if they reflected continued use of the strategy that was rewarded in the preceding trial block, or regressive if in line with the strategy rewarded in the block prior to that. There was very little incidence of older participants regressing to the earlier strategy (2.50%), but they did persevere with the immediately previous strategy on 32.50% of error trials. Where other types of error were made, older participants again used both incorrect place (37.50%) and response strategies (27.50%), suggesting that they were not simply reverting to a preferred response strategy.

4.2.4 Discussion

Summary of findings

Overall, older participants performed worse than young at the VPM in terms of the

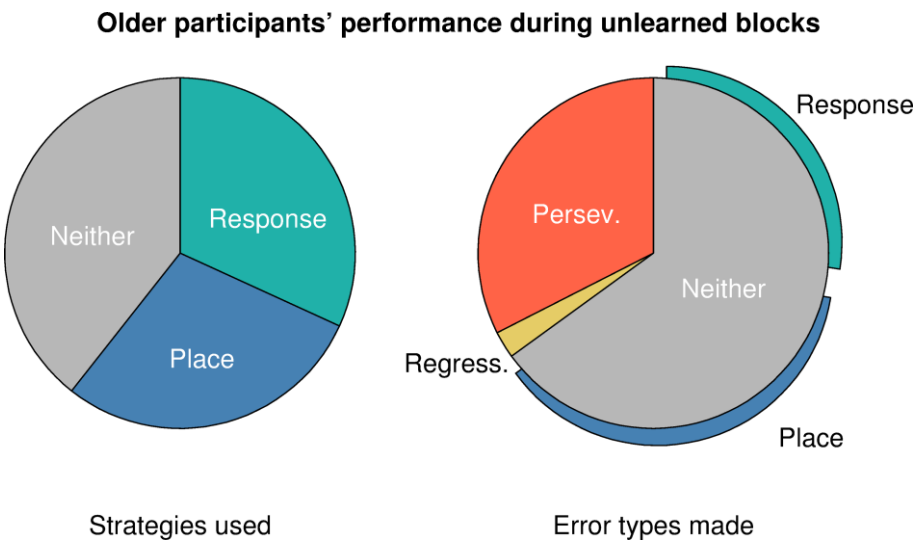

Figure 4.5 Older participants' performance during unlearned blocks. *Left:* Incorrect strategies used by older participants during unlearned blocks. Participants sometimes responded consistently in accordance with an incorrect place (red) or response (blue) strategy, and sometimes did not (grey). *Right:* Types of error made by older participants during unlearned blocks in which they did consistently use an incorrect strategy. Participants sometimes persevered with the previous strategy (green), sometimes regressed to the strategy that preceded that one (orange), and sometimes used another incorrect strategy.

proportion of trials to which they responded correctly, the proportion of trial blocks for which they learned the correct strategy, and the proportion of trials on which they stably used the correct strategy. Stepwise regression analyses for each measure confirmed that performance was predicted by age alone, not gender, computing experience, place or response recall, or reward sensitivity. Dividing VPM data by strategy then showed that older participants performed worse during place blocks, but not response blocks. However, dividing the data by change type demonstrated that they also performed worse after strategy switches, but not after reversals. Separating the data by both strategy and change type revealed that these results were due to a more specific deficit in switching to the place strategy. During blocks where older participants failed to learn the correct strategy, they often adopted an incorrect strategy. They used an incorrect place strategy as often as an incorrect response strategy, and these errors were perseverative only a minority of the time. Older participants were also slower to respond than young, but this did not seem to relate to performance.

Interpretation of findings

The age difference in overall VPM performance, and, more specifically, the age difference in performance following strategy switches, provided evidence of a strategy switching deficit among older people. This was consistent with our hypothesis, as well as with previous findings outside the context of navigation using tasks such as the WCST (Ashendorf & McCaffrey, 2008; Gamboz et al., 2009), and can be interpreted in terms of the NA hypothesis of strategy switching (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005). As older participants usually did not exhibit perseverative errors, and as VPM performance was not predicted by reward sensitivity, it is unlikely that the age-related switching deficit is attributable to a failure of the OFC or ACC to detect changes in reward. It could, however, be explained by LC-NA dysfunction, as observed in ageing (Manaye et al., 1995; Grudzien et al., 2007), as NA depletion, in PFC in particular, has been shown to have similar effects on strategy switching performance (Tait et al., 2007; McGaughy et al., 2008; Caetano et al., 2013). Alternatively, it could be accounted for by PFC failing to engage a new strategy despite normal NA input, simply due to age-related PFC degradation (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011).

We also found that older participants performed worse on place blocks, but not response blocks, which seemed indicative of an allocentric processing deficit. This was not unexpected, as previous work has demonstrated that allocentric navigation is impaired in ageing (Moffat & Resnick, 2002; Antonova et al., 2009; Iaria et al., 2009), and it can be accounted for by age-related hippocampal dysfunction (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009). This finding did not necessarily affect our hypothesis or supporting results regarding a general strategy switching deficit, but further analyses of performance divided by both change type and strategy revealed a much more specific deficit than hypothesised, with older people performing worse only on switch-to-place blocks. Their performance therefore could not be explained by a general strategy switching deficit, as switching to the response strategy was unaffected. Similarly, it could not be attributed solely to

impaired allocentric processing, as performance throughout place blocks following reversals was also unaffected. This was the first study to demonstrate this specific impairment, although it may still relate to previous findings reflecting a general strategy switching deficit, with the asymmetry of the age difference across switch directions resulting from a discrepancy between strategies in terms of difficulty. Strategy difficulty could influence participants' decisions regarding the best strategy to use, which may be affected by age-related decision making deficits (Denburg et al., 2005; Fein et al., 2007; Bauer et al., 2013), associated with PFC dysfunction (Bechara et al., 1994; Manes et al., 2002; Denburg et al., 2007). Others have reported unidirectional switching deficits (Maintenant et al., 2011), especially when switching to a more difficult strategy (Floresco et al., 2008), and the allocentric strategy may have been particularly difficult for older participants due to age-related allocentric impairments (Moffat & Resnick, 2002; Antonova et al., 2009; Iaria et al., 2009) and preference for egocentric strategies (Nicolle et al., 2003; Rodgers et al., 2012; Konishi et al., 2013). However, there was no difference between place and response reversals to suggest that allocentric impairments made the place strategy more difficult.

As switch-to-response and reverse-place data indicated that older participants had retained normal functionality of PFC and hippocampus, respectively, another explanation for the specific switch-to-place deficit is a decline in the functional interaction between these two contributing systems. In this case, when a response strategy is no longer rewarded, a switch would still be initiated by the LC-NA system, and the hippocampal place strategy would still be available to switch to, but, perhaps due to reduced weighting of inputs from the hippocampus, PFC would be less inclined to select an allocentric strategy when required. Once an allocentric strategy is engaged, reversals would be performed normally, and, assuming no such decline in functional interaction between PFC and the caudate nucleus, switches in the opposite direction would also be unaffected. There is some existing evidence of a change in functional connectivity between the hippocampus and PFC in ageing and early dementia (Grady et al., 2003; Wang et al., 2006; Bai et al., 2009), and it could explain the age-related preference for egocentric strategies observed in Study 1

(section 3.2) and other previous studies (Nicolle et al., 2003; Rodgers et al., 2012; Konishi et al., 2013). Furthermore, it is possible that a deficit in switching to an allocentric strategy could explain some previous findings interpreted as evidence of age-related decline in allocentric navigation abilities.

Limitations

This study demonstrated that older people were impaired at switching from a response strategy to a place strategy. However, one limitation of the study is that these strategies are the simplest possible representations of allocentric and egocentric navigation. Real-world navigation involves much more complex forms of allocentric and egocentric strategies, to which the results of this study may not necessarily relate. I addressed this limitation in the study presented in the next section of this chapter. Another problem is that the behavioural data is unable to differentiate between alternative possible neural bases of the switch-to-place deficit. It remains to be determined whether the deficit is caused by an age-related decline in functional connectivity between hippocampus and PFC, or whether it actually reflects a general strategy switching deficit (masked by strategy preferences) caused by LC-NA or PFC dysfunction. The neural mechanisms underlying the behavioural age differences reported here require further investigation.

Conclusion

This study was the first to demonstrate a navigational strategy switching deficit among older people. The deficit was more specific than expected, as older people were impaired at switching from the egocentric response strategy to the allocentric place strategy, but not in the opposite direction. As switches to the response strategy and place reversals were unaffected, the deficit may reflect a decline in functional connectivity between intact prefrontal and hippocampal systems. Alternatively, the results may still reflect a general strategy switching deficit, caused by LC-NA or PFC dysfunction, but masked by a preference among older people for egocentric strategies and/or age-related decision making deficits. To determine which of these

accounts is more accurate, the underlying neural mechanisms require further investigation. Importantly, the specific switch-to-place deficit may have contributed to previous findings reported as allocentric navigation impairments, and is likely to contribute more generally to the navigational difficulties experienced by older people.

4.3 Study 4: An age-related deficit in switching to an allocentric wayfinding strategy

4.3.1 Introduction

Recapitulation

As introduced in section 4.2.4, ageing has a profound effect on navigation abilities, partly due to dysfunction of brain regions such as the hippocampus (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009) and entorhinal cortex (Du et al., 2003, 2006), leading to deficits in navigational processes such as cognitive mapping (Moffat & Resnick, 2002; Moffat et al., 2006; Antonova et al., 2009; Iaria et al., 2009) and path integration (Allen et al., 2004; Mahmood et al., 2009; Harris & Wolbers, 2012). However, everyday navigation is dependent upon various navigational strategies, some allocentric and some egocentric, so the ability to flexibly switch between navigational processes may also be important. My doctoral research was therefore based on the idea that age-related deficits in strategy switching (Moore et al., 2003; Ashendorf & McCaffrey, 2008; Young et al., 2010) contribute to the navigational difficulties experienced by older people. Study 3 (section 4.2) was the first study to support this, demonstrating that older people were impaired at navigational strategy switching, specifically at switching from an egocentric to an allocentric strategy. I discussed this finding in terms of Aston-Jones and Cohen's (2005) model of switching behaviour, suggesting that the deficit could be attributed to reduced functional connectivity between PFC and hippocampus, or dysfunction of PFC or the LC-NA system. One limitation of the study was that it

assessed navigational strategy switching using the relatively abstract VPM, which may or may not relate well to real-world navigation.

Current study

The main aim of this study was to address a limitation of the previous study by assessing navigational strategy switching in a more realistic context. I designed two realistic virtual town environments in which participants performed a novel shortcutting task. Participants were repeatedly trained on indirect routes to several landmarks, then, during testing, they were asked to take the shortest possible route to the same locations. Participants therefore used a more complex sequential egocentric response strategy during testing (Iglói et al., 2009), and had to switch to a wayfinding strategy depending on allocentric processing. I hypothesised that older participants would take longer routes to goal locations, using the available shortcuts less frequently than young participants, due to an impaired ability to switch from an egocentric route-following strategy to an allocentric wayfinding strategy. Participants also completed a short form of the VPM, and I expected that the results would replicate those of the previous study, and that they would relate to use of shortcuts in the main task.

4.3.2 Methods

Participants

Twenty-five (12 female) young participants (aged 18-29, M=21.8) and 25 (11 female) old participants (aged 61-79, mean 68.7) were recruited from the PPLS panel of research volunteers and from the local Edinburgh student population, and were reimbursed for their time at a rate of £7 per hour. Most had prior experience of participating in research, and all had normal or corrected-to-normal vision and no known neuropsychological disorders.

Procedure

Participants completed the Montreal Cognitive Assessment (MoCA) to screen for mild cognitive impairment (MCI), the National Adult Reading Test (NART) as a measure of crystallised intelligence, and a computer-based version of the Corsi blocks task as a measure of spatial working memory. They then completed the main shortcutting task, followed by a short form of the VPM, on a desktop computer with a 24in widescreen monitor and a standard UK keyboard. Finally, participants completed a simple cognitive mapping test (CMT) as a measure of allocentric processing, which involved matching landmark labels to locations on paper maps of the VEs encountered during the shortcutting task (similar to those shown in *figure 4.6)*. Due to time constraints, not all participants completed the VPM. All participants were made fully aware of the details of the study and provided consent before participating.

Shortcutting task

This task was based in two realistic virtual town environments, designed in 3ds Max, each consisting of houses and salient buildings as landmarks (supermarkets, restaurants, etc.) along roads in a grid formation (*figure 4.6*). The task, programmed and run in Vizard, involved training participants on long, indirect routes to four goal locations, then testing their ability to find available shortcuts. The first two routes each ran from a different start point to a different goal location, but overlapped in the middle of the first VE, and included four junctions between start and end points. The other two routes ran through and overlapped in the middle of the second VE, and included six junctions.

During training, participants actively navigated the routes by using the keyboard's arrow keys to choose whether to go left, right or straight ahead at each junction. However, they were not allowed to deviate from the set routes, which, to begin with, were indicated by arrows at each junction. Training also incorporated probe trials, which involved placing the participants at a point in the VE facing a particular

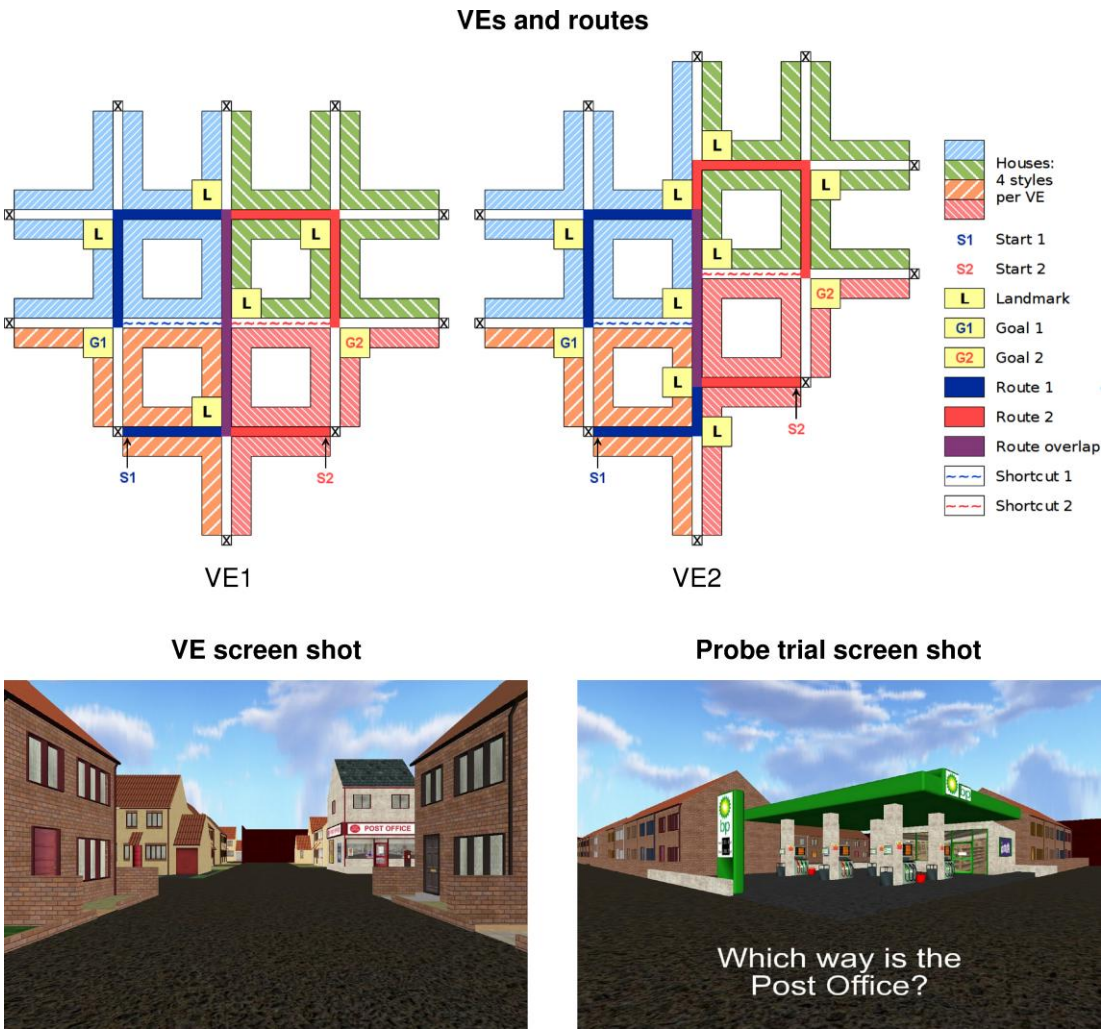

Figure 4.6 Shortcutting task. *Top:* Maps of the two VEs, with the four long routes to each goal location (followed during training) and the shortcuts (available during testing) marked. *Bottom left:* Screen image captured from VE1 during training, approaching one of the goal locations. *Bottom right:* Screen image captured during a probe trial (in which the post office was directly to the left).

landmark and asking them to point to another landmark, again using the arrow keys. These probe trials were designed to both promote and test the use of landmark information and allocentric processing while the routes were being learned. Each training cycle consisted of two repetitions of a traversal of each of the four routes in turn, followed by a set of three probe trials for each of the two VEs. Participants progressed to testing once they were able to traverse all four routes without directions or errors, and to respond correctly to a full set of probe trials for each VE. Route learning was also measured in terms of the number of training cycles before

able to navigate each route without directions or errors. As the direction arrows gradually disappeared throughout the first two training cycles, the minimum number of training cycles was three, while the maximum, due to time constraints, was seven.

Participants were then tested on each of the four original routes, as well as four new routes, which crossed from each start point to the opposite goal location in the same VE. These eight trials were presented twice in a random order, producing a total of 16 test trials. Before testing, participants were explicitly informed that they were no longer restricted to the long training routes, and that the objective during testing was to find the shortest route to each goal location. They were then also reminded of this at the start of every trial. I assessed task performance in terms of the lengths of the routes taken to each goal location in number of junctions (adjusted for VE differences in training route length), as well as whether or not the shortcut was used on each trial.

VPM

This study used a short version of the VPM, as described in Chapter Two (section 2.3.3) and above (section 4.2.2). The original VPM was shortened by reducing the length of each trial (5-8s) and the number of trials (155) in terms of both trials per block (15 or 20, varied pseudorandomly) and total blocks (nine, allowing four switches and four reversals). The VE differed from the one used in the previous study in that there were no longer any transparent walls around the plus maze (as participants could not deviate from the path anyway), nor were there any reward wells (instead the reward signal simply appeared at the end of the goal arm on correct trials). The task also differed from the previous version in that participants always started on the place strategy, rather than a pseudorandomly selected strategy, in order to avoid exaggerating any age-related allocentric processing deficits.

Data analysis

Data were analysed in Matlab. Results of the MoCA, NART, Corsi blocks task and

CMT were each represented as a single-value score. CMT scores for each VE were corrected to account for the fact participants could not give only one incorrect answer, then combined to produce a score out of 15. VPM results were processed in terms of the proportion of correct trials per block. For the shortcutting task, I assessed route learning in terms of number of training cycles, and testing performance in terms of route length (in junctions) and shortcut use. I performed mixed model ANOVAs and paired t-tests to assess age differences across routes and VEs, and used stepwise regression and generalised linear modelling (GLM) to assess the contribution of secondary measures to shortcut use. For multiple comparisons, p values were corrected using the Holm-Bonferroni method. I also used the Bayesian learning analysis, described in Chapter Two (section 2.5.3), to identify if and when each participant switched to an allocentric wayfinding strategy in the shortcutting task. Participants were to be excluded if they scored below 23 on the MoCA, if they failed to learn all of the routes in the maximum training period allowed, or if their average testing route length was further than 2.5 SDs from the group mean, but no participants met any of these exclusion criteria.

4.3.3 Results

Control measures

All participants scored 23 or above on the MoCA so none were excluded for showing signs of MCI. The older group performed significantly better than the young at the NART (young: M=33.96, SD=6.37; old: M=42.24, SD=5.51; t_{48}=5.02, p<.001), as observed in previous studies (Strauss et al., 2006), and significantly worse than the young at the Corsi blocks task (young: M=6.32, SD=1.35; old: M=4.76, SD=1.01; t_{48}=4.73, p<.001), indicating that the participants represented typical samples of the young and old populations. A stepwise regression analysis revealed that, of age group, gender, NART score and Corsi blocks task performance, only age group was retained in the model as a significant predictor of shortcut use during the main task *(table 4.4)*, so gender, NART score and Corsi blocks task performance were not considered in further analyses.

Shortcut use stepwise regression results

Predictor	β	SE	In	p
Age group	-.685	.049	1	<.001
Gender	.014	.049	0	.772
NART	.006	.004	0	.163
Corsi blocks	.008	.021	0	.694

Table 4.4 Shortcut use stepwise regression results. A stepwise regression analysis assessed how well age, gender, NART score and Corsi blocks task performance predicted use of shortcuts during the main task. Variables that were retained in the model as significant predictors are highlighted in blue.

Shortcutting task performance

Performance during training was assessed in terms of how long participants took to learn the routes, demonstrated by their ability to traverse each route without directions or errors. The third training cycle was the first to include training trials with no direction arrows, so, by this definition, routes could not be learned in fewer than three training cycles. *Figure 4.7* summarises young (orange) and old (green) participants' route learning performance in terms of how many training cycles it took them to learn each of the four routes. The young group generally learned the routes in the lowest possible number of training cycles, while the older group took slightly longer, particularly for the more complex routes 3 and 4. A mixed model ANOVA therefore revealed a significant main effect of age group on route learning ($F_{1,48}$=28.33, p<.001), although no effect of route ($F_{3,144}$=2.30, p=.080) and no significant interaction ($F_{3,144}$=.82, p=.485). Post-hoc t-tests confirmed that the effect of age was driven mainly by older participants taking significantly longer to learn the two routes in the more complex VE (route 3: t_{48}=3.22, p_{HB}=.009; route 4: t_{48}=2.88, p_{HB}=.018), although they did also tend to take longer to learn the routes in the simpler VE (route 1: t_{48}=2.03, p_{HB}=.097; route 2: t_{48}=1.88, p_{HB}=.067). However, while the older group took slightly longer than the young to learn the routes, most learned the routes reasonably quickly, and all participants successfully learned all routes during the training period. On the other hand, while most participants – 22

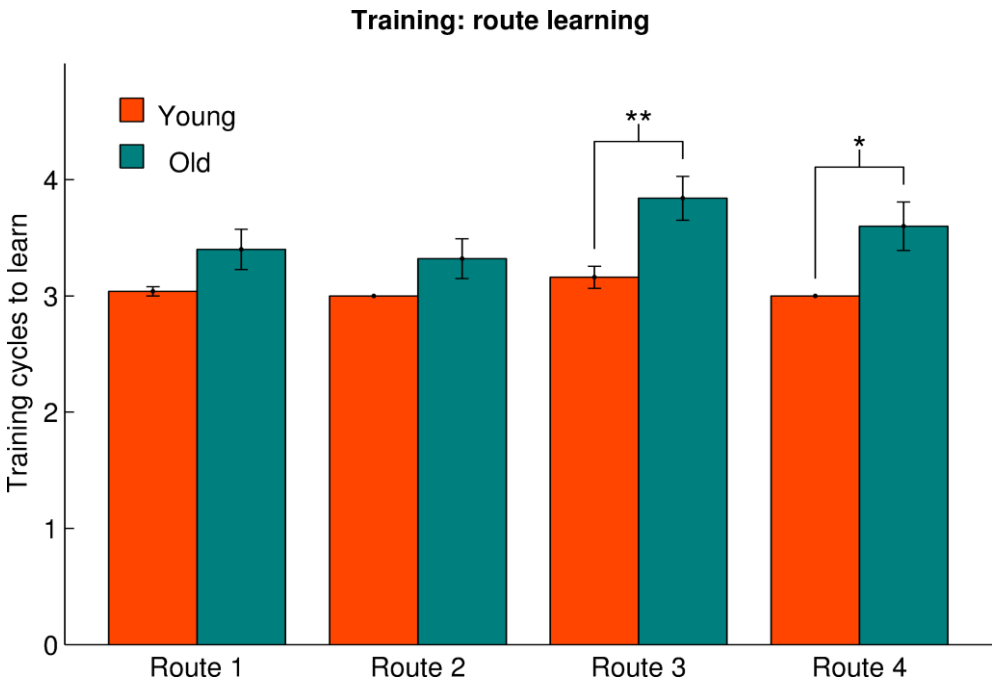

Figure 4.7 Shortcutting task route learning performance. Speed of route learning during training by route for young (orange) and old (green) participants, in terms of mean number of training cycles until the route could be followed without directions or errors. The minimum possible number of training cycles in which this criterion could be reached was three. Error bars represent SEM. * and ** represent statistically significant age differences at $p_{HB}<.05$ and $p_{HB}<.01$.

young and 18 old – managed to respond correctly to a full set of probe trials for at least one of the VEs, many – nine young and 23 old – did not do so for both VEs, and consequently performed the maximum number of training cycles.

Performance during testing was assessed in terms of the lengths of routes taken by participants, measured in number of junctions visited, as well as the proportion of trials on which participants used the newly available shortcuts. The top panel of *figure 4.8* shows the mean length of routes taken by young and old participants in each VE (adjusted for each trial according to the length of the shortest possible route). As illustrated, older participants took much longer routes in both VEs, which may indicate that they tended to use the available shortcuts less frequently. The bottom panel of the same figure addresses this directly, depicting the mean proportion of trials on which young and older participants used the shortcuts. As shown, while the young group used the available shortcuts on the majority of test

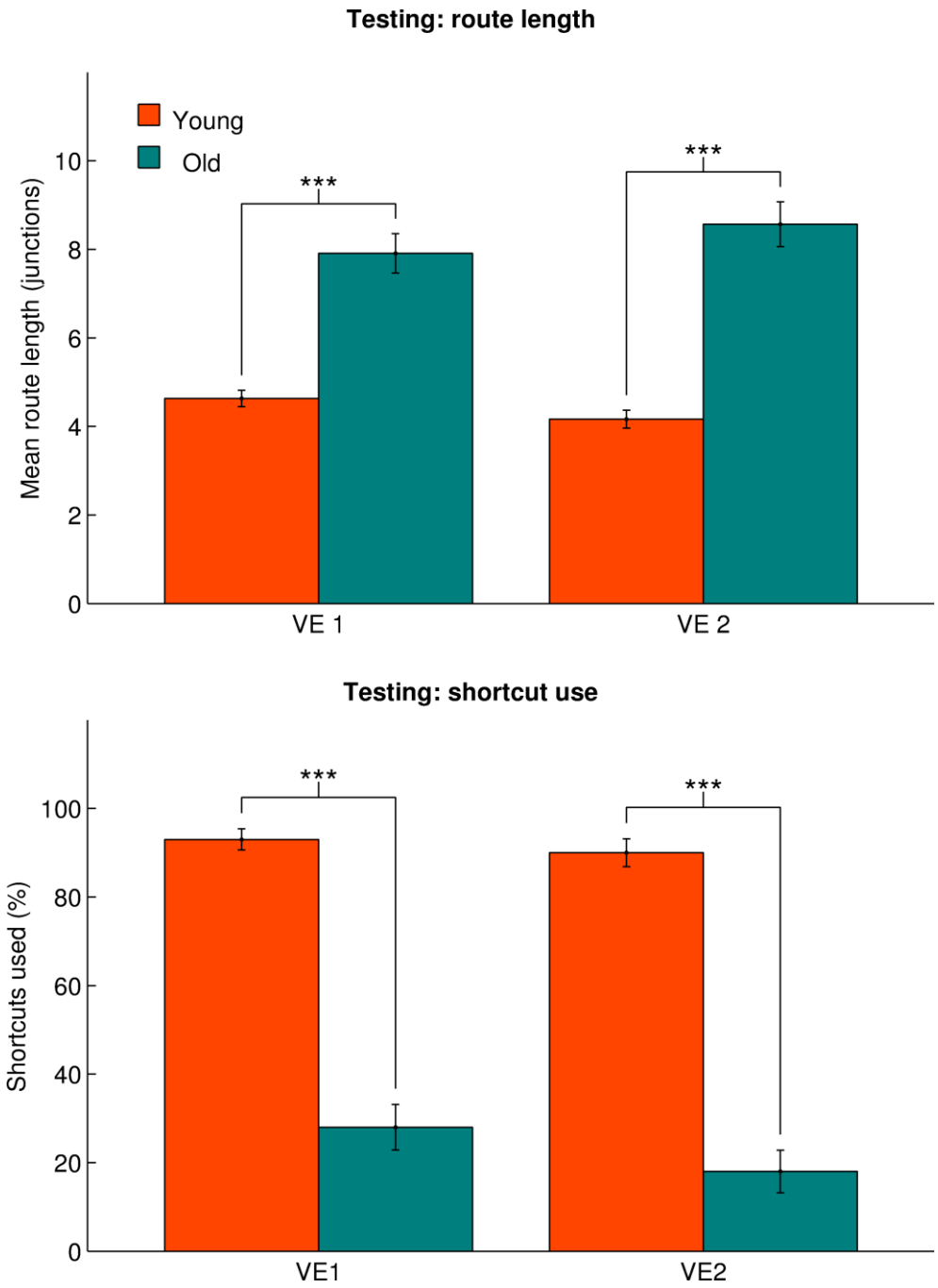

Figure 4.8 Shortcutting task testing performance. *Top:* Length of routes (in number of junctions; adjusted for VE differences) taken during testing by VE for young (orange) and old (green) participants. *Bottom:* Percentage of test trials on which the available shortcut was used by VE and age group. Error bars represent SEM. *** represents statistically significant age differences at p_{HB}<.001.

trials, the older group used the shortcuts on only a small proportion of trials.

A mixed model ANOVA with age and VE as factors demonstrated a significant main effect of age on test trial route length ($F_{1,48}$=104.94, p<.001), but no effect of VE ($F_{1,48}$=.07, p=.789) and no significant interaction ($F_{1,48}$=2.51, p=.120). Post-hoc t-tests confirmed that older participants took significantly longer routes in both VE1 (t_{48}=6.80, p_{HB}<.001) and VE2 (t_{48}=8.06, p_{HB}<.001). A second ANOVA showed an even stronger effect of age on shortcut use ($F_{1,48}$=199.54, p<.001), as well as a small effect of VE ($F_{1,48}$=4.62, p=.037), but no significant interaction ($F_{1,48}$=1.34, p=.253). Again, post-hoc testing confirmed that the age effect was driven by older participants using the available shortcuts much less often in both VE1 (t_{48}=11.41, p_{HB}<.001) and VE2 (t_{48}=12.56, p_{HB}<.001). The difference between VEs was not significant for each age group individually (young: t_{24}=1.30, p_{HB}=.207; old: t_{24}=1.79, p_{HB}=.173).

On probe trials, participants had to point to unseen landmarks, hence successful completion indicated that they had formed a survey representation of that particular VE. This means that, as some participants were unable to complete a full set of probe trials successfully, the deficit in shortcut use among older participants might have been caused by an inability to learn the layout of the environments. To address this problem, I performed an additional analysis in which I compared shortcut use between younger and older participants only for those VEs for which participants correctly responded to a full set of probe trials during training. There was still a large age difference in use of shortcuts across both VEs (t_{38}=14.33, p<.001).

I applied the Bayesian learning analysis described in Chapter Two (section 2.5.3) to the data on shortcut use, in order to assess whether each participant stably switched from an egocentric route-following strategy to an allocentric wayfinding strategy during testing. Based on the results, I was able to divide all participants into four categories: those that switched immediately and used the shortcuts for all test trials; those that switched at some point during testing and used the shortcuts for the majority of subsequent trials; those that used the shortcuts on some trials, but either not enough or not consistently enough to suggest that they had stably switched to a wayfinding strategy; and those that never used the shortcuts. *Figure 4.9* represents each age group in terms of the proportion of participants that were assigned to each

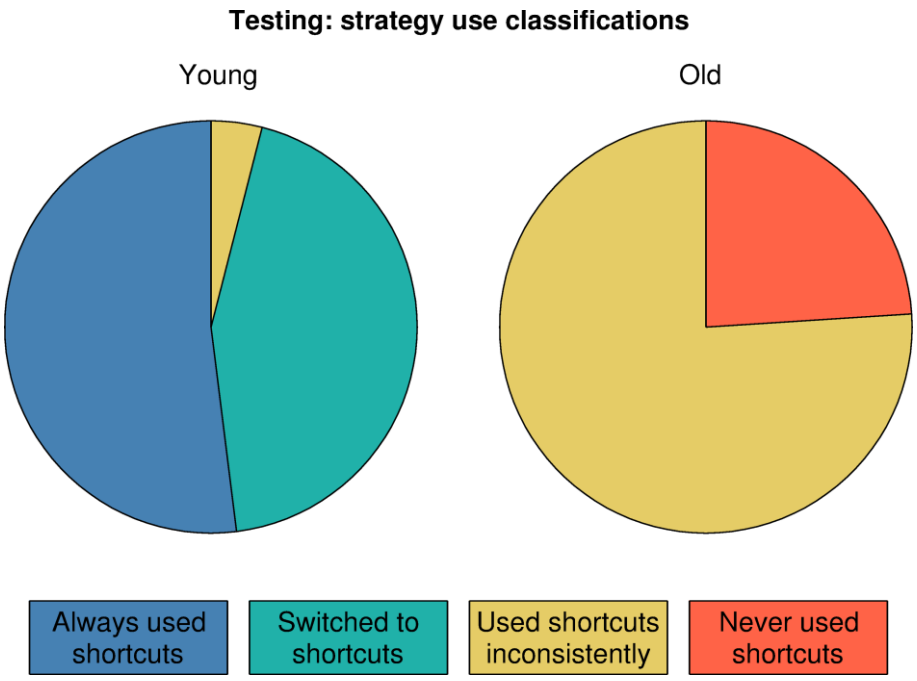

Figure 4.9 Shortcutting task strategy use classifications. *Always used shortcuts:* Participants that used the available shortcuts from the first test trial and throughout testing (blue). *Switched to shortcuts:* Participants that followed the long training routes at the beginning of testing, but stably switched to a shortcutting strategy at some point during testing (green). *Used shortcuts inconsistently:* Those that occasionally used the available shortcuts, but not consistently enough to be classified as having stably switched to a shortcutting strategy (yellow). *Never used shortcuts:* Those that employed a route following strategy throughout testing and never used the shortcuts (orange).

of these categories. As depicted, the vast majority of young participants stably switched to the allocentric strategy, either immediately or at some point during testing, with only one participant using the shortcuts inconsistently. On the other hand, not one of the older participants stably switched to the allocentric strategy, although most did use the available shortcut on at least one test trial.

Finally, I explored the effects of the novel testing routes, which involved crossing from the start point of one training route to the end point of another. As these new test routes were not repetitively trained, I expected that they would make it easier for participants to switch from using a route-following strategy, and to start using the available shortcuts. I investigated this by assessing the trial type upon which each participant first used a shortcut. Participants who never used the shortcuts could not

be included in this analysis. Of those that did use a shortcut during testing, 17 of 25 young and six of 19 old participants first did so on a crossing route test trial (χ^2_1=21.18, p<.001), suggesting only the young were thus prompted to start using shortcuts. I also assessed the effect of crossing routes on the length of routes taken during testing (excluding trials on which the shortcut was taken), but found no effect of route type ($F_{1,48}$=2.52, p=.119).

VPM and CMT performance

The results of the VPM also suggest that the older group was less able to switch between egocentric and allocentric strategies. The top panel of *figure 4.10* represents mean performance of young and older participants, in terms of trials correct, for each of the four more specific change types. Older participants performed at least slightly worse throughout all block types, but particularly during switch-to-place and, most of all, switch-to-response blocks. A mixed ANOVA therefore showed main effects of age ($F_{1,38}$=10.11, p=.003) and change type ($F_{1,38}$=7.78, p=.008) on trials correct, as well as a significant age by change type interaction ($F_{1,38}$=6.72, p=.014), which seemed to be due to impaired performance among the older group during blocks following a switch (t_{38}=3.47, p_{HB}=.003). More specifically, this difference was significant for switch-to-response blocks (t_{37}=3.20, p_{HB}=.011), although, after correcting for multiple comparisons, not for switch-to-place (t_{34}=2.01, p_{HB}=.156), nor for reverse-place (t_{36}=1.48, p_{HB}=.297) or reverse-response (t_{29}=.83, p_{HB}=.412) blocks. Post-hoc testing also revealed no significant performance differences between change types, including between switch-to-place and switch-to-response blocks (t_{34}=.21, p_{HB}=.840).

However, as shown in the bottom panel of *figure 4.10*, older participants also performed worse at the CMT, suggesting that an allocentric processing deficit may have contributed to the age difference in use of shortcuts. A t-test confirmed that this difference in CMT performance was significant (t_{48}=7.30, p<.001). To assess the effects of strategy switching and cognitive mapping on shortcut use, I performed a GLM analysis, modelling use of shortcuts in terms of age group, VPM switching

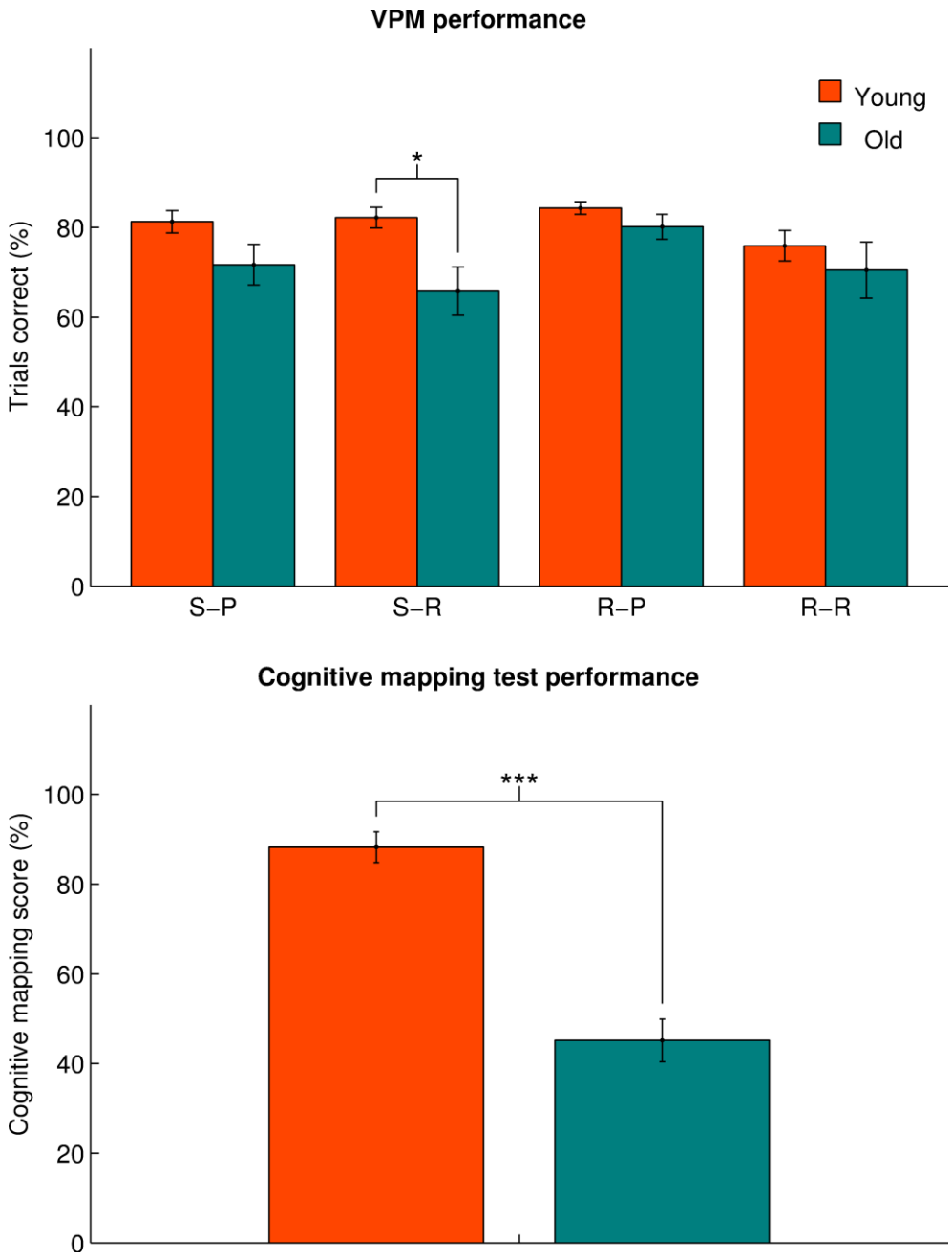

Figure 4.10 VPM and cognitive mapping test performance. *Top:* VPM performance, in terms of percentage of trials correct by change type for young (orange) and old (green) participants. *Bottom:* CMT performance by age group in terms of (corrected) percentage of landmarks correctly labelled. Error bars represent SEM. * and *** represent statistically significant age differences at p_{HB}<.05 and p_{HB}<.001.

performance and cognitive mapping score. While both age group (β=-.548, t_{36}=-6.43, p<.001) and strategy switching (β=.445, t_{36}=2.38, p=.023) showed significant independent effects on use of shortcuts, there was no significant contribution of

cognitive mapping (β=.001, t_{36}=.92, p=.365). These results are consistent with the finding that shortcut use was deficient in older participants even where successful probe trial performance indicated that they *had* formed an allocentric representation of the VE. Although these combined findings do not rule out the possibility that allocentric impairments may have affected use of shortcuts, they do suggest that it was primarily a strategy switching deficit that led to impaired performance at the shortcutting task in the older group.

4.3.4 Discussion

Summary of findings

Participants performed normally on measures of crystallised intelligence and spatial working memory, and these did not predict performance at the shortcutting task. During training, older participants learned the routes to goal locations almost as quickly as the young, demonstrating a significant difference only for the more complex routes. However, during testing, the older group took longer routes to goal locations, primarily because they used the available shortcuts much less often than the young group. Furthermore, while the vast majority of young participants stably switched from using a route-following strategy to a wayfinding strategy either on the first test trial or at some point during testing, the older participants used the shortcuts either sporadically or not at all, so that not one could be said to have stably switched to the wayfinding strategy. Crossing routes may have prompted young participants to use the shortcuts, but not old. A GLM analysis confirmed that older participants' much lower use of the shortcuts was predicted by both age and switching performance, as measured by the VPM, but not allocentric processing ability, as measured by the CMT.

Interpretation of findings

The main finding of this study, that older people were less able to switch from following a learned route to finding a novel shortcut, is consistent with my primary

hypothesis and the results of the previous study, which also demonstrated a specific deficit in switching from an egocentric to an allocentric navigational strategy. This study therefore corroborates this earlier finding, but also, due to the more realistic nature of the shortcutting task, provides support for the assumption that a strategy switching deficit observed in the relatively abstract VPM does translate to a real-world navigational impairment. As discussed in section 4.2, strategy switching is thought to be coordinated by PFC and the LC-NA system (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005; Caetano et al., 2013). This means that the navigational strategy switching deficit observed in this study and the last can be explained in terms of age-related dysfunction of PFC (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011), perhaps causing an underlying deficit in the ability to decide which strategy to use, and/or the LC-NA system (Manaye et al., 1995; Grudzien et al., 2007), affecting the ability to initiate a switch and to engage the correct strategy. More specifically, if the deficit does only affect switching from an egocentric to an allocentric strategy, it may relate to reduced functional connectivity between PFC and the hippocampus. Unfortunately, the design of the shortcutting task did not facilitate assessing switching in the opposite direction, which meant that it was unable to confirm the specificity of the switching deficit.

The VPM, on the other hand, did assess switching in the opposite direction, but contrary to my expectations and to the results of the previous VPM study, switching to the response strategy was impaired. In fact, the apparent age difference in switching to the place strategy did not remain significant after correcting for multiple comparisons – although there was no significant difference between these two change types. These results are more concordant with a general strategy switching deficit, which would not relate to reduced prefrontal-hippocampal connectivity, as suggested in the previous section, but instead to dysfunction within the LC-NA system or PFC, as above. As discussed earlier, the previous findings may have been due to a discrepancy between the two strategies in terms of difficulty (Floresco et al., 2008), which I may have alleviated in this study by ensuring that all participants started on the more difficult place strategy. As the GLM also demonstrated an age-independent relationship between switching performance and use of shortcuts, it may

be more reasonable to infer that the observed impairment in shortcutting reflects a general strategy switching deficit, rather than a specific deficit in engaging an allocentric strategy. The main finding of this study may therefore relate more directly to previous work on age-related switching deficits in other cognitive domains (Ashendorf & McCaffrey, 2008; Gamboz et al., 2009).

In addition to deficits in switching between strategies, the large age difference in performance on the CMT is indicative of allocentric processing deficits among the older participants. Similar map sketching tests have been criticised as measures of cognitive mapping, because survey maps can theoretically be generated from a quantitatively scaled route representation (Montello et al., 2004). However, the results are consistent with previous work demonstrating allocentric processing deficits in older people (Moffat & Resnick, 2002; Antonova et al., 2009; Iaria et al., 2009). Furthermore, many more older participants than young failed to respond correctly to a full set of probe trials for both VEs, also indicating an impairment in formation or use of a cognitive map. It seems likely that an allocentric processing impairment would have contributed to the age difference in use of shortcuts, as older people may have been less able to use a wayfinding strategy. However, while only two older participants responded correctly to a full set of probe trials for both VEs, most of them managed to do so for at least one, suggesting that they *were* able to form and use allocentric representations of the environments. Moreover, when only assessing shortcut use within VEs for which each participant *did* pass a set of probe trials, I still found a large age difference, suggesting that older participants failed to switch to a wayfinding strategy even when they had formed an allocentric representation of the environment. Similarly, while none of the older participants stably switched to the wayfinding strategy, the majority did use a shortcut at least once, confirming that they were able to do so. Furthermore, navigating overlapping routes has been shown to depend more heavily upon the hippocampus (Brown et al., 2010), yet older participants did not seem to find the crossing routes more difficult. Finally, while the GLM demonstrated an age-independent effect of strategy switching, it did not show a specific effect of cognitive mapping on use of shortcuts. This does not prove that allocentric processing deficits did not affect use of shortcuts,

and in fact it is likely that they did. However, taken together, the results indicate that the large age difference we observed in use of shortcuts does reflect a strategy switching deficit.

Limitations

A limitation of the shortcutting task, as mentioned above, was that it did not assess switching from an allocentric strategy to an egocentric strategy. A related problem was that the VPM did, but the results did not match those of the previous VPM study. As discussed, it may be that the previous results were due to a difference in difficulty between the two studies, which was to some extent alleviated in this study by keeping the starting strategy fixed on the place strategy. However, another problem with this study was that there was less VPM data, partly because not all participants completed the VPM, but also because it was shorter, incorporating fewer switches and reversals. It may still be the case that the results of the previous study were more accurate, and that older people are specifically impaired at switching to an allocentric strategy. This could be determined by directly assessing the neural processes underlying navigational strategy switching, but, as with the last study, this study was also limited in that it only assessed behavioural data.

Conclusion

The results of this study reflect a large effect of age on the ability to switch from following a known route to using a novel shortcut in order to take the optimal route to a goal location. This confirms that the age-related deficit in navigational strategy switching identified using the VPM in the previous study does affect performance on a more realistic navigational task, and provides an illustration of how real-world navigation might be affected by this deficit. Older participants also showed evidence of allocentric processing difficulties, which are likely to contribute as well, but their perseverance with the route-following strategy was more closely related to strategy switching performance. A general strategy switching impairment may result from degradation of PFC or dysfunction of the LC-NA system, causing underlying deficits

in decision making, or in initiating a switch or engaging a behavioural strategy. However, it is still possible that older participants are impaired specifically at switching to an allocentric strategy due to reduced prefrontal-hippocampal functional connectivity. Exactly how age-related changes in functionality or connectivity of the PFC-LC switching network lead to navigational strategy switching deficits remains to be explored. Overall, the results of this study confirm that strategy switching deficits affect navigation in a more realistic context than the VPM, and show how a relatively subtle age-related impairment in a single executive process can contribute to much more substantial effects on navigational performance and on the everyday lives of older people.

4.4 Chapter conclusion

The two studies presented in this chapter assessed navigational strategy switching deficits in older people. The first to do so was Study 3, which measured navigational strategy switching using the VPM, involving switching between an allocentric place strategy and an egocentric response strategy. Older participants were specifically impaired at switching to the allocentric place strategy. Performance was unaffected in place blocks following a reversal, suggesting that the age difference in switch-to-place performance could not be explained by an allocentric processing deficit, caused by hippocampal degeneration. Similarly, switching to a response strategy was unimpaired, indicating that a general strategy switching deficit, due to prefrontal or noradrenergic dysfunction, could not account for the finding either. Instead, the specific deficit may be attributable to reduced functional connectivity between PFC and hippocampus. Alternatively, a discrepancy between the two strategies in terms of difficulty may have distorted the effects of a general strategy switching deficit.

One limitation of this study stemmed from the relatively simple and abstract nature of the VPM as a navigational task. In Study 4, I investigated navigational strategy switching using a more realistic shortcutting task, involving switching from an egocentric route-following strategy to an allocentric wayfinding strategy. Throughout

testing, older participants took longer routes and used shortcuts much less frequently, as they were unable to switch to the wayfinding strategy. This difference remained even when participants that failed to form an allocentric representation of both VEs were excluded. Furthermore, shortcut use was not related to performance on a test of cognitive mapping, and most older participants did use the shortcuts at least once. These findings all suggesting that the large age difference in switching to the wayfinding strategy was not attributable to impairments in allocentric processing. On the other hand, performance following switches on a short version of the VPM did predict shortcut use, confirming that the effect did relate to deficient navigational strategy switching. However, the results of the VPM did not match those of the previous study, as switch-to-response performance was impaired, suggesting that older people are generally impaired at switching between navigational strategies, rather than only in one direction.

In conclusion, the results of both studies demonstrated that older people are impaired at navigational strategy switching, and Study 4 in particularly illustrated how this can have a substantial effect on real-world navigational performance. The exact nature of the impairment is unclear, as the results of Study 3 demonstrate a specific deficit in switching to an allocentric strategy, the VPM results from Study 4 suggest a more general deficit in switching either way, and the results of the shortcutting task, which did not assess switching to an egocentric strategy, could be concordant with either. The underlying neural mechanisms also remain to be explored.

Chapter Five
Further Behavioural Studies of Navigational Strategy Switching in Ageing

5.1 Chapter overview

In Chapter Four, I presented data from two behavioural studies in virtual reality (VR) demonstrating that older people are impaired at navigational strategy switching. Study 3 first used the virtual plus maze (VPM) to investigate the ability of older people to switch between an allocentric place strategy and an egocentric response strategy. I found a specific deficit in switching in one direction only – from the response strategy to the place strategy. Study 4 used a more realistic task, set in a town-like virtual environment (VE), to demonstrate that older people are similarly impaired at switching from an egocentric route-following strategy to an allocentric wayfinding strategy. The remaining studies I have to present aimed to explore the mechanisms underlying age-related decline in the ability to switch to an allocentric strategy, although the first two, reported in this chapter, used behavioural methods to do so.

In Study 5, presented in section 5.2, I assessed the relationship between decision making deficits, caused by prefrontal dysfunction, and impairments in navigational strategy switching in ageing. I used two altered versions of the VPM, one of which eliminated the decision making aspect of the task by informing participants of which strategy they had to switch to. I expected the results of the standard version to replicate those of Study 3 by demonstrating a specific deficit among older participants in switching to the place strategy. The purpose of the no-DM version of the task was to identify whether this deficit persisted even when decision making was not required. I also tested decision making abilities using a navigational adaptation of the Iowa Gambling Task (IGT), in order to directly measure age-related impairments in decision making, and to assess whether these impairments related to the specific deficit in switching to a place strategy. This study was intended to explore the

relationship between ageing-related deficits in decision making and switching to an allocentric strategy, in order to provide insight into the role of prefrontal dysfunction in navigational strategy switching impairments in ageing.

In section 5.3, I cover Study 6, in which I briefly investigated whether decline in navigational strategy switching is caused by lack of practice. I used a sample of participants involved in orienteering, a physically and cognitively challenging sport dependent on navigational strategy switching. Orienteers and control participants were tested on the VPM in order to assess whether orienteering practice protects against ageing-related decline in navigational strategy switching abilities. They were also tested on Raven's Standard Progressive Matrices (RSPM), a test of general fluid intelligence, in order to assess whether any such effects were specific to navigational strategy switching, or more general. I hoped that this study would provide a preliminary indication that navigational strategy switching impairments could be amenable to a practice-based intervention.

Again, a number of undergraduate students assisted with data collection for both studies, and Rachel Armitage in particular, through her involvement in orienteering, also provided access to orienteering participants. However, I was responsible for designing and actively involved in conducting both studies, and solely responsible for performing the data analyses reported in this chapter, which is also entirely my own work.

5.2 Study 5: Impaired decision making and navigational strategy switching

5.2.1 Introduction

Decision making in ageing

While neurodegeneration is evident throughout the brain in ageing, the frontal ageing

hypothesis (Dempster, 1992; West, 1996) suggests that the majority of cognitive impairments evident in early ageing reflect degeneration or dysfunction of prefrontal cortex (PFC). This is mainly because PFC supports executive processing (Robbins, et al., 1996; Funahashi, 2001; Rodríguez-Aranda & Sundet, 2006), responsible for the management of other cognitive and behavioural processes. Decision making in particular is impaired in ageing (Denburg et al., 2005; Fein et al., 2007; Brown & Ridderinkhof, 2009; Eppinger et al., 2011), which can have a serious impact on the lives of older people, for example, by affecting important choices about financial arrangements and medical treatment (Moye & Marson, 2007). Decision making deficits have been associated with neurodegeneration and neuromodulatory dysfunction within medial and dorsolateral PFC (Bechara et al., 1994; Manes et al., 2002; Denburg et al., 2007; MacPherson et al., 2009), orbitofrontal cortex (OFC; Marschner et al., 2005; Denburg et al., 2007; Doya, 2008) and anterior cingulate cortex (ACC; Botvinick, 2007; Doya, 2008; Grabenhorst & Rolls, 2011). They have therefore been explained in terms of an increase in noise in these regions and a consequent decrease in signal-to-noise ratio (Milosavljevic et al., 2010), affecting the speed (Walker et al., 1997), accuracy (Denburg et al., 2005; Fein et al., 2007) and adaptability (Worthy & Maddox, 2012) of decision making.

Decision making and navigational strategy switching

Decision making plays a role in many processes that are fundamental to behaviour, but some have suggested that age-related decision making deficits may be particularly relevant to behavioural flexibility (Marschner et al., 2005; Eppinger et al., 2011). As discussed previously, flexibly switching between behavioural strategies is thought to be coordinated by noradrenaline and many of the prefrontal regions also associated with decision making (Aston-Jones & Cohen, 2005). Navigational strategy switching certainly does involve decision making, primarily in terms of selecting the appropriate strategy. For example, on the VPM, in response to a change in reward, participants have to decide whether to use a place or response strategy, and specifically which place or response strategy to use. Decision making impairments – and underlying prefrontal dysfunction – may therefore be able to

explain the navigational strategy switching deficits presented in the previous chapter.

Cued switching

Switching strategy involves a sequence of several sub-processes. Referring to the VPM by way of example, participants first have to detect a change in reward, disengage the old strategy, select a new strategy and then engage that new strategy. It is the engaging and disengaging of strategies that is thought to be mediated by the locus coeruleus-noradrenergic (LC-NA) system (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005), while OFC and ACC are responsible for detecting changes in reward (Rolls, 2000; Botvinick et al., 2004; Kennerley et al., 2011). Selection of the appropriate strategy is the part of the process that relates to decision making, mediated by other regions of PFC (Bechara et al., 1994; Kim & Shadlen, 1999; Manes et al., 2002; Denburg et al., 2007), and it is this aspect of strategy switching that the present study was concerned with. In order to be able to study navigational strategy switching both with and without this component of the process, as described in more detail below, I also had to remove the reward monitoring aspect of the task, by providing a cue to prompt strategy changes. However, the altered task still related well to the original VPM, as it was just as dependent upon the other sub-processes and associated brain regions. Also, cued switching has been studied previously in other contexts (Monsell, 2003; Kiesel et al., 2010), and, while some research suggests the switch costs associated with explicitly cued switching are lower (Van Loy et al., 2010), age-related switching deficits are still evident (Kray et al., 2002; Arrington et al., 2007; Eppinger et al., 2007). In fact, following a meta-analysis of data on age differences in task switching from 36 participant groups, Wasylyshyn, Verhaeghen and Sliwinski (2011) concluded that cueing does not affect age differences in switching.

Current study

In this study, I assessed the role of decision making in navigational strategy switching using a decision making task and two variations of the VPM. One variant,

the standard VPM, was similar to the versions used in the previous chapter, with some differences, as described below. The other was specifically designed to remove the decision making component of the task, by including instructions at each switch or reversal about which strategy to use throughout the following block of trials. The decision making task, a navigational gambling task (NGT), was heavily based on an established measure of decision making, the IGT (Bechara et al., 1994). I expected to replicate the finding of Study 3 by demonstrating a specific deficit among older participants in switching to the place strategy during the standard VPM. Further, I hypothesised that this deficit would relate to a deficit in decision making, as measured by the NGT. On the other hand, I anticipated that switching to the place strategy would not be impaired during the no-DM version of the VPM.

5.2.2 Methods

Participants

Twenty-seven (15 female) young participants (aged 20-25, M=21.9) and 23 (12 female) old participants (aged 65-85, M=71.4) were recruited from the university's student population, the local community and the existing PPLS database of research volunteers. Each was paid £7 for their participation, lasting approximately 1h. Many had previous experience of participating in research, none were known to suffer from any cognitive or neurological disorders, and all had normal or corrected-to-normal vision.

Procedure

All participants were fully informed about the study and provided written consent before participating. They then began by completing the Mini Mental State Examination (MMSE) to screen for mild cognitive impairment (MCI), but none were excluded on this basis. Following this, participants completed three tasks – the standard VPM, a no-DM version of the VPM, and the NGT, each described below. These tasks were run in Vizard on a standard desktop computer with a 24in

widescreen monitor and a standard UK keyboard. Each participant completed the three tasks in a pseudorandomised order, balanced within each age group. The study was approved by the university's psychology research ethics committee and conformed to the ethical guidelines of the BPS.

Virtual plus mazes

Participants completed two variations of the VPM, a standard version and a no-DM version. These were the latest incarnations of the VPM that I used, and even the standard version differed substantially from the original. Firstly, as in the version used in Study 4, the plus-shaped pathway was not surrounded by transparent walls, and there were no reward wells at the end of goal arms. Secondly, in contrast to the original plus maze, adjacent rather than opposite start arms were used, and participants were allowed to continue straight ahead at the central junction. This meant that it was possible to avoid rewarding the previous strategy following a strategy switch (as shown in *figure 2.5*). Thirdly, in contrast to all other variations of the VPM, the adjacent pair of start arms used throughout each trial block varied from block to block (with one of the two retained across consecutive blocks). This study was also the only one to use trial blocks of the same size throughout the VPM, with both variations used comprising nine blocks of 15 trials. Both versions allowed a maximum decision time of 2s on each trial.

The no-DM version differed even more by excluding the decision making component of the task. At the beginning of each trial block, participants were presented with an on-screen message instructing them to use a particular strategy throughout the next trial block, for example “Turn left”. With the addition of landmarks at the end of each arm of the maze (also included in the standard version of the task), I was able to provide simple instructions for the place strategy, for example “Go towards the car park”. These instructions eliminated the need for a decision making process to select the appropriate strategy to use, but also reduced the emphasis on reward monitoring, as participants were no longer required to notice when the current strategy was no longer being rewarded. In order to equate the two variations of the task in terms of

reward monitoring requirements, I also included instructions at the beginning of each block during the standard VPM, which simply read “New strategy”. Although strategy switches and reversals were prompted, in both versions of the task, the changes still had to be executed (in terms of disengaging the previous strategy and engaging the new strategy), and in the standard version of the task the appropriate strategy still had to be selected by a decision making process. Furthermore, it was the removal of the reward-monitoring aspect of the task that allowed me to vary start arm pairs across trial blocks, and to use a consistently low number of trials per block.

Navigational gambling task

This task was based on an established measure of decision making, the IGT, which involves choosing cards from one of four decks, each associated with a constant reward in combination with a variable penalty. Higher decision making ability is reflected by gravitation across numerous trials towards 'good decks' – those associated with a lower constant reward, but also lower penalties, and thus overall higher average net profit. In the NGT, the four reward/penalty options were associated with landmarks at locations along an arc, set in a VE comprising a ground plane and the same mountain scenery as in the VPMs (*figure 5.1*). On each of a total of 100 trials, participants had to navigate to their chosen location by using the left and right arrow keys on the keyboard to align their view with the respective landmark, before pressing the up arrow key to proceed towards it. The virtual monetary rewards and penalties, which differed slightly from those used in the IGT (*table 5.1*), as well as the participant's current balance (initially $3000), were displayed on-screen upon arrival at the chosen landmark. The locations of landmarks and of reward/penalty options were separately pseudorandomised for each participant, in order to counterbalance any potential location or landmark biases.

Data analysis

I assessed VPM performance in terms of the percentage of trials correct and the percentage of stable trials for switch-to-place (S-P), switch-to-response (S-R),

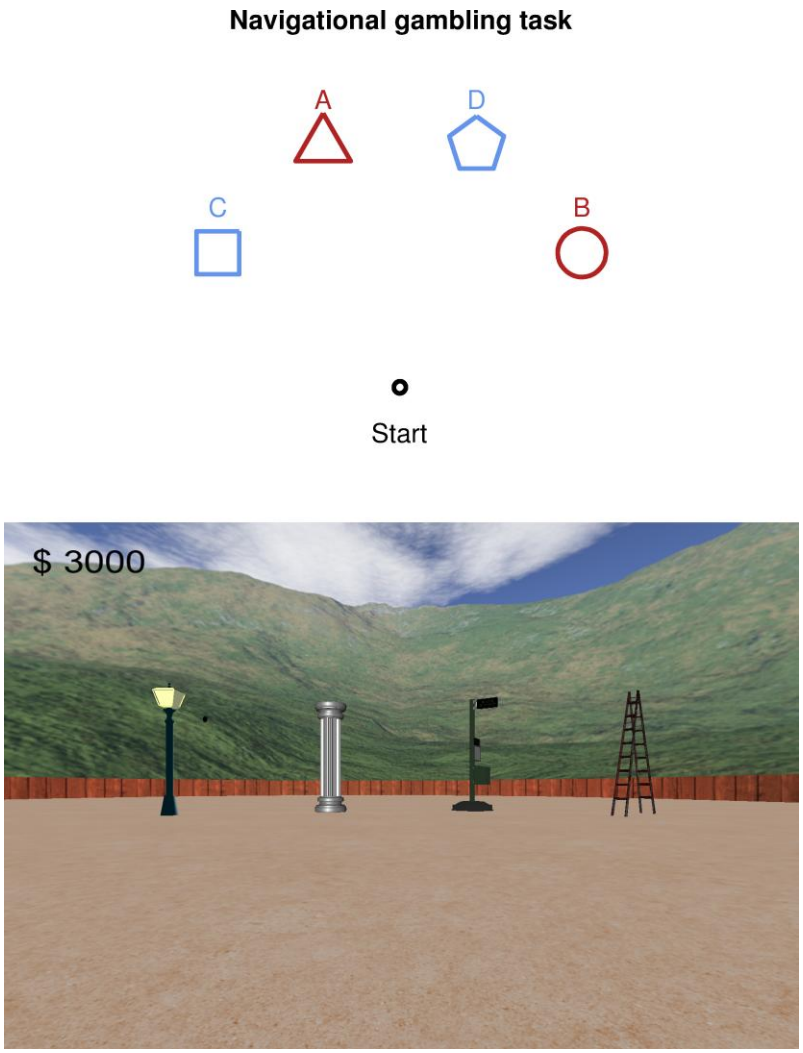

Figure 5.1 Navigational gambling task. *Top:* Diagram of the NGT VE showing the four landmarks and positions, each associated with one of the four reward/penalty options. The positions of landmarks and reward/penalty options were randomised separately for each participant. *Bottom:* Screen image captured during a development version of the NGT. In the experimental version of the task was that the landmark positions were spread across a wider arc, as shown in the diagram.

reverse-place (R-P) and reverse-response (R-R) change types. I used the Bayesian learning analysis described in Chapter Two (section 2.5.3) to estimate the point during each block of trials at which the correct strategy was stably acquired, and all following trials were counted as stable trials. NGT performance was assessed in terms of percentage of choices for options A to D separately, and in terms of the percentage of good choices (options C and D combined). Outliers were defined as more than 2.5 standard deviations from the group mean in terms of standard VPM

NGT rewards and penalties

Option	A	B	C	D
Reward	$100	$100	$50	$50
Penalties	$0	$0	$50	$0
	$200	$0	$0	$0
	$250	$625	$50	$0
	$0	$0	$50	$125
	$0	$0	$0	$0
	$300	$0	$0	$0
	$0	$0	$0	$0
	$350	$0	$50	$0
	$0	$625	$50	$0
	$150	$0	$0	$125
Mean net value	-$25	-$25	$25	$25

Table 5.1 NGT rewards and penalties. Each option was associated with a set reward, which remained constant across trials. Penalties were presented in pseudorandom patterns throughout blocks of 10 trials – examples are included in the table. The mean net value of each option (which remained constant for any given block of 10 trials) is also shown, illustrating that, overall, options A and B were bad choices, while options C and D were good choices.

total trials correct or NGT total good choices. Accordingly, two young female, one older male and two older female participants were excluded from further analyses. Data from each task were then analysed using mixed ANOVAs and paired and independent t-tests, after which the relationship between the three tasks was assessed by calculating Pearson's correlation coefficient and using a generalised linear model (GLM). Following multiple comparisons, p values were adjusted according to the Holm-Bonferroni method (subsequently denoted p_{HB}).

5.2.3 Results

VPMs

Performance on the two versions of the VPM produced three key findings. Firstly,

older participants performed worse than young following a switch to the place strategy on the standard VPM. *Figure 5.2* summarises young (brown) and older (purple) participants' performance in terms of trials correct for switch-to-place, switch-to-response, reverse-place and reverse-response trial blocks. The bottom two lines, which represent performance throughout the standard VPM, show a marked difference between age groups in S-P trials correct. The top two lines represent performance throughout the no-DM VPM, and illustrate the second key finding, that both groups performed better on this version of the task. Finally, as shown, the age difference in S-P trials correct was much lesser on the no-DM version of the VPM. Although not illustrated, these same three results were corroborated by stable trials performance data.

These findings were supported by a series of statistical analyses. For the standard VPM, a mixed ANOVA with age group (young, old) and change type (S-P, S-R, R-P, R-R) as factors, revealed significant main effects of age group ($F_{1,31}$=7.25, p=.011) and change type ($F_{3,93}$=4.09, p=.009), as well as a significant interactive effect ($F_{3,93}$=6.42, p=.001) on trials correct. Post-hoc tests confirmed that this effect was due to the older group achieving significantly fewer trials correct during S-P blocks (t_{41}=4.37, p_{HB}<.001), but not S-R (t_{41}=1.81, p_{HB}=.234), R-P (t_{36}=1.59, p_{HB}=.121) or R-R (t_{37}=1.61, p_{HB}=.232) blocks. I assessed stable trials in the same way, finding significant main effects of age group ($F_{1,31}$=7.99, p=.008) and change type ($F_{3,93}$=3.37, p=.022), and a significant interaction ($F_{3,93}$=5.30, p=.002), again due to significantly fewer stable trials among older participants during S-P blocks (t_{41}=4.10, p_{HB}<.001), but not S-R (t_{41}=1.83, p_{HB}=.225), R-P (t_{36}=1.30, p_{HB}=.203) or R-R (t_{37}=1.53, p_{HB}=.269) blocks.

While performance during the no-DM VPM was more similar for the two groups than during the standard VPM, analyses still revealed a significant effect of age group ($F_{1,38}$=6.77, p=.013) on trials correct. However, there was no significant effect of change type ($F_{3,114}$=2.62, p=.055), nor a significant interaction ($F_{3,114}$=1.10, p=.353). Although the age difference in S-P performance was reduced in comparison to the standard VPM, post-hoc tests indicated that older participants still performed

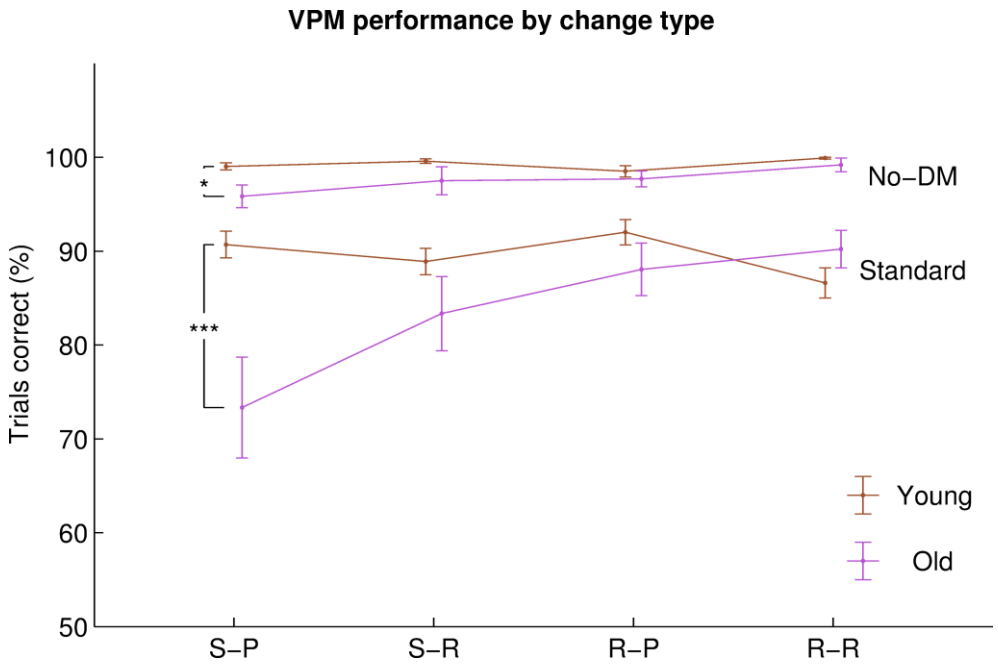

Figure 5.2 VPM performance by change type. Mean performance in terms of percentage of trials correct throughout S-P, S-R, R-P and R-R blocks of the standard (bottom) and no-DM (top) variations of the VPM for young (brown) and old (purple) participants. Error bars represent SEM. * and *** represent significant age differences at p<.05 and p<.001.

significantly worse during S-P blocks (t_{42}=2.90, p_{HB}=.024), but not S-R (t_{42}=1.64, p_{HB}=.328), R-P (t_{40}=.84, p_{HB}=.404) or R-R (t_{40}=1.15, p_{HB}=.518) blocks. In terms of stable trials, again I found a significant effect of age group ($F_{1,38}$=6.58, p=.014) but not of change type ($F_{3,114}$=1.22, p=.307), nor a significant interaction ($F_{3,114}$=1.05, p=.372). Here, post-hoc tests showed no significant differences, although older participants did tend towards significantly worse performance during S-P blocks (t_{42}=2.51, p_{HB}=.065; S-R: t_{42}=1.36, p_{HB}=.548; R-P: t_{40}=.55, p_{HB}=.584; R-R: t_{40}=1.15, p_{HB}=.518).

VPM difference

I calculated the difference in performance between the two VPMs as an index of the positive effect that removing the decision making component of the task had upon performance. The improvement in trials correct is shown for each change type by age group in *figure 5.3*. As depicted, improvement was similar for the two groups for

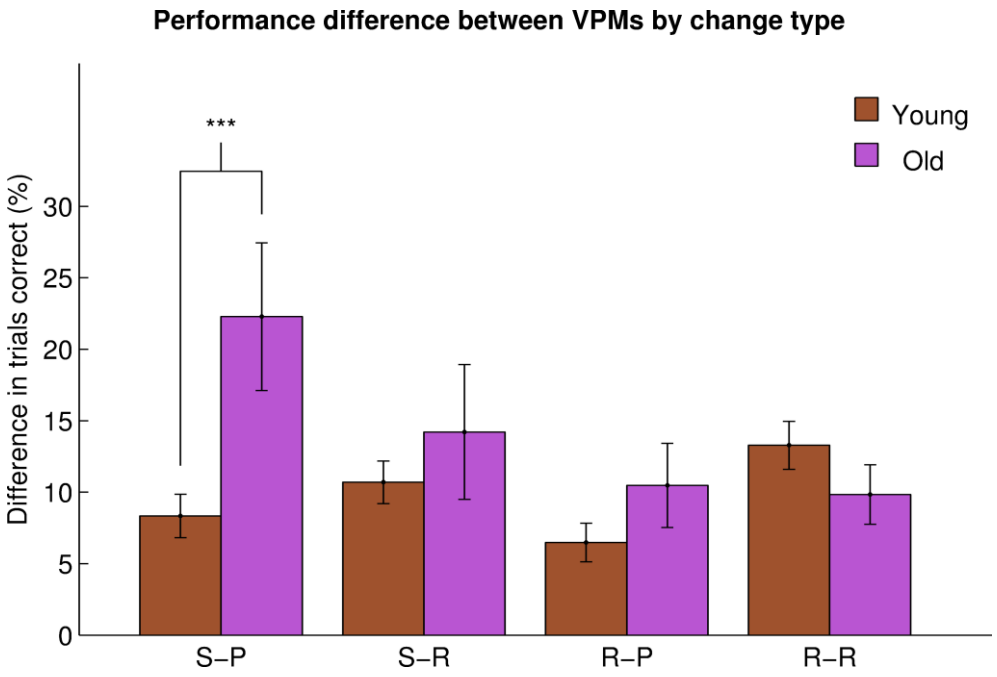

Figure 5.3 Performance difference between VPMs by change type. Mean difference between the standard and no-DM variants of the VPM in percentage of trials correct throughout blocks following each of the four change types for young (brown) and old (purple) participants. Error bars represent SEM. *** represents a significant age difference at p<.001.

switch-to-response, reverse-place and reverse-response blocks. Young participants also showed a similar improvement during switch-to-place blocks, but for this change type only, improvement in trials correct was much greater among older participants. This is consistent with the interpretation that removing the decision making aspect of the task specifically alleviated the age-related switch-to-place deficit. As before, improvement in stable trials showed the same pattern.

Again, I performed statistical analyses in order to confirm these findings. In terms of both trials correct (TC) and stable trials (ST), there was a significant effect of age group on improvement (TC: $F_{1,29}$=4.49, p=.043; ST: $F_{1,29}$=6.59, p=.016) and, although no significant effect of change type (TC: $F_{1,29}$=2.49, p=.066; ST: $F_{1,29}$=2.23, p=.090), also a significant interaction between the two (TC: $F_{1,29}$=3.77, p=.014; ST: $F_{1,29}$=3.75, p=.014). Post-hoc tests revealed significantly greater improvement within the older group during S-P blocks (TC: t_{41}=3.74, p_{HB}=.002; ST: t_{41}=3.93, p_{HB}=.001)

but not S-R (TC: t_{41}=1.02, p_{HB}=.313; ST: t_{41}=1.35, p_{HB}=.186), R-P (TC: t_{35}=1. 60, p_{HB}=.359; ST: t_{35}=1.44, p_{HB}=.477) or R-R (TC: t_{35}=1.48, p_{HB}=.296; ST: t_{35}=1.40, p_{HB}=.339) blocks. These results confirm that the switch-to-place deficit apparent in the standard VPM was specifically reduced by removal of the decision making aspect of the task during the no-DM version.

NGT

NGT performance was assessed in terms of how often participants chose to visit each of the four landmarks. Although to be clear, options A, B, C and D represent choices in terms of rewards and penalties, which were associated with different landmarks and different positions for each participant. As shown in *figure 5.4*, older participants chose to visit option A as often as young participants, options C and D less often, and option B more often. Options A and B were bad choices, associated with an average net loss, while options C and D were good choices, associated with an average net profit. Older participants therefore made good choices less often and bad choices more often, which is indicative of poorer decision making.

In support of these age differences in performance, mixed ANOVAs with age group and option (A, B, C, D) as factors revealed significant effects of age group ($F_{1,42}$=10.05, p=.003) and option ($F_{3,126}$=6.47, p<.001) on percentage of choices throughout the task, as well as a significant interaction ($F_{3,126}$=4.11, p=.008). Although post-hoc tests showed no significant age differences for any of the four options, older participants did tend towards choosing option D significantly less often than young participants (t_{42}=2.60, p_{HB}=.052; A: t_{42}=.91, p_{HB}=.367; B: t_{42}=2.05, p_{HB}=.139; C: t_{42}=1.98, p_{HB}=.108). However, I then combined options C and D to assess overall proportion of good choices, and demonstrated that older participants (M=43.25%, SD=11.36%) made significantly fewer good choices than young participants (M=56.58%, SD=11.71%; t_{42}=3.90, p_{HB}<.001), confirming that they were impaired on this measure of decision making abilities.

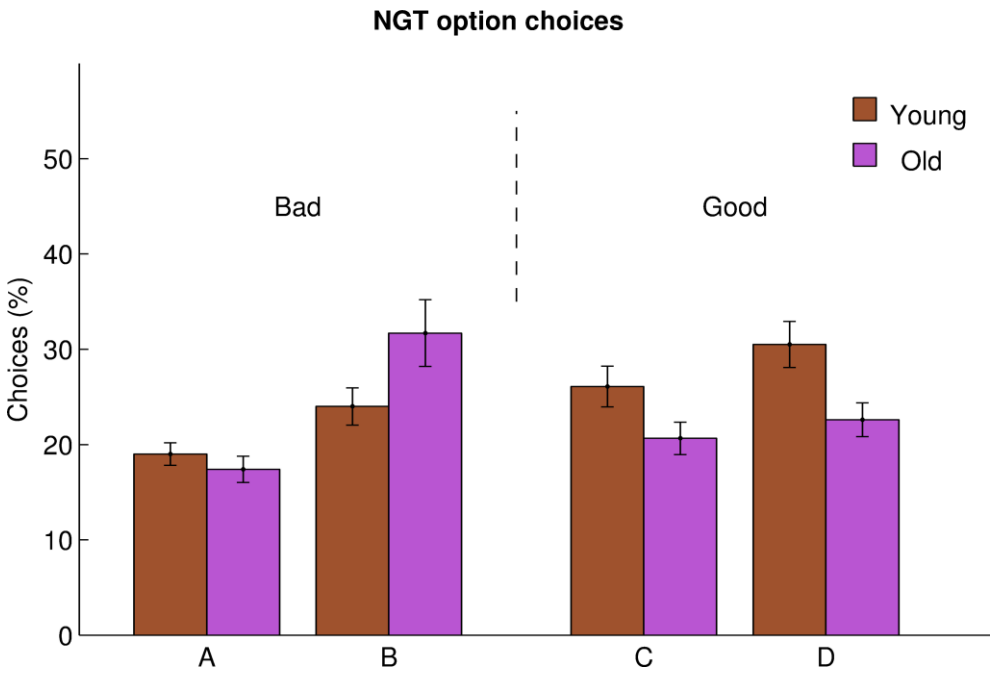

Figure 5.4 NGT option choices. Mean percentage of choices for each of the four reward/penalty options throughout the task for young (brown) and old (purple) participants. A and B were bad choices while C and D were good choices. Error bars represent SEM.

Task relations

As the only difference in task requirements between VPMs was in decision making, performance differences between VPMs should have been greater for those with more severely impaired decision making abilities. I therefore expected to observe a negative correlation between NGT performance and VPM performance difference. *Figure 5.5* plots good choices throughout the NGT against the difference between VPMs in S-P trials correct. Both young (brown stars) and old (purple stars) are included on the same plot, which demonstrates exactly the relationship expected. This demonstrates that, while performance on the no-DM version of the VPM seemed to relate to performance on the standard version, NGT performance was also associated with VPM performance, and specifically the greater deficit in switching to the place strategy on the standard version.

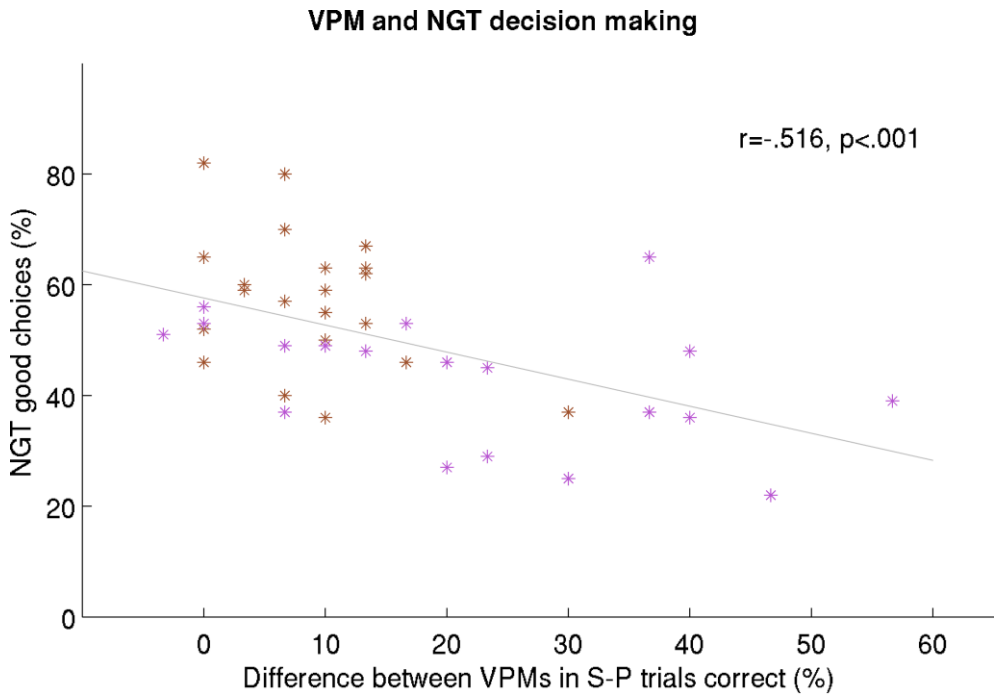

Figure 5.5 VPM and NGT decision making. Correlation between the difference between VPM variants in S-P performance, as an assumed index of decision making impairment, and the percentage of good choices made during the NGT, as a direct measure of decision making ability. Young (brown) and old (purple) are marked separately, but the regression line and correlation statistics apply to the sample as a whole.

I calculated Pearson's correlation coefficient for the relationship between NGT good choices and VPM improvement in S-P trials correct and confirmed that the negative correlation was significant ($r=-.52$, $p<.001$). I also assessed the contributions of decision making (NGT good choices) and other aspects of navigational strategy switching (no-DM VPM S-P trials correct) to standard VPM switch-to-place performance (trials correct) using a GLM. Both NGT ($\beta_{39}=.365$, $p=.027$) and no-DM VPM ($\beta_{39}=1.181$, $p=.022$) performance were significant predictors of standard VPM performance, indicating that while decision making is important to navigational strategy switching, other factors are too.

5.2.4 Discussion

Summary of findings

As found in Study 3, older participants performed significantly worse during switch-to-place blocks, in terms of both trials correct and stable trials, despite the fact that switches (and reversals) were explicitly cued. Also as expected, performance was higher and more similar across change types and age groups during the no-DM VPM. Contrary to my hypothesis, there was still an age difference in terms of accuracy during S-P blocks, as well as a tendency towards a significant difference in terms of learning speed. However, assessing the difference between the two variations of the task demonstrated that older participants exhibited significantly greater difference – in terms of both trials correct and stable trials – only for switch-to-place blocks. During the NGT, older participants tended to choose option D less frequently, and overall chose good options (C and D) significantly less than younger participants, indicating diminished decision making abilities. A negative correlation between NGT good choices and the S-P performance difference between VPMs provided evidence that the greater S-P impairment among older participants during the standard VPM was related to deficient decision making. A GLM confirmed that decision making ability predicted standard VPM S-P performance, although no-DM VPM S-P performance also predicted standard VPM S-P performance, confirming that other factors are important as well.

Interpretation of findings

The age-related deficit in switching to an allocentric place strategy observed in this study is a reproduction of the main finding of Study 3, but also relates to previous work studying the effects of ageing on switching (Ashendorf & McCaffrey, 2008; Gamboz et al., 2009), including cued switching (Kray & Lindenberger, 2000; Terry & Sliwinski, 2010; Wasylyshyn et al., 2011). Although it is difficult to attribute a specific switch-to-place deficit to impaired reward monitoring, as this would affect all change types similarly, the standard VPM results definitively show that impaired

reward monitoring and underlying decline in OFC and ACC function are not responsible. The decision making deficit detected using the NGT also reflects the findings of previous studies using the IGT (Denburg et al., 2005; Fein et al., 2007; Bauer et al., 2013) and other decision making tasks (Brown & Ridderinkhof, 2009; Eppinger et al., 2011). However, the important aspect of this study's results is the association between the two, which supports previous implications of an important role for decision making in strategy switching (Marschner et al., 2005; Eppinger et al., 2011), and suggests that the impairments may reflect deterioration of a common neural substrate. As regions of PFC have been implicated in both switching (Aston-Jones & Cohen, 2005) and decision making (Bechara et al., 1994; Kim & Shadlen, 1999; Manes et al., 2002; Denburg et al., 2007), it is likely that prefrontal dysfunction underlies the age differences observed in this study. This is also concordant with previous observations of prefrontal dysfunction in ageing and the frontal ageing hypothesis (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011).

Decision making studies have demonstrated that older people take longer to make decisions (Walker et al., 1997) and that their decisions are more strongly influenced by previous successful choices (Worthy & Maddox, 2012). These impairments can be understood in terms of the Diffusion Drift Model of decision making (Ratcliff & Rouder, 1998). In brief, the model proposes that the integration of new information causes a decision signal to drift between alternative response-associated thresholds – originally two, but the model has been extrapolated and successfully applied to multiple alternatives (Krajbich & Rangel, 2011). In ageing, as PFC deteriorates (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011), a poorer signal-to-noise ratio means that more information is required for the decision signal to drift towards a particular threshold, reducing the speed and accuracy of decision making (Milosavljevic et al., 2010). Within the context of this study, at the beginning of each trial block, older participants' response choices would have been more heavily influenced by their rewarded responses to trials in the previous block, i.e. by the previous strategy, and it would have taken more trials (in some cases more than were available) for them to reach the threshold for the new strategy. This explanation

provides an account of how impaired decision making, mediated by prefrontal dysfunction, might have a negative effect on navigational strategy switching in general (Marschner et al., 2005; Eppinger et al., 2011).

The specificity of the switch-to-place deficit may arise from a pre-existing difference in change type difficulty. Decision making theory also suggests that action choices are based on cost-benefit analyses that focus on minimising cognitive demand (Kahneman & Tversky, 1979; Stephens & Krebs, 1986; Kool et al., 2010). In the VPM, the response strategy simply involves making the same egocentric response on each trial. The place strategy is much more complex, depending upon recalling the rewarded place and its position within the environment, identifying one's current position within the environment, calculating the spatial relationship between the two, and translating this into an egocentric response. As a result, the cost of using the place strategy is higher, and performing a switch to the place strategy, in contrast to the three other possible change types, is associated with an increase in cognitive load. This change type is therefore more difficult, represented in terms of the Diffusion Drift Model by a much higher threshold for the decision signal to cross before choosing to switch to the place strategy. This may have little effect on performance when decision making abilities are intact, but, once impaired in old age, the higher threshold could substantially exacerbate the effects of reduced signal-to-noise. In summary, I suggest that age-related decision making impairments have a general impact on navigational strategy switching, but that this effect is much more severe for switching to an allocentric strategy, being the most demanding change type. This is not necessarily relevant only to navigational strategy switching, as indicated, for example, by a previous rodent prefrontal lesion study, which also demonstrated a deficit in switching specifically from an easier strategy to a more difficult strategy (Floresco et al., 2008). Additionally, ageing is associated with impaired allocentric processing (Moffat & Resnick, 2002; Moffat et al., 2006; Antonova et al., 2009; Iaria et al., 2009) and a related preference for egocentric strategies (Rodgers et al., 2012; Konishi et al., 2013). These could inflate the increase in cognitive demand associated with performing a switch to the place strategy, raising the threshold for choosing to make this switch, and further increasing the effect of ageing on switch-to-place

performance.

A final point worth discussing is that a reduced switch-to-place deficit was apparent during the no-DM VPM, and S-P performance on this variant of the task still predicted S-P performance on the standard version. As this effect occurred when participants did not have to determine the appropriate strategy themselves, it is likely attributable to difficulties with engaging the appropriate strategy. Impairments in engaging behavioural strategies may reflect noradrenergic dysfunction (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005), but this would also affect other change types. Instead, the residual switch-to-place deficit detected by the no-DM VPM could have been related to a reduction in functional connectivity between PFC and hippocampus, which some evidence does suggest occurs in ageing (Grady et al., 2003).

Limitations

In removing the decision making requirements involved in selecting the appropriate strategy from the no-DM version of the VPM, I also removed the emphasis on reward monitoring throughout the task. I balanced this by providing non-specific cues during the standard VPM, but this was one limitation of the study design. However, the standard VPM results replicated those of Study 3, indicating that the switch/reversal cues did not have a substantial impact on task performance. As for Study 3, another limitation may have been that the tasks used were inadequately simple representations of real world navigational strategy switching and decision making – although Study 4 demonstrated that more realistic tasks do produce similar results. Perhaps the most significant limitation of this study is that, while it demonstrated an association between impaired decision making and the switch-to-place deficit, pointing to dysfunction of PFC as the underlying cause, it still did not directly assess the neural mechanisms. This limitation is addressed in the following chapter. Finally, even assuming the inference that prefrontal dysfunction accounts for the switch-to-place deficit is correct, this study did not explore how this information can be used to prevent age-related decline in navigational strategy switching abilities.

This is addressed in the next section of this chapter.

Conclusion

In this study I replicated the findings of Study 3 by demonstrating a specific switch-to-place deficit among older participants. This was despite explicitly cueing switches/reversals, confirming that reward monitoring impairments do not explain the deficit. Removing the decision making component of the task alleviated the deficit, suggesting that decision making impairments may be responsible. In accordance with this inference, the NGT separately identified decision making impairments within the same group of older participants. Furthermore, a correlation between these impairments and the effect that removing decision making requirements had upon VPM S-P performance provided further evidence that decision making deficits underlie navigational strategy switching impairments. The results of a GLM analysis conclusively demonstrated that decision making ability predicted switch-to-place performance during the standard VPM. I suggest that prefrontal dysfunction is responsible for suboptimal decision making and consequent navigational strategy switching deficits. Within the context of the Diffusion Drift Model, reduced signal-to-noise may impair switching by requiring more information for the decision signal to reach a choice threshold. The specificity of the deficit in switching to an allocentric strategy may be attributable to exacerbation of this effect for the inherently more complicated change type. Age-related hippocampal degeneration may also increase the difficulty of this change type, further exacerbating the specific effects of age-related prefrontal noise. However, it is necessary to explore this further by assessing the underlying neural mechanisms directly. I also found that there was a residual switch-to-place deficit in the no-DM version of the VPM, and that no-DM VPM S-P performance predicted standard VPM S-P performance as well. Other factors, such as noradrenergic dysfunction or reduced functional prefrontal-hippocampal connectivity, are therefore likely to contribute too.

5.3 Study 6: Orienteering practice and navigational strategy switching

5.3.1 Introduction

Cognitive ageing interventions

An important facet of cognitive ageing research focuses on developing or identifying possible interventions that could ameliorate decline in fluid intelligence. Some research has worked towards developing pharmacological treatments, with some success (Landfield et al., 1981; Andrade & Radhakrishnan, 2009; Koh, 2012). However, something as simple as regular physical exercise could also prove highly beneficial. Meta-analyses of numerous randomised controlled trials have concluded that aerobic exercise interventions lead to modest improvements in cognitive facets such as processing speed, executive function and memory (Smith et al., 2010; Ahlskog et al., 2011). Even short-term exercise interventions have produced improvements in cognitive functioning (Aguiar et al., 2011; Chapman et al., 2013). Exercise has been associated with increases in hippocampal volume and neurogenesis (Ahlskog et al., 2011; Erickson et al., 2011) and retention of prefrontal grey matter volume (Colcombe et al., 2006; Ahlskog et al., 2011). Moderate exercise in middle to late life has also been associated with decreased risk of developing MCI and dementia in old age (Geda et al., 2010; Ahlskog et al., 2011)

Cognitive training has been demonstrated as effective as well (Gates & Valenzuela, 2010; Belleville & Bherer, 2012; Park & Bischof, 2013). Training methods include practising visual searching and problem solving (Gräsel, 1994; Ball et al., 2002), learning mnemonic strategies (Ball et al., 2002; Brehmer et al., 2008), playing spatial navigational games (Lövdén et al., 2012), and using commercially available 'brain training' games (Gates & Valenzuela, 2010; McDougall & House, 2012; Nouchi et al., 2012). Such mental training has effectively reduced age-related decline in memory (Brehmer et al., 2008; McDougall & House, 2012; Maseda et al., 2013), reasoning (Ball et al., 2002; Boron et al., 2007), processing speed (Ball et al., 2002;

Nouchi et al., 2012; Wolinsky et al., 2013) and, of particular significance, executive processes such as switching (Basak et al., 2008; Nouchi et al., 2012). However, some evidence suggests that the benefits of cognitive training are limited to the particular cognitive abilities that are trained (Ball et al., 2002; Park & Bischof, 2013). Associated neurophysiological effects include preserved hippocampal volume (Lövdén et al., 2012), cortical thickness and white matter integrity (Belleville & Bherer, 2012), and even increases in neural volume (Park & Bischof, 2013).

Orienteering

Orienteering is an outdoor activity and competitive sport that involves racing through a number of checkpoints across rough terrain in wild environments, such as forests and moorland. Participants are provided with maps, indicating the locations of checkpoints, but have to plan their own routes through or around terrain, obstacles and ascents, before running – or often while already running – over long distances. Orienteering is therefore both highly physically and cognitively challenging (Eccles et al., 2002), and such multi-modal training may serve as a particularly effective and ecologically valid cognitive ageing intervention (Belleville & Bherer, 2012). Competitive orienteering has been used to study complex decision making in natural settings (Omodei & McLennan, 1994), and depends heavily upon interpretation and inter-translation of cartographic representations and visual perception of landscapes and terrain, as well as spatial organisation and memory (Guzman et al., 2008). Involvement in the sport is therefore likely to benefit a range of cognitive abilities. However, as orienteering involves using multiple navigational strategies and switching between them (Eccles et al., 2002), practice may improve or preserve navigational strategy switching abilities in particular. While one study has demonstrated a positive effect of orienteering practice on spatial cognition in children (Notarnicola et al., 2012), the potential of orienteering to prevent or alleviate age-related cognitive decline, particularly in navigational strategy switching abilities, has not yet been explored.

Current study

This study was intended to explore whether decline in navigational strategy switching ability was caused by lack of practice, or whether practice could prevent, alleviate or reverse this decline. I therefore assessed the specific benefits of orienteering practice, in relation to general benefits to fluid intelligence, by testing young and old orienteers and controls on the VPM, as well as an abridged form of the RSPM. I expected older controls to perform worse at the VPM, again due to a specific deficit in switching to the place strategy, as well as at the RSPM. However, I hypothesised that older orienteers would perform better than older controls on both tasks, and perhaps even as well as young participants. Due to the involvement of switching between navigational processes in orienteering, I expected that the benefit of practice to navigational strategy switching ability would be greater than the general benefit to fluid intelligence, i.e. that the difference between older orienteers and controls would be greater on the VPM than on the RSPM.

5.3.2 Methods

Participants

Seventeen (nine female) young orienteers (aged 18-25, M=21.0), 18 (nine female) young controls (aged 20-24, M=21.0), 18 (eight female) older orienteers (aged 65-80, M=68.6) and 19 (10 female) older controls (aged 65-78, M=71.0) participated in the study. Orienteers were recruited through numerous orienteering clubs in and around Edinburgh. Controls were recruited from the university's student population, the local community and the existing PPLS database of research volunteers. Each received £7 as reimbursement for their time – approximately 1h. Some of the control participants, but few of the orienteers, had previous experience of participating in research. No participants were known to suffer from any cognitive or neurological disorders, and all had normal or corrected-to-normal vision.

Procedure

After providing informed consent and some general information, participants began by completing the MMSE to screen for MCI, but none were excluded on this basis. Participants then completed the Corsi blocks task as a measure of spatial working memory, as described in Chapter Two (section 2.3.2), followed by the RSPM and finally the VPM, as described below. Each task was run in Vizard on a standard desktop computer with a 24in widescreen monitor and a standard UK keyboard. The study was approved by the university's psychology research ethics committee and conducted in accordance with the BPS code of ethics.

VPM

The variation of the VPM used in this study used the same VE and the same general procedure as in all other versions of the task. As in many of the later versions of the task, such as those used in Study 4 and Study 5, there were no transparent walls or reward wells. As in some of the latest variations of the task, such as those used in Study 5, adjacent start arms were used, and participants were allowed to go straight ahead at the central junction, so that it was possible to avoid rewarding the previous strategy following a switch. Unlike the VPMs used in Study 5, the incarnation used in this study retained the reward monitoring component, providing no cues prior to a switch/reversal. Specifically, there were no instructions between blocks, the same two adjacent start arms were used, and the number of trials per block was varied. This version of the VPM used 13 blocks of 17, 20 or 23 trials, and a maximum decision time of 3s.

Raven's Standard Progressive Matrices

The RSPM is an established non-verbal test of fluid intelligence, consisting of five sets of twelve items, each more difficult than the last (Raven, 1996; Raven et al., 1996). Each test trial presents a two-dimensional pattern in a three-by-three grid, with the bottom right item missing, along with six (sets A & B) or eight (sets C-E)

pieces that could complete the pattern (*figure 5.6*). Participants must determine which piece fits into the bottom right space and completes the pattern correctly. For this study, I computerised the task in Vizard, and participants simply clicked on the piece that they thought completed the pattern. I also used only the first four items from each set, due to time constraints, allowing participants 10min to complete all 20 items. Their performance was recorded as a score out of 20.

Data analysis

For this study I used the percentage of trials correct as the only measure of VPM performance, as well as the measure of RSPM performance, and Corsi block span as the measure of spatial working memory. Before beginning, a 21-year-old female control, a 68-year-old male orienteer and a 71-year-old female control were excluded as outliers, performing further than 2.5 SDs from their group mean on either the VPM or RSPM. Following this, I first performed two stepwise regression analyses, assessing the contributions of age group, orienteering group, gender and Corsi block span to VPM and RSPM performance. I then assessed age differences in VPM performance across the four change types among control participants only. As before, I used a two-way mixed ANOVA, followed by post-hoc independent t-tests, correcting for multiple comparisons according to the Holm-Bonferroni method. I then explored the effects of age and orienteering on performance during VPM switch-to-place blocks and the RSPM, using data from all participants. Similarly, I used two-way between-groups ANOVAs, followed by post-hoc t-tests, correcting for multiple comparisons. Finally, I assessed the independent contributions of age and length of involvement in orienteering (orienteering years) on RSPM performance within the older orienteering group using a GLM.

5.3.3 Results

Control variables

Initially, I assessed the effects of gender and spatial working memory (Corsi block

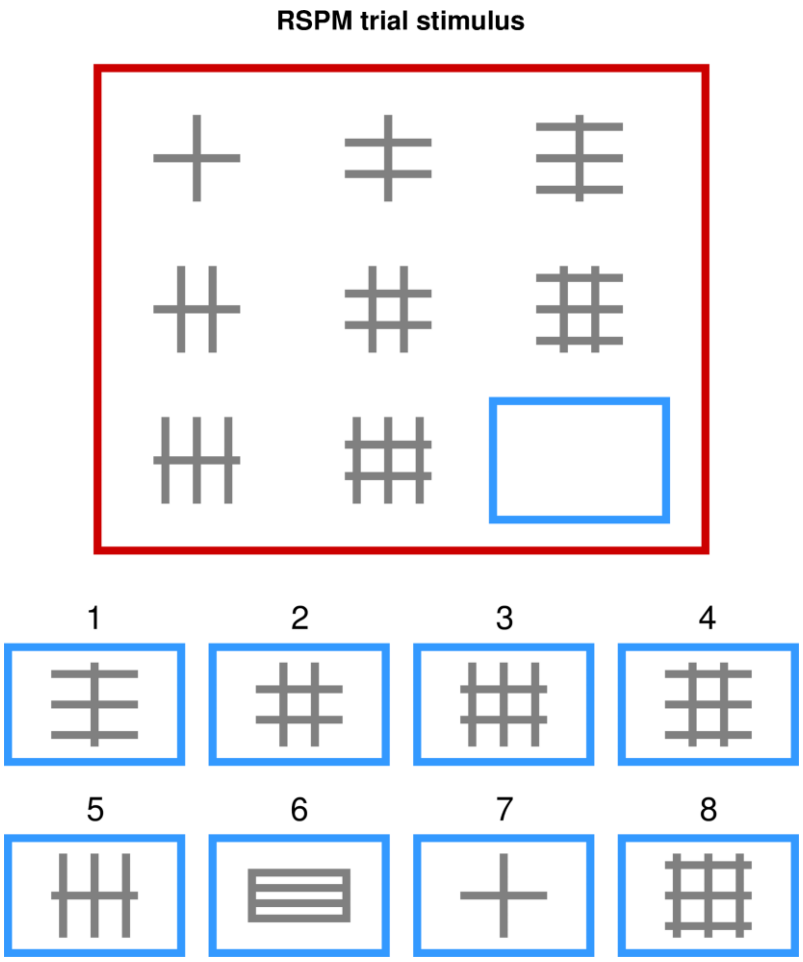

Figure 5.6 RSPM trial stimulus. An example of a test trial used in the RSPM and included in the short version used in this study. Participants have to choose which of the eight pieces at the bottom fit in the space left in the stimulus at the top to complete the pattern. For this trial the correct answer was 8. This test item was selected from set C; in earlier sets there were only six pieces to choose from.

span), as well as age and orienteering groups, on overall VPM and RSPM performance, using stepwise regression analyses. As shown in *table 5.2*, age and gender were retained in the model as significant predictors of overall VPM performance. This was the only indication across all studies of any gender difference in VPM performance. However, the effect was much smaller than that of age, and an independent t-test indicated that the difference between males (M=82.10, SD=9.67) and females (M=77.25, SD=12.42) across age and orienteering groups did not quite achieve significance (t_{67}=1.84, p=.070). A three-way ANOVA did show a modest effect of gender ($F_{1,62}$=4.84, p=.032), but no significant interaction between gender

and age group ($F_{1,62}$=1.01, p=.319) or orienteering group ($F_{1,62}$=1.40, p=.242). Additionally, all four participant groups were evenly and similarly balanced in terms of gender. I therefore did not include gender in any subsequent analyses of VPM performance. Older orienteers (M=5.29, SD=1.05) and particularly controls (M=4.83, SD=.71) achieved lower Corsi block spans than younger orienteers (M=6.47, SD=1.23) and controls (M=6.53, SD=1.12), but as this measure of spatial working memory did not predict VPM performance, I did not consider it in any further analyses either. On the other hand, I continued to explore potential effects of orienteering group, despite it being excluded from the stepwise regression model, as it was one of the two main factors of interest in this study.

I performed the same stepwise regression analysis for RSPM performance. In this case, age, orienteering and gender groups were all included as significant predictors. Again, the effect of gender was smaller than those of age and orienteering, and a t-test showed that the difference between males (M=92.57, SD=10.53) and females (M=87.65, SD=12.51) across all participants was not quite significant (t_{67}=1.80, p=.077). As for VPM performance, while an ANOVA revealed a modest effect of gender ($F_{1,62}$=5.67, p=.020), there was no significant interaction with age ($F_{1,62}$=1.47, p=.230) or orienteering ($F_{1,62}$=1.06, p=.308). So again, as the effect of gender was relatively small, and the participant groups were gender balanced, I did not include gender in any further analyses of RSPM performance.

Overall VPM performance stepwise regression results

Predictor	β	SE	In	p
Age	-.121	.023	1	<.001
Orienteer group	.033	.022	0	.140
Gender	.050	.023	1	.029
Corsi blocks	.003	.009	0	.109

Table 5.2 Overall VPM performance stepwise regression results. A stepwise regression analysis assessed how well age, orienteering, gender, and Corsi block span predicted VPM performance in terms of overall trials correct. Factors retained in the model as significant predictors of performance are highlighted in blue.

RSPM performance stepwise regression results

Predictor	β	SE	In	p
Age group	.130	.022	1	<.001
Orienteer group	.066	.022	1	.003
Gender	-.052	.022	1	.019
Corsi blocks	.008	.009	0	.348

Table 5.3 RSPM performance stepwise regression results. A second stepwise regression analysis assessed how well age, orienteering, gender, and Corsi block span predicted RSPM performance in terms of proportion of correct responses. Factors retained in the model as significant predictors of performance are highlighted in blue.

VPM

Before exploring the effect of orienteering on VPM performance, I assessed age differences in accuracy by change type among controls only. *Figure 5.7* summarises performance in terms of trials correct throughout switch-to-place, switch-to-response, reverse-place and reverse-response trial blocks, for both young (brown) and old (purple) control participants. As shown, older controls performed at least slightly worse than young following all change types, the age difference was greatest for switching to the place strategy, which is consistent with the results of both Study 3 and Study 5. I therefore assessed the effects of age and orienteering specifically on performance during S-P blocks. VPM S-P performance is summarised in terms of trials correct by age and orienteering groups in *figure 5.8*. Young controls and orienteers are represented by the brown and purple bars on the left, respectively, while older participants are represented by those on the right. Young groups performed similarly, and older orienteers still performed worse than young, but they also performed slightly better than older controls. This may indicate that orienteering moderates decline in navigational strategy switching abilities.

Statistical analyses confirmed that older controls tended to perform worse than young controls across most change types (S-R: $t_{31}=2.30$, $p_{HB}=.057$; R-P: $t_{29}=2.54$, $p_{HB}=.050$; R-R: $t_{30}=1.74$, $p_{HB}=.092$), but particularly on switch-to-place blocks ($t_{32}=4.04$,

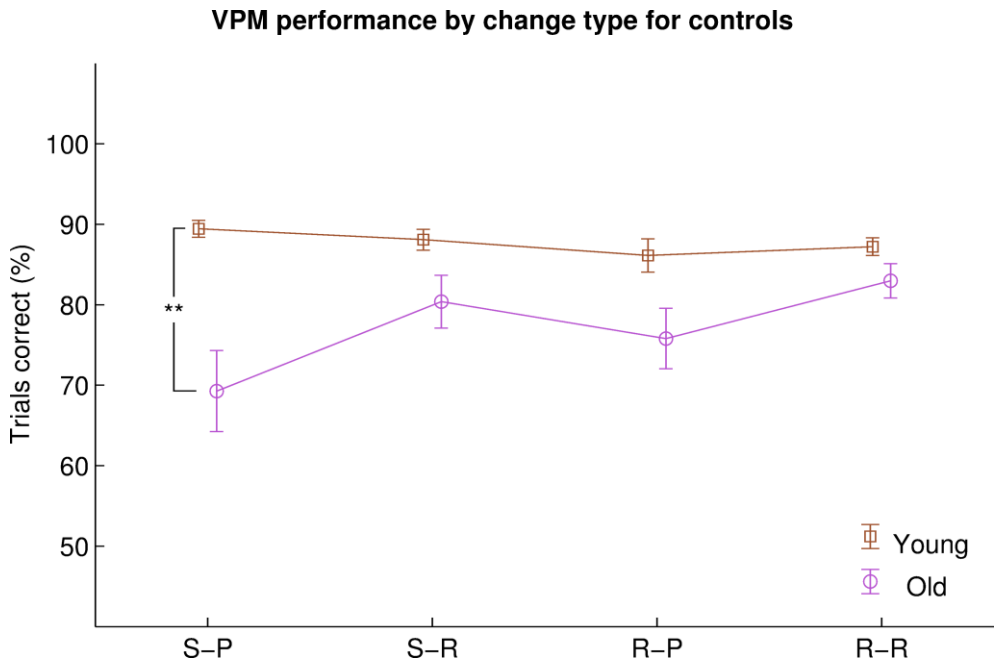

Figure 5.7 VPM performance by change type. Mean VPM performance in terms of percentage of trials correct throughout switch-to-place (S-P), switch-to-response (S-R), reverse-place (R-P) and reverse-response (R-R) trial blocks for young (brown) and old (purple) control participants. Error bars represent SEM. ** represents a significant age difference at p<.01.

p_{HB}=.001). However, while a two-way ANOVA with age and orienteering as factors confirmed a significant effect of age on S-P performance for all participants ($F_{1,64}$=24.06, p<.001), there was no significant main effect of orienteering ($F_{1,64}$=1.00, p=.320), nor a significant interaction ($F_{1,64}$=2.59, p=.113). Likewise, post-hoc t-tests confirmed that older controls performed significantly worse than young controls (t_{32}=3.91, p_{HB}=.003) and young orienteers (t_{32}=3.57, p_{HB}=.006), that older orienteers, although the differences were smaller, also performed worse than both young controls (t_{32}=3.48, p_{HB}=.006) and young orienteers (t_{32}=2.97, p_{HB}=.017), and that young controls and orienteers performed similarly (t_{32}=1.32, p_{HB}=.196). However, analyses demonstrated that there was not actually a significant difference in S-P trials correct between older controls and orienteers (t_{32}=1.34, p_{HB}=.378).

RSPM

I assessed RSPM performance in the same way as VPM S-P performance, by age and

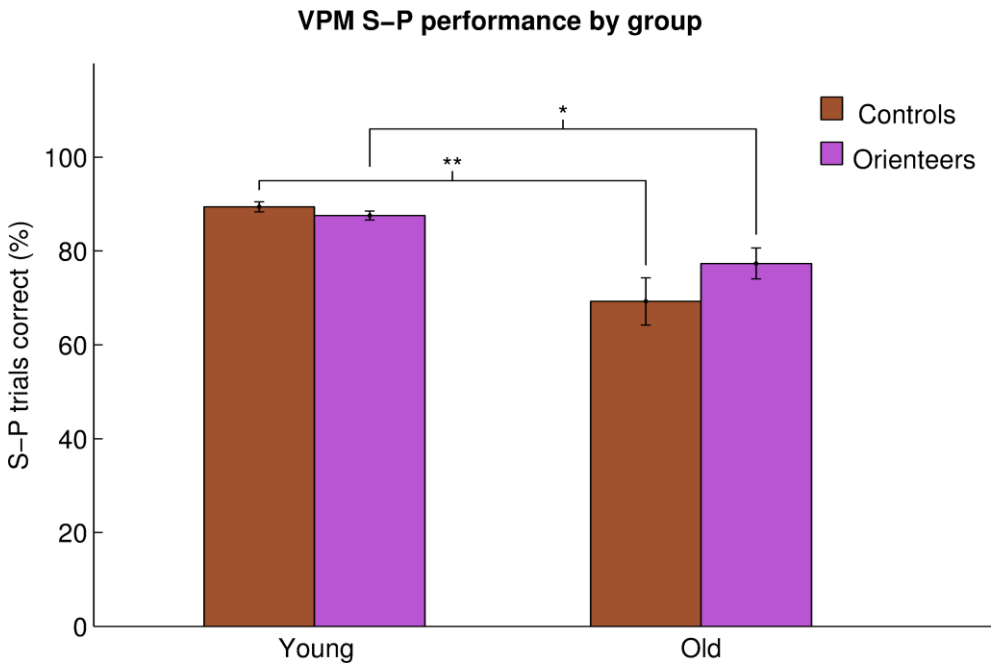

Figure 5.8 VPM S-P performance by group. Mean VPM performance in terms of percentage of trials correct during switch-to-place blocks for young and old controls (brown) and orienteers (purple). Error bars represent SEM. * and ** represent significant age differences at p<.05 and p<.01.

orienteering groups. *Figure 5.9* similarly represents the mean performance of young (left) and older (right) controls (brown) and orienteers (purple). This figure shows that, as for VPM S-P performance, young groups performed similarly on the RSPM, and older controls performed worse. However, for RSPM performance, the difference between older orienteers and young participants was smaller, while the difference between the two older groups was greater. This suggests that practising orienteering may have a greater protective effect on general fluid intelligence. *Figure 5.10* plots older orienteers' RSPM performance against the number of years they had been involved in orienteering, demonstrating a correlation between the two, which provides further evidence that the difference between older groups in fluid intelligence was due to the protective effects of orienteering practice.

In support of these findings, a two-way ANOVA revealed significant main effects of both age ($F_{1,65}$=36.41, p<.001) and orienteering ($F_{1,65}$=9.01, p=.003) on RSPM performance, as well as a significant interaction between the two ($F_{1,65}$=7.43,

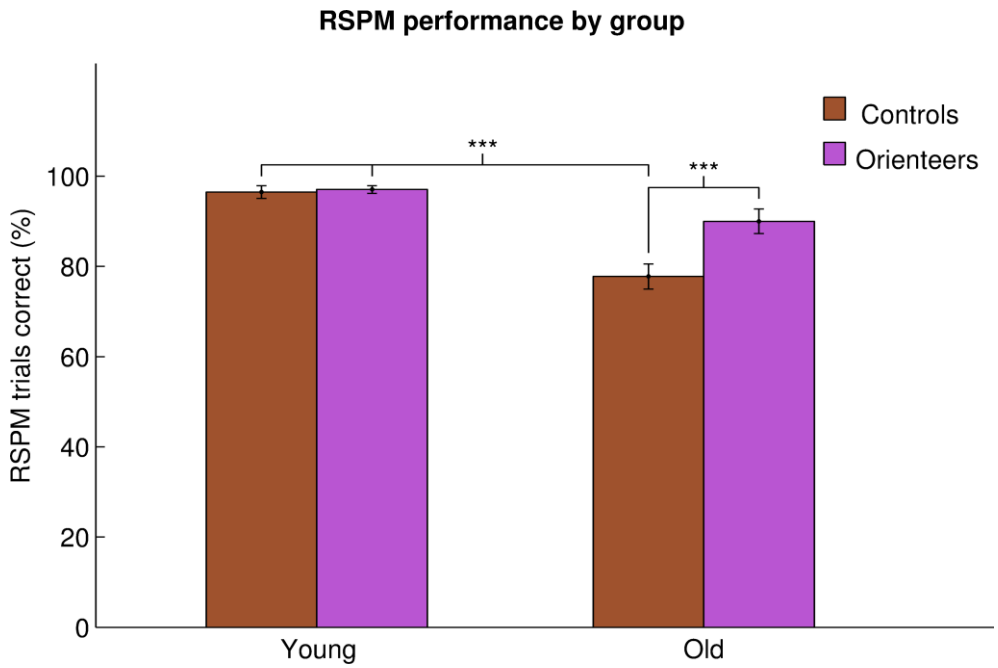

Figure 5.9 RSPM performance by group. Mean RSPM performance in terms of percentage of trials correct for young and old controls (brown) and orienteers (purple). Error bars represent SEM. *** represents significant group differences at p<.001.

p=.008). Post-hoc t-tests confirmed that older controls performed significantly worse than young controls (t_{33}=5.90, p_{HB}<.001) and young orienteers (t_{33}=6.47, p_{HB}<.001). On the other hand, although older orienteers still tended to perform worse than the younger groups, they did not differ significantly either from young orienteers (t_{32}=2.48, p_{HB}=.056) or young controls (t_{32}=2.12, p_{HB}=.084). Young orienteers performed very similarly to young controls (t_{32}=.36, p_{HB}=.724), but, importantly, in terms of RSPM performance, older orienteers did perform significantly better than older controls (t_{33}=3.14, p_{HB}=.014).

I assessed the separate effects of age and orienteering years on general fluid intelligence, within the older orienteering group only, using a GLM. Both age (B_{14}=-.317, p=.002) and orienteering years (B_{14}=.095, p=.015) were significant predictors of RSPM performance, suggesting that, while fluid intelligence still decreases with ageing among orienteers, the extent to which practising orienteering alleviates this effect increases with years of involvement in the sport.

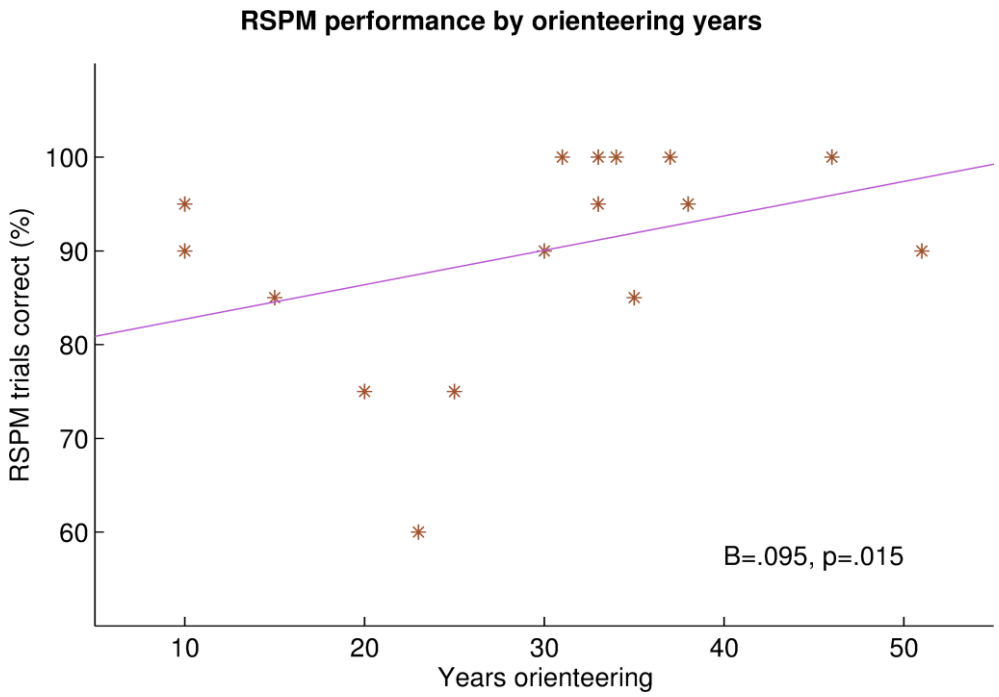

Figure 5.10 RSPM performance by orienteering years. Relationship between years involved in orienteering and RSPM performance within the older orienteering group only. The purple line represents a standard regression line, but the reported statistics are derived from the GLM assessing the effect of years orienteering on RSPM performance while controlling for the effect of age.

5.3.4 Discussion

Summary of findings

Within the control group, older participants performed significantly worse at the VPM during switch-to-place blocks, as expected and as found in Studies 3 and 5. During VPM S-P blocks, older orienteers also performed worse than young participants, and did not significantly outperform older controls. However, in terms of RSPM performance, while older controls were again significantly worse than young participants, older orienteers were not, and in fact performed significantly better than older controls. Within the older orienteering group, despite a strong negative effect of age, there was a significant positive effect of length of involvement in orienteering on RSPM performance.

Interpretation of findings

Data from this study's control participants provided further evidence of an age-related deficit in switching to an allocentric navigational strategy, relating to studies presented earlier and to previous work on switching impairments in ageing (Ashendorf & McCaffrey, 2008; Gamboz et al., 2009). RSPM data demonstrated an impact of ageing on fluid intelligence, also observed in numerous previous studies (Horn & Cattell, 1967; Bors & Forrin, 1995; Kaufman & Horn, 1996; Bugg et al., 2006). But, as hypothesised, this study also demonstrated a beneficial effect of orienteering practice on fluid intelligence in ageing. Although samples were not selected randomly, there was no difference in RSPM performance between the young orienteers and controls, providing some indication that the difference between older groups was due to an effect of orienteering, rather than a sampling bias. On the other hand, there was a ceiling effect among young participants, which may have masked a difference between the orienteers and controls. The finding does relate to previous work demonstrating an effect of orienteering practice on cognitive ability in children (Notarnicola et al., 2012). However, it could also relate to previous work showing a cognitive benefit of exercise in general (Smith et al., 2010; Ahlskog et al., 2011), as it may be that it was simply the physical activity involved in orienteering that produced the observed effect.

Regarding the main focus of this study, I also hypothesised that older orienteers would perform significantly better than controls on the VPM, and furthermore that the benefit of orienteering practice to navigational strategy switching would be greater than the general effect on fluid intelligence. My results did not support this hypothesis, as older orienteers did not differ significantly from older controls, and still performed worse than young participants. It may be that orienteering did not benefit VPM performance in particular because the two do not involve the same cognitive processes. However, this does not seem consistent with previous implications that orienteering is dependent upon navigational strategy switching (Eccles et al., 2002). On the other hand, it may be that the brain regions whose dysfunction accounts for impaired navigational strategy switching are less likely to

benefit from multi-modal cognitive and physical training. As previous studies have demonstrated benefits throughout PFC (Colcombe et al., 2006; Ahlskog et al., 2011), and RSPM performance is also highly dependent upon PFC, this may suggest that deterioration of LC (Manaye et al., 1995; Grudzien et al., 2007) or prefrontal-hippocampal connections (Grady et al., 2003) is responsible for the age-related switch-to-place deficit. The other explanation is that there is a positive effect of orienteering practice on navigational strategy switching ability, but that this was masked by variance in VPM S-P performance among the older groups, which was higher than variance in RSPM performance.

Limitations

With this study I intended to assess the benefit of practising orienteering on navigational strategy switching ability in ageing, and whether age-related deficits might be related to lack of practice. I did so by comparing participants that were involved in orienteering to those that were not. The major limitations of this study were therefore that the orienteering practice was not administered as a controlled intervention and that participants were not randomly assigned to conditions. A longitudinal study would have been more appropriate, but was not feasible within the time I had. Considering the effects that physical and cognitive training have upon cognitive decline separately, it would also have been useful to assess navigational strategy switching in young and old runners or chess players, for example. I decided not to test additional control groups, as orienteering did not appear to have a significant ameliorative effect on decline in navigational strategy switching ability. Another concern was the ceiling effect that young participants exhibited on the RSPM. It may have been better to use the advanced version of this test, or another more difficult assessment to measure fluid intelligence. Finally, in investigating the efficacy of cognitive ageing interventions, it is useful to assess their effects on neural structure, integrity and activity, as well as behavioural performance, which this study did not.

Conclusion

This study replicated the findings of Study 3 and Study 5, revealing a switch-to-place deficit among older control participants, and demonstrated a beneficial effect of orienteering practice on fluid intelligence in ageing. However, contrary to my hypothesis, older orienteers showed no advantage in switching to the place strategy in the VPM, suggesting that decline in ageing is not related to lack of practice. It may be that the age-related impairment in switching to an allocentric strategy is caused by neurodegeneration that is not slowed or reversed by physical or mental exercise, perhaps in LC or prefrontal-hippocampal connections. However, the cross-sectional study design was not the most suitable for assessing orienteering as a potential cognitive ageing intervention, and this study should really be considered as a pilot study. Still, as these preliminary results did not demonstrate any significant effect of orienteering on decline in navigational strategy switching ability, they do not indicate that a more controlled longitudinal study would be worthwhile.

5.4 Chapter conclusion

In this chapter I reported two further behavioural studies assessing the mechanisms underlying decline in navigational strategy switching ability. In Study 5, I used two variations of the VPM together with the NGT to explore the relationship between deficient decision making, caused by prefrontal dysfunction, and impaired navigational strategy switching. As in Study 3, older participants were specifically impaired at switching to the place strategy. They also showed impaired decision making, which predicted switch-to-place performance during the standard VPM. This indicates that the switch-to-place deficit is mediated by decision making impairments, and in turn prefrontal degeneration. However, older participants were still impaired, though to a lesser extent, at switching to the place strategy during the no-DM variation of the VPM, and performance at this task also predicted standard VPM S-P performance. This suggests that other factors, such as LC-NA dysfunction or reduced prefrontal-hippocampal connectivity, are also involved.

In Study 6, I used a sample of participants involved in orienteering to assess the effects of practice on decline in navigational strategy switching ability. Although orienteering seemed to benefit fluid intelligence, as measured by the RSPM, it did not significantly improve switch-to-place performance in the VPM. The study was limited by a number of factors, most critically its cross-sectional design, but the results still suggest that navigational strategy switching is not preserved by relevant practice, and is less responsive to physical and mental training than fluid intelligence in general. Deficits in switching to an allocentric strategy may therefore be mediated by dysfunction of brain regions other than PFC, which does benefit from training interventions.

Overall, Study 5 indicates that age-related navigational strategy switching impairments are related to, but not entirely explained by, decision making deficits and underlying prefrontal dysfunction. Study 6 demonstrated that relevant practice does not prevent decline in navigational strategy switching ability, even though the associated regular physical and mental exercise does appear to preserve fluid intelligence. This may suggest that the navigational strategy switching deficits relate to degeneration of brain regions less responsive to training interventions, possibly LC. These studies therefore provide some insight into the mechanisms underlying the deficit in switching to an allocentric strategy (a finding that both studies also replicated). The studies presented in the remaining two experimental chapters were designed to more directly assess the roles of prefrontal regions and the LC-NA system in navigational strategy switching and ageing-related deficits therein.

Chapter Six
Functional Magnetic Resonance Imaging of Navigational Strategy Switching

6.1 Chapter overview

In Chapter Four, I presented Study 3, which used the virtual plus maze (VPM) to assess navigational strategy switching in young and older participants, demonstrating an age-related deficit in switching to an allocentric strategy. In Chapter Five, I presented Study 5, which indicated that deficits in cognitive processes supported by prefrontal cortex (PFC) underlie navigational strategy switching impairments in ageing. However, in order to better understand the neural mechanisms of age-related decline in navigational strategy switching ability, it is important to directly assess brain activity throughout the process. An excellent way of directly assessing neural activity related to cognitive processes in humans is functional magnetic resonance imaging (fMRI). In this chapter, I present an fMRI study that assessed navigational strategy switching in young participants using the VPM, and a pilot study that tested a revised version of the VPM to be used in a later fMRI study, using both young and older participants. Unfortunately, this later study was never completed and is therefore not included.

In section 6.2, I present Study 7, which used an early version of the VPM to assess navigational strategy switching ability in a small number of young participants at the University of California Santa Barbara (UCSB), in collaboration with Mario Mendoza and Brendan McHugh. I explored the effects of strategy switching on activation of dorsolateral PFC (dlPFC), orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC), as well as the effects of strategy on activation of the hippocampus and caudate nucleus. I also attempted to decode switching, strategy and change type from the same regions of interest (ROIs), and explored hippocampal prospective and retrospective coding, using multi-voxel pattern analysis (MVPA). However, the main objective of the study was to demonstrate that dlPFC, OFC and

ACC are involved in navigational strategy switching. I planned to assess age differences in activity of these regions during navigational strategy switching in a later fMRI study at the German Center for Neurodegenerative Diseases in Magdeburg.

This later study would use older participants as well as young, in order to be able to assess age differences in the neural processes involved in navigational strategy switching. I also planned to use a 7T MRI scanner, with higher spatial resolution, which would enable imaging of the locus coeruleus (LC) as well as of prefrontal ROIs. In response to some issues with the original VPM identified by the first fMRI study, I developed a quite different version of the task to be used in the second. In section 6.3, I present Study 8, which piloted the revised VPM in a small sample of young and older participants, in order to ensure that it was suitable for use with fMRI. The new variant of the VPM divided trial blocks into three, and participants were expected – and required – to learn the correct strategy for each block during the middle sub-block. Unfortunately, the preliminary results did not match this expectation, and I did not complete the planned study in Magdeburg.

6.2 Study 7: Navigational strategy switching during fMRI

6.2.1 Introduction

Recapitulation

This study also used the VPM, a task that involves finding a reward using either an allocentric place strategy or an egocentric response strategy, and periodically switching or reversing strategy. In previous chapters I have presented behavioural results suggesting that older people are impaired at switching between navigational strategies. Older people may be specifically impaired at switching from the response to the place strategy, as indicated by the results of Study 3, or may have a more general deficit in navigational strategy switching. I have already discussed some

potential neural mechanisms underlying age-related navigational strategy switching impairments, mainly in terms of Aston-Jones and Cohen's (2005) adaptive gain theory of LC-noradrenaline (NA) function. Their model suggests that the overall benefit of a behavioural strategy is monitored by OFC and ACC, which signal to LC when a change in strategy is required. In response, the LC changes to a high-tonic mode of NA output, which facilitates the coordination of a strategy switch in PFC. Bouret and Sara (2005) suggest that a subsequent increase in phasic NA promotes functional reorganisation of cortical networks, and the engaging of a new strategy. To provide a relevant example, when switching from the place to the response strategy, weightings of inputs to PFC from the hippocampus and caudate nucleus are decreased and increased, respectively (Doeller et al., 2008).

BOLD fMRI

MRI takes place within a strong magnetic field, produced by a massive electromagnet. Within an MRI scanner, the spins of any atomic particles with magnetic moment – such as hydrogen nuclei, abundant in water throughout the body – are aligned with the magnetic field (Hendee & Morgan, 1984; McKinstry, 1986). During scanning, a transmitting coil emits a radio frequency (RF) pulse, which temporarily alters the spin alignments. Following the RF pulse, as the nuclei relax and realign with the magnetic field, they produce a small electromagnetic signal, detected by receiver coils (Hendee & Morgan, 1984; Carpenter & Williams, 1999; Weishaupt et al., 2008). The magnetic field is homogenised by a series of weaker electromagnets called shim coils (Roméo & Hoult, 1984; Patton, 1994), and then distorted by gradient coils throughout the imaging sequence in order to systematically vary spin relaxation times, allowing localisation of the relaxation signals within three-dimensional space (Hendee & Morgan, 1984; Carpenter & Williams, 1999; Weishaupt et al., 2008). MRI can therefore be used to generate detailed three-dimensional images of bodily structures, including the brain, or, as in fMRI, to observe physiological changes related to activity throughout the brain. Following neuronal activation (and energy consumption), a corresponding haemodynamic response within surrounding blood vessels increases local cerebral

blood volume (CBV), cerebral blood flow (CBF) and cerebral metabolic rate of oxygen ($CMRO_2$; Fox & Raichle, 1986; Buxton et al., 2004; Kim & Bandettini, 2010). Blood oxygen level dependent (BOLD) fMRI exploits changes in blood oxygenation and the difference in magnetic properties between oxygenated and deoxygenated blood (Pauling & Coryell, 1936; Thulborn et al., 1982) to produce contrast images highlighting brain regions that have recently been active (Ogawa et al., 1990; Kwong et al., 1992; Gore, 2003; Kim & Bandettini, 2010). BOLD fMRI usually uses echo planar imaging (EPI), which involves following the RF pulse with a rapid oscillation of gradient coil frequencies, producing multiple nuclear spin relaxation signals, and allowing quicker acquisition of images (Poustchi-Amin et al., 2001).

In the early 1990s, the first human fMRI studies simply used neural responses to sensory stimulation to demonstrate the utility of BOLD contrast imaging (Belliveau et al., 1991; Ogawa et al., 1992; Kwong et al., 1992). Since then, BOLD fMRI has been applied to investigations of the neural mechanisms underlying a range of cognitive processes, including both navigation and switching behaviour, as well as age-related cognitive decline. Within the context of navigation, several studies have demonstrated that allocentric and egocentric studies are supported by the hippocampus and caudate nucleus, respectively (Hartley et al., 2003; Iaria et al., 2003), while studies of path integration and spatial updating have shown that other brain regions, including the human motion complex (hMT+), medial PFC (mPFC), dorsal premotor cortex (PMd) and the precuneus, are also important (Wolbers et al., 2007, 2008). fMRI has also been used to confirm the role of prefrontal regions in set-shifting (Monchi et al., 2001; Moll et al., 2002; Hampshire & Owen, 2006) and task switching (Dove et al., 2000; DiGirolamo et al., 2001). In studying cognitive decline (and preserved cognitive functioning) in ageing, fMRI has revealed a range of regional activity differences between young and old participants (Cabeza, 2001; Eyler et al., 2011). In particular, ageing has been associated with differences in BOLD signal from the hippocampus, caudate nucleus, PFC and retrosplenial cortex (RSC) during virtual navigation (Moffat et al., 2006, 2007), and from frontal and parietal cortex during task switching and attention shifting (DiGirolamo et al., 2001;

Townsend et al., 2006).

Hippocampal prospective and retrospective coding

The hippocampus serves as the neural basis of the cognitive map by representing current position information (O'Keefe & Dostrovsky, 1971; O'Keefe & Nadel, 1978). However, hippocampal place cells fire not only while within certain place fields, but also before and after visiting these place fields (Ferbinteanu & Shapiro, 2003; Shapiro et al., 2006), known, respectively, as prospective and retrospective coding. Prospective coding seems to be important in navigational decision making in terms of planning trajectories. For example, in rodents running a T-maze, prospective coding hippocampal cells may fire in relation to locations on one of the maze's goal arms while the animal is still on the start arm. Johnson and Redish (2007) demonstrated that when rats reach the junction of a T-maze, activation of prospective coding cells sweeps down one goal arm and then the other as the rats consider following each trajectory. Retrospective coding shows that the hippocampus encodes not only spatial locations, but also episodic relations between locations. The plus maze, which is of course similar to the T-maze but with multiple start arms as well as multiple goal arms, has been used to study both prospective and retrospective coding, demonstrating hippocampal cell firing related to current, recent and imminent position, during use of both hippocampal and non-hippocampal strategies (Ferbinteanu et al., 2011).

Current study

In this study I used data collected from young participants who completed the VPM during fMRI to explore the neural mechanisms underlying navigational strategy switching. I intended to verify that component regions of the switching model postulated by Aston-Jones and Cohen (2005) are involved in navigational strategy switching. I expected to see increased activation within dlPFC, OFC and ACC during strategy learning periods (while participants would be performing strategy switches) in comparison to stable strategy periods (during which participants would be stably

using a single strategy and no longer switching). Demonstrating that these regions are involved in navigational strategy switching in young people would provide a foundation for interpretations of navigational strategy switching deficits among older people in terms of degradation or dysfunction of the PFC-LC switching network, as well as an indication of how best to continue exploring the neural mechanisms underlying age-related deficits. While I anticipated changes in activation of these ROIs during reversals as well as switches, I expected to see different patterns of activation changes, as these two change types are mediated by different subregions of PFC (Young & Shapiro, 2009). I also intended to confirm that the place and response strategies utilised during the VPM are supported by the hippocampus and caudate nucleus, respectively, and used the data to explore hippocampal prospective and retrospective coding, expecting to show that future and past locations could be decoded from hippocampal activity before and after participants made a decision at the VPM central junction.

6.2.2 Methods

Participants

Eight (two female) healthy young participants (aged 19-31, M=23.1) were recruited from the UCSB Brain Imaging Center's database of imaging research volunteers. All participants reported normal or corrected-to-normal vision, no known neurological disorders or cognitive deficits, and previous experience of fMRI. One 24-year-old male participant's data were discarded, as he did not complete the entire experiment due to a technical error during acquisition.

Procedure

Participants received information about the study and provided informed consent before beginning the experiment. Although all had previous experience of fMRI, prior to scanning, they were again screened for pacemakers or other metal implants, claustrophobia, pregnancy and any other conditions that would have made them

unsuitable for MRI. They then received more detailed instructions on the VPM and completed one full session as practice, before entering the MRI scanner. In the scanner, following a single scan localiser, scout and shimming, participants completed four sessions of the VPM during functional EPI, with five minute breaks between sessions. The scanning concluded with a T_1-weighted anatomical scan, after which participants were allowed out of the scanner and debriefed. The study was approved by the UCSB Institutional Review Board and conducted in accordance with the Declaration of Helsinki.

VPM

This study, as one of the earliest I ran, used the first incarnation of the VPM. As described and illustrated in Chapter Two (section 2.3.3), the VPM was set in a virtual environment (VE) comprising a grass-textured plain, surrounding mountain scenery, a plus-shaped pathway and, in this version, transparent walls at the sides of the pathway and reward wells at the end of the east and west goal arms. On each trial, participants were positioned at either the north arm or the south arm of the maze, and then automatically moved towards the central junction. Stopping just before the central junction, participants pressed either the top or bottom button on a button pad to indicate whether they wanted to proceed to the left or right. Which button related to which direction was randomised for each trial and indicated on-screen while participants were stopped at the junction. After 3s, automatic movement continued through the central junction in their chosen direction and towards the reward well at the end of either the east or west maze arm. A yellow ball emerged from the well as a reward signal if participants had made the correct choice, which also increased a running total displayed in the top corner of the screen. Sometimes participants were rewarded for visiting the same place on each trial, i.e. the east or west reward well, regardless of which direction they had to turn to get there. At other times participants were rewarded for making the same response on each trial, i.e. turning left or right, regardless of which reward well this led them to. Participants used the same place or response strategy for 20 trials, after which the strategy was either switched, e.g. from place to response, or reversed, e.g. from left to right. The experiment consisted of

four sessions, each including four blocks, producing a total of 320 trials, incorporating six switches and six reversals. This was preceded by a single session (80 trials) as an introduction to the task, completed outside the scanner. The timescale of the experiment, of each session and of each individual trial are illustrated in *figure 6.1*.

fMRI equipment and parameters

fMRI data were acquired using a 3T Siemens Magnetom Trio Tim System with a 32-channel head coil at the UCSB Brain Imaging Center. Functional EPI volumes comprised 25 interleaved 2.5mm slices of 2.0x2.0mm voxels with 1.0mm gap (TR=2170ms, TE=35ms, FA=70°), covering the entire brain. Anatomical scans followed a standard T_1-weighted sequence (TR=2300ms, TE=2.98ms, FA=9°, 1.0mm isotropic). The VPM, running in Vizard on a high performance laptop, was projected onto a screen behind the scanner, viewed by participants using a mirror angled at 45°. Participants provided input using a Current Designs Inline four-button fibre optic response pad.

Data analysis

All data analyses were performed in Matlab. For each trial, the predetermined strategy (place/response), polarity (east/west or left/right) and start arm (north/south) were logged, along with the participant's chosen direction (left/right) and dependent goal arm (east/west) and outcome (correct/incorrect). The primary measure of performance was the proportion of trials to which participants responded correctly. I also used the Bayesian learning analysis described in Chapter Two (section 2.5.3) to identify if and when participants stably acquired the correct strategy for each block, producing two further measures of performance; proportion of blocks learned and proportion of stable trials, related to learning speed. Behavioural data were divided by block change type, excluding blocks following unlearned blocks, as participants could not be said to have switched or reversed from the previous strategy if they had not necessarily been using that strategy.

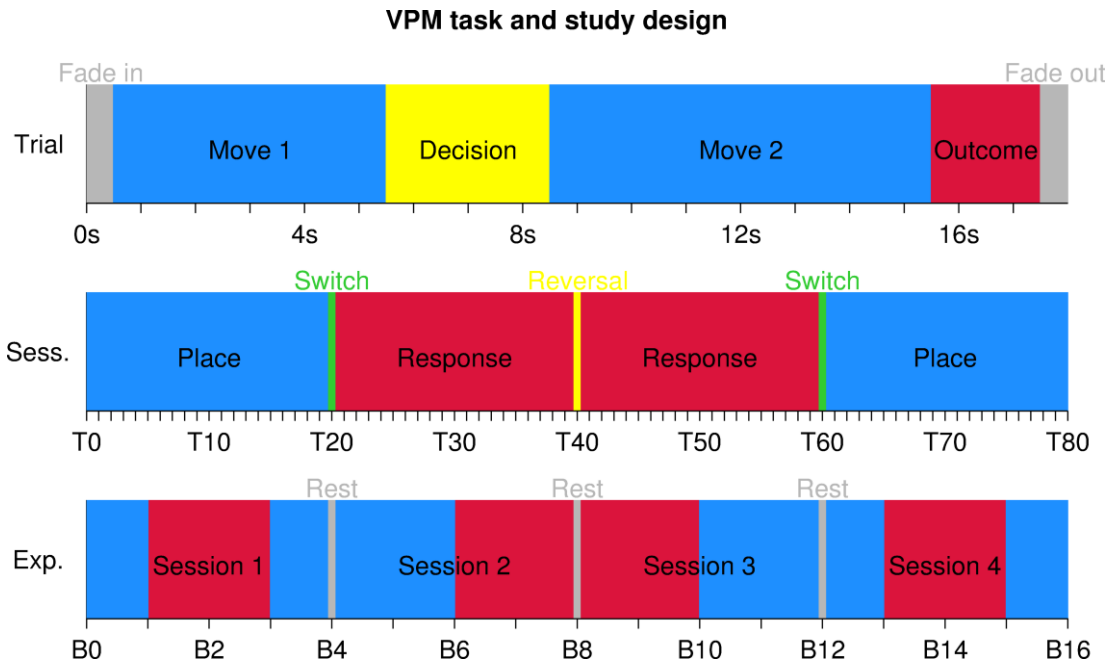

Figure 6.1 VPM task and study design. Timescales of a single trial in seconds (*top*), showing the four trial phases (during which participants moved to the junction, decided which direction to proceed in, moved to the reward well and either did or did not receive a reward); of a session in trials (*centre*), incorporating four blocks and three strategy changes; and of the experiment in blocks (*bottom*), comprising four sessions, 16 blocks and 12 changes.

fMRI data were preprocessed in SPM 8. This involved slice timing correction to account for changes in activity throughout the TR, realignment of all subsequent functional images to the first in order to compensate for minor head movements during scanning, and coregistration (without reslicing) of functional and structural images. I used the ArtRepair SPM toolbox to check for bad volumes, but none were discarded on this basis. Images were also normalised to a standard anatomical template, in order to perform group analyses, and smoothed with a 5mm FWHM kernel. Finally, I created ROI masks by segmenting structural images using FreeSurfer, writing out and combining segments using FSL and, where necessary, splitting larger segments into smaller ROIs using the MarsBaR SPM toolbox and the built-in SPM ImCalc function.

I also used SPM to perform first and second level general linear model (gLM) analyses. For these purposes, trials were divided into three phases; pre-decision

(during which participants moved to and waited at the junction before providing a response), post-decision (during which participants waited at the junction after providing a response and then moved to the reward well) and outcome (during which participants either did or did not receive a reward from the well). Trial phase onsets and durations were further divided into 12 regressors per session, also modelling the data in terms of strategy learning status (unlearned/learned) and either change type (switch/reversal) or strategy (place/response). Realignment parameters were also included for each session. Regressors were automatically convolved during model estimation in order to compensate for the haemodynamic response function (HRF). I then performed F and t contrasts for each participant, and subsequently for the whole group, assessing activation differences between switch learning and stable strategy periods, and between place and response stable strategy periods. These analyses were restricted to ROIs by applying masks, and I used small volume correction (SVC) to correct for familywise error (FWE) within each ROI.

Finally, I used the Princeton MVPA toolbox to perform MVPA in attempt to decode switch learning status, change type and strategy from ROIs. I also tried to decode future and past locations from hippocampus, in order to assess prospective and retrospective coding, respectively, as well as movement type (forward/rotational) from primary visual cortex (V1), simply as a procedural verification. Data were high pass filtered, z-scored and averaged, and regressors were shifted by three TRs to account (more approximately) for the HRF. Following ANOVA-based feature selection with a threshold of p=.05 and low weight penalisation, I used ridge regression and n-minus-one cross-validation to classify data from the four sessions. I then checked whether the resulting classification accuracies were significantly higher than chance using the 'wavestrapper_results' function, which compares the classifier outputs to a null distribution, created by scrambling the same data.

6.2.3 Results

Behavioural results

I used behavioural data to assess whether participants performed the task similarly, as well as the effects of change type on performance among young people. The top left chart included in *figure 6.2*, represents each participant's overall VPM performance, in terms of mean proportion of trials correct across the four sessions. As shown, there was, of course, some inter-individual variability in performance, but overall performance was quite similar. The other three charts included in the same figure summarise the sample's mean performance across the four change types; switch-to-place (S-P), switch-to-response (S-R), reverse-place (R-P) and reverse-response (R-R). As in previous studies, blocks following a block during which the correct strategy was not learned were excluded. Performance was assessed in terms of the same measures used in Chapter Four (section 4.2.3); trials correct (*figure 6.2 top right*), blocks learned (*bottom left*) and stable trials (*bottom right*). As illustrated, each measure indicated that participants performed worse during switch-to-place and particularly switch-to-response trial blocks than throughout reverse-place and reverse-response blocks.

Overall performance ranged from 81.14% to 92.76% across participants, so all performed well above chance (50%). Mean trials correct was 87.74% and standard deviation in performance was 4.43%, so all participants performed within 1.5 SDs of the group mean, well within most outlier definitions. All seven remaining participants were therefore included in subsequent analyses. A one-way ANOVA then revealed a significant main effect of change type on trials correct ($F_{3,24}$=3.94, p=.020), and post-hoc tests confirmed that participants performed significantly worse during switch-to-place blocks than during reverse-place blocks (t_6=5.45, p_{HB}=.006), and throughout switch-to-response blocks compared to both reverse-place (t_6=6.96, p_{HB}=.003) and reverse-response blocks (t_6=5.72, p_{HB}=.006), suggesting that participants found switches more difficult than reversals.

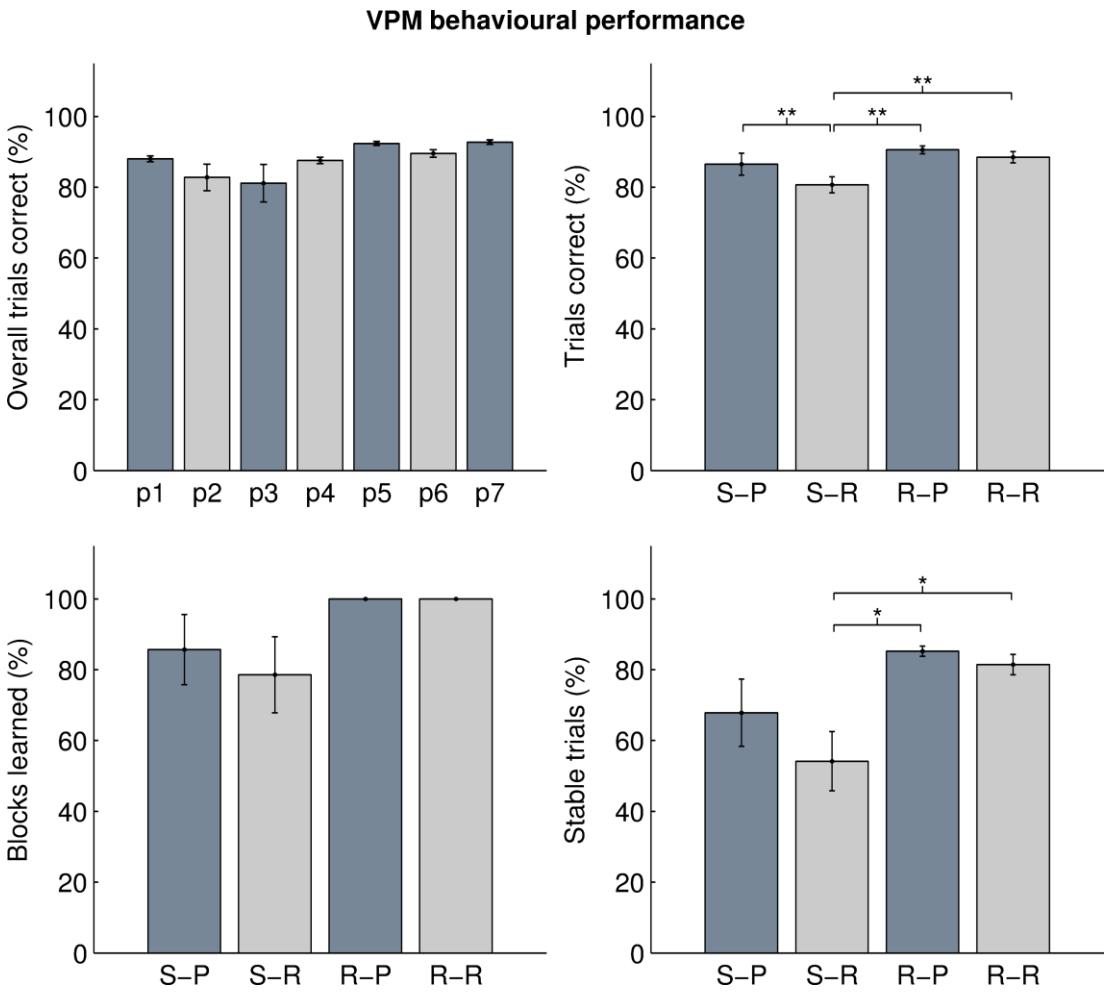

Figure 6.2 VPM behavioural performance. *Top left:* Overall trials correct by participant. Error bars represent SEM across sessions. *Top right:* Trials correct by change type; S-P=switch to place; S-R=switch to response; R-P=reverse place; R-R=reverse response. Error bars represent SEM across participants. *Bottom left:* Blocks learned by change type. *Bottom right:* Stable trials by change type.

Participants always learned the correct strategy after a reversal, but sometimes failed to do so following a switch, again indicating that they found switches more difficult. However, the effect of change type on blocks learned was not significant ($F_{3,24}$=2.15, p=.120). On the other hand, there was significant main effect of change type on stable trials ($F_{3,24}$=4.67, p=.011), and post-hoc tests confirmed that switch-to-response performance differed significantly from reverse-place (t_6=3.75, p_{HB}=.047) and reverse-response (t_6=4.57, p_{HB}=.023) performance. Again, this suggests that participants found switches harder than reversals. However, stable trials performance during switch-to-place blocks did not differ significantly from reverse-place (t_6=1.86,

Switching v stable in dlPFC

Trial phase	ROI	Cluster	Peak		
			x, y, z	T	p_{FWE}
Pre-decision	Left dlPFC	97	-30, 38, 31	4.81	.913
		12	-6, 50, 28	4.39	.959
		11	-3, 32, 31	3.10	1.000
		2	-6, 56, 1	3.03	1.000
	Right dlPFC	28	3, 41, 28	8.06	**.067**
		47	36, 32, 43	7.76	**.083**
		33	33, 44, 19	5.23	.675
		22	6, 59, 1	4.26	.970
Post-decision	Left dlPFC	27	-33, 35, 34	4.38	.955
		18	-15, 32, 46	3.62	.995
		5	-9, 47, 25	3.62	.995
		12	-18, 50, 37	3.33	.998
		9	-3, 53, 10	2.99	1.000
		2	-3, 62, 28	2.27	1.000
		2	-3, 53, 22	2.20	1.000
		2	-33, 47, 28	2.16	1.000
		3	-27, 44, 40	2.16	1.000
	Right dlPFC	21	33, 41, 37	5.69	.438
		9	33, 47, 19	4.30	.963
		15	6, 53, 25	3.79	.991
		11	3, 59, -8	3.51	.997
		2	45, 44, 22	2.86	1.000
		2	9, 65, 16	2.84	1.000
		2	6, 59, 31	2.63	1.000
Outcome	Left dlPFC	191	-36, 35, 37	6.84	.166
		48	-6, 35, 37	5.40	.578
	Right dlPFC	161	45, 47, 10	6.12	.300
		11	3, 59, -8	5.48	.532
		29	6, 29, 37	4.54	.896
		3	3, 26, 55	3.89	.972

Table 6.1 Switching v stable in dlPFC. Clusters of multiple neighbouring voxels within left and right dlPFC showing significant activation differences between strategy switching and stable strategy periods at p<.05 (uncorrected). The coordinates (in normalised mm), effect sizes and FWE corrected p values (corrected within each ROI using SVC) are included for the peak voxel of each cluster. Peak activation differences close to achieving significance (p_{FWE}<.1) are shown in bold.

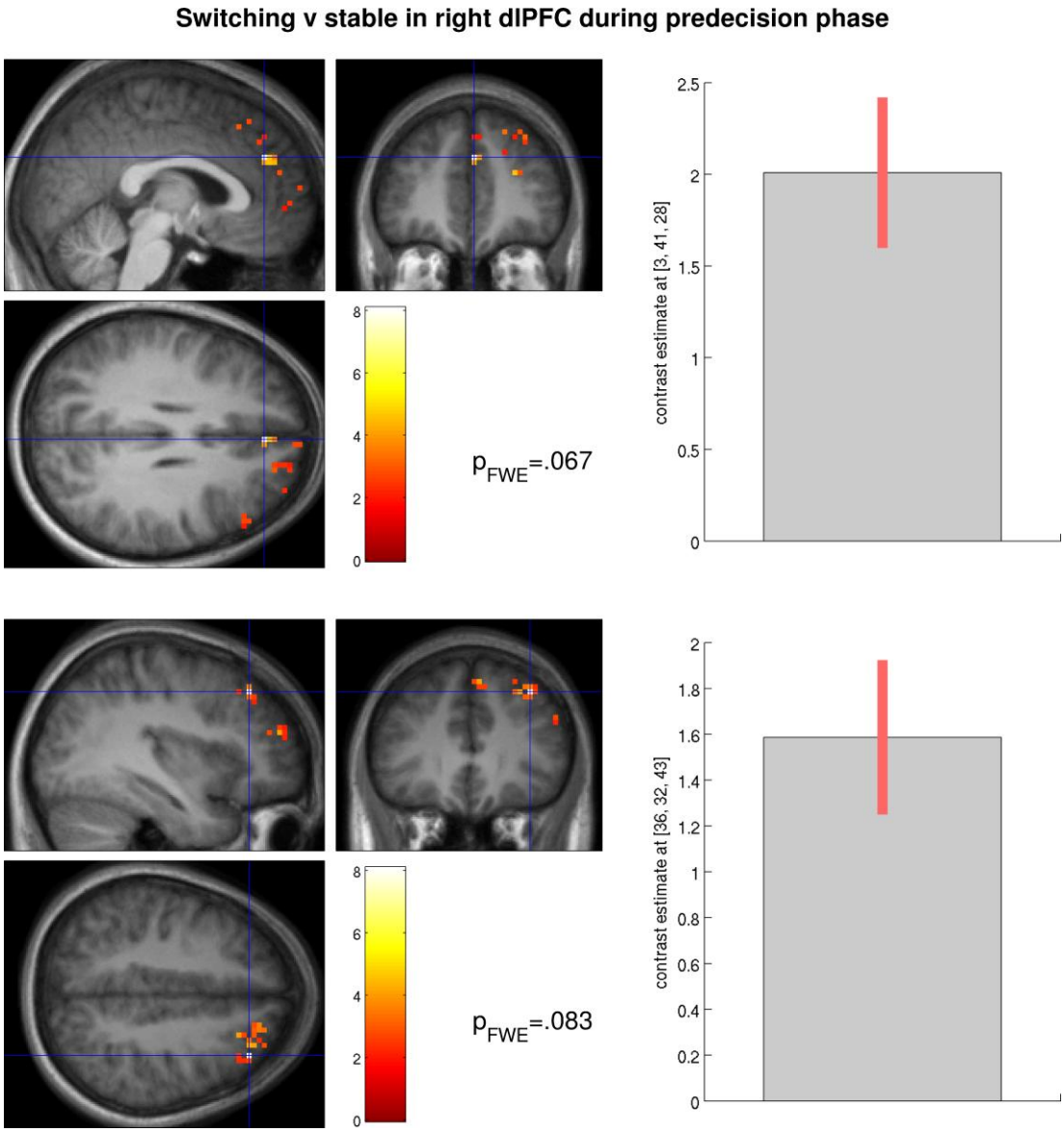

Figure 6.3 Switching v stable in right dlPFC (masked) during pre-decision phase. Clusters of greater than five voxels within dlPFC showing a significant activation difference between switching and stable periods at p<.05 (uncorrected) are marked in colour. The crosshairs in the top and bottom images are centred on the peak voxels of the two clusters closest to achieving significance following SVC. Contrast estimates at these points are depicted by the accompanying bar charts on the right.

p_{HB}=.224) or reverse-response (t_6=1.97, p_{HB}=.290) blocks, demonstrating that, in terms of this measure at least, the difference in apparent difficulty between switches and reversals depended upon the direction of the switch.

Switching v stable in OFC

Trial phase	ROI	Cluster	Peak x, y, z	Peak T	Peak p_{FWE}
Pre-decision	Left OFC	8	-36, 20, 14	4.06	.536
		2	-24, 23, 17	3.30	.995
		11	-6, 50, 8	3.19	.997
	Right OFC	4	24, 47, -14	3.08	.998
		5	27, 20, -17	2.91	.999
		3	21, 29, -14	2.36	1.000
		6	33, 23, -11	2.35	1.000
		2	9, 50, -5	2.26	1.000
Post-decision	Left OFC	12	-21, 38, 14	4.86	.227
		10	-27, 20, -11	3.66	.853
		18	-9, 50, -8	3.49	.989
	Right OFC	3	27, 20, -20	4.17	.449
		7	21, 32, -14	3.60	.870
		11	3, 41, -11	3.42	.991
		5	3, 56, -8	3.04	.998
		2	12, 38, -5	2.74	.999
		7	30, 38, -8	2.49	1.000
Outcome	Left OFC	26	-33, 23, -11	5.44	.128
		11	-12, 50, 5	2.81	.996
		5	-30, 35, -17	2.68	.998
		2	-3, 47, -11	2.63	.998
		2	-9, 35, -11	2.35	.999
	Right OFC	6	24, 47, -14	5.85	**.084**
		15	12, 38, -5	5.38	.130
		39	36, 26, -5	4.96	.196
		6	3, 56, -5	2.95	.995
		2	33, 26, 1	2.91	.996

Table 6.2 Switching v stable in OFC. Clusters of voxels within left and right OFC showing significant activation differences between strategy switching and stable strategy periods at p<.05 (uncorrected). The coordinates (in mm), effect sizes and FWE corrected p values (corrected within each ROI) are included for the peak voxel of each cluster. Peak activation differences close to achieving significance (p_{FWE}<.1) are shown in bold.

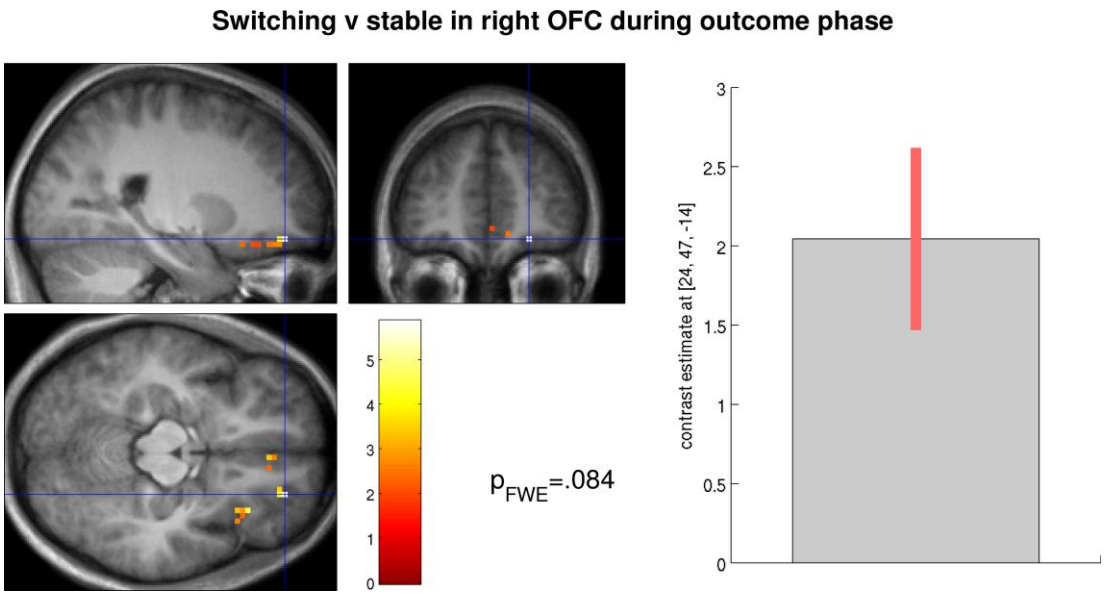

Figure 6.4 Switching v stable in right OFC (masked) during outcome phase. Clusters of greater than five voxels within OFC showing a significant activation difference between switching and stable periods at p<.05 (uncorrected) are marked in colour. The crosshairs are centred on the peak voxel of the cluster closest to achieving significance following SVC. The contrast estimate at this point is depicted by the bar chart on the right.

fMRI gLM results

I investigated differences in activation between switch learning and stable strategy periods throughout three trial phases – pre-decision, post-decision and outcome – for each participant using first level gLM analyses in SPM. I then entered these results into second level analyses in order to assess activation differences that were consistent throughout the sample. I identified clusters of voxels showing significant activation differences at p<.05 (uncorrected) within ROIs, then used SVC to correct for FWE within these ROIs. Results for left and right dlPFC are summarised by cluster in *table 6.1*, showing that no activation differences remained significant after SVC. However, those clusters showing the largest differences, and closest to achieving significance (p_{FWE}=.067; p_{FWE}=.083), were identified in right dlPFC during the pre-decision phase. These two clusters are depicted in *figure 6.3*, mapped onto a group average T_1-weighted anatomical image, each alongside a bar chart showing the effect size for the same peak voxel.

Switching v stable in ACC

Trial phase	ROI	Cluster	Peak		
			x, y, z	T	p_{FWE}
Pre-decision	Left ACC	37	-6, 29, -8	3.98	.546
		5	0, 32, 13	2.38	.981
	Right ACC	14	6, 11, 37	4.39	.384
		21	3, 29, -11	4.33	.410
		3	3, 32, 22	2.29	.993
Post-decision	Left ACC	1	-6, 29, -8	4.39	1.000
	Right ACC	40	3, 26, -11	4.88	.230
		4	6, 11, 40	2.50	.983
		2	6, 2, 31	1.86	.993
Outcome	Left ACC	55	-6, 41, 1	6.51	**.047**
		13	-3, 26, 25	3.85	.635
		9	-6, 11, 37	3.43	.758
	Right ACC	42	3, 29, -11	4.39	.385
		51	6, 35, 16	4.01	.588

Table 6.3 Switching v stable in ACC. Clusters of voxels within left and right ACC showing significant activation differences between strategy switching and stable strategy periods at p<.05 (uncorrected). Clusters of one voxel are included only where no larger clusters were identified. The coordinates (in mm), effect sizes and FWE corrected p values (corrected within each ROI) are included for the peak voxel of each cluster. Significant peak activation differences at p_{FWE}<.05 are shown in bold.

Results were similar for OFC. As summarised in *table 6.2*, numerous clusters of voxels showed switching-stable activation differences in left and right OFC before correcting for FWE. But again, after SVC, these differences did not remain significant. In right OFC, the peak activation difference in one cluster was relatively close to achieving significance during the outcome phase (p_{FWE}=.084). This cluster's peak voxel is shown on the group average structural image in *figure 6.4*, with effect size represented by the accompanying bar chart.

Table 6.3 summarises results for ACC. Again, numerous clusters were identified

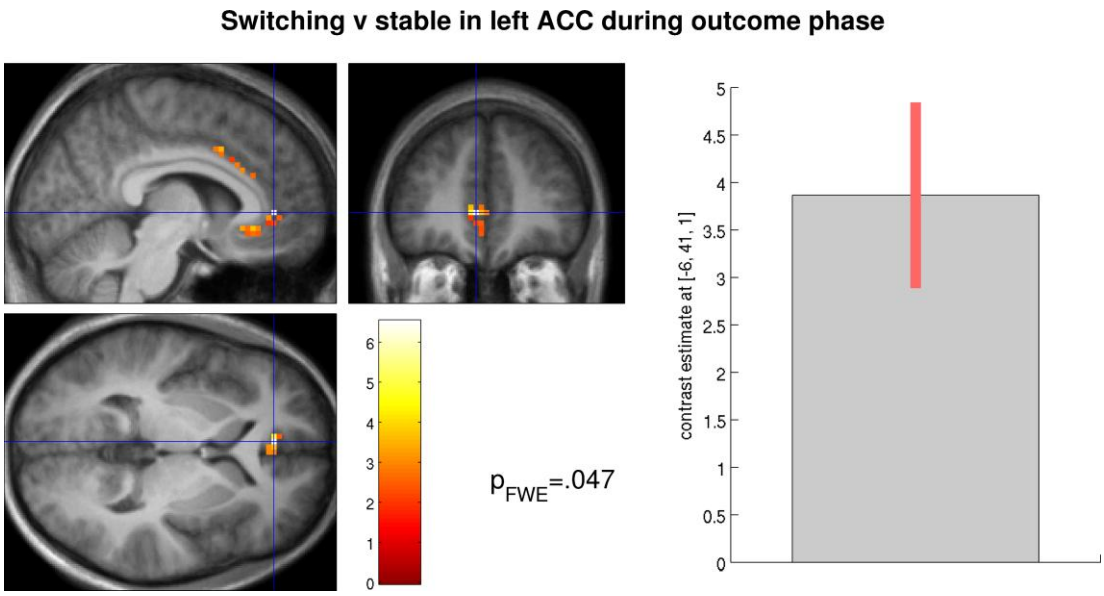

Figure 6.5 Switching v stable in left ACC (masked) during outcome phase. Clusters of greater than five voxels within ACC showing a significant activation difference between switching and stable periods at p<.05 (uncorrected) are marked in colour. The crosshairs are centred on the peak voxel that still showed a significant activation difference after SVC. The contrast estimate at this point is depicted by the bar chart on the right.

before FWE correction, but most activation differences did not remain significant after SVC. However, in left ACC, also during the outcome phase, the peak activation difference within one cluster did remain significant (p_{FWE}=.047), providing evidence in support of ACC's involvement in error detection. This cluster's location and the effect size of its peak voxel's activation difference are illustrated in *figure 6.5*.

I also assessed differences in activation between place and response blocks, during stable periods only, and throughout the same three trial phases. Second level analyses again identified some clusters of voxels showing activation differences within ROIs – left and right hippocampus and caudate nucleus – summarised in *table 6.4*. However, fewer clusters were identified even before SVC, and no peak activation differences remained significant after FWE correction. These results therefore did not support the role of the hippocampus in use of the allocentric place strategy, nor that of the caudate nucleus in use of the egocentric response strategy.

Place v response in hippocampus and caudate

Trial phase	ROI	Cluster	Peak		
			x, y, z	T	p_{FWE}
Pre-decision	Left hippo.	1	-30, -25, -14	2.54	.860
	Right hippo.	4	36, -31, -8	2.82	.790
	Left caudate	3	-6, 8, 10	2.67	.815
	Right caudate	1	21, -25, 22	1.99	.933
Post-decision	Left hippo.	-	-	-	-
	Right hippo.	1	36, -31, -11	2.16	.920
	Left caudate	8	-9, 5, 7	3.20	.712
		3	-18, 14, 10	2.61	.842
	Right caudate	12	12, 2, 13	3.74	.591
		2	21, -25, 22	2.73	.826
Outcome	Left hippo.	7	-27, -13, -17	3.31	.715
	Right hippo.	2	36, -31, -11	1.99	.940
	Left caudate	2	-6, 8, 7	2.23	.908
	Right caudate	-	-	-	-

Table 6.4 Place v response in hippocampus and caudate. Clusters of voxels within left and right hippocampus and caudate nucleus showing significant activation differences between place and response stable strategy periods at $p<.05$ (uncorrected). Results for caudate are actually derived from a response v place contrast. Clusters of one voxel are included only where no larger clusters were identified. Where no voxels showed significant activation differences, no clusters are listed. The coordinates (in mm), effect sizes and FWE corrected p values (corrected within each ROI) are included for the peak voxel of each cluster. No activation differences were close to achieving significance following SVC.

fMRI MVPA results

After identifying few significant effects of strategy switching and no significant differences between strategies within ROIs using a mass univariate approach, I used MVPA to explore the data further. Firstly, I decoded forward linear and rotational movement from V1, simply to verify the analytical procedure. As shown in *table 6.5*, the classifier was able to decode movement direction well above chance level for all participants.

Classification of movement type in V1

Participant	1	2	3	4	5	6	7
Accuracy	.64	.83	.79	.76	.88	.92	.93
p	**<.001**	**<.001**	**<.001**	**<.001**	**<.001**	**<.001**	**<.001**

Table 6.5 Classification of movement type in V1. Forward/rotation decoding accuracies and associated p values are included for each participant. Bold font represents classification performance significantly better than chance (p<.001, uncorrected).

I then applied the same technique to switching status (switching/stable) across all trial blocks following a switch, in prefrontal ROIs. As shown in *table 6.6*, the classifier was able to decode strategy switching during the outcome phase from participant 4's dlPFC (59.84%, p=.007) and ACC (54.18%, p=.018) data, and during the pre-decision phase from participant 6's dlPFC (68.63%, p=.002) and OFC (68.6%, p=.010) data. The classifier did not perform above chance level for any ROIs during other trial phases for those participants, or during any trial phase for any of the other participants.

I next attempted to classify strategy change type (switches/reversals) during learning periods in dlPFC, OFC and ACC. Results are summarised in *table 6.7*. The classifier was able to decode change type from participant 1's dlPFC data during the post-decision trial phase with 63.30% accuracy, which was significantly better than chance (p=.003). It was also able to decode change type from participant 2's dlPFC (58.64%, p=.041) and OFC (58.64%, p=.028) data during the post-decision phase, and from OFC during the outcome phase (69.75%, p=.039). However, in all other ROIs, trial phases and for all other participants the classifier performed at (or below) chance level.

By the same method, I then tried to classify strategy (place/response) during stable strategy periods in hippocampus and caudate nucleus. Strategy was successfully decoded from hippocampal data for participant 3 during pre-decision (56.50%, p=.006) and post-decision (54.12%, p=.007) trial phases, as shown in *table 6.8.*

Classification of switching status in PFC

Trial phase	dlPFC		OFC		ACC	
	Accuracy	p	Accuracy	p	Accuracy	p
Pre-decision	.47	.882	.49	.867	.53	.069
	.20	.999	.21	.578	.45	.467
	.51	.740	.47	.870	.52	.759
	.53	.262	.55	.490	.55	.808
	.55	.525	.54	.858	.53	.271
	.68	**.002**	.73	.246	.68	**.010**
	.62	.659	.58	.419	.49	.307
Post-decision	.51	.134	.33	.950	.49	.883
	.26	.419	.20	.999	.47	.531
	.47	.455	.48	.922	.50	.994
	.44	.525	.49	.873	.43	.664
	.58	.537	.58	.153	.55	.746
	.61	.063	.57	.820	.62	**.044**
	.44	.482	.20	.883	.39	.564
Outcome	.50	.621	.52	.500	.51	.412
	.33	.297	.33	.577	.53	.240
	.45	.805	.50	.747	.48	.585
	.59	**.007**	.54	**.018**	.50	.116
	.53	.176	.49	.368	.53	.940
	.56	.272	.55	.312	.52	.313
	.55	.165	.52	.660	.55	.308

Table 6.6 Classification of switching status in PFC. Switching/stable decoding accuracies and associated p values are included for each ROI, for each trial phase and for each participant. Bold font represents classification performance significantly better than chance (p<.05, uncorrected).

However, hippocampal strategy classification was no better than chance for any other participants during any trial phase; nor could strategy be decoded from caudate data for any participant during any trial phase.

Finally, I assessed hippocampal prospective and retrospective coding by using MVPA to decode future location (east/west goal arm) from activity during movement along the start arm, and past location (north/south start arm) from activity during movement along the goal arm, respectively. As shown in *table 6.9*, the classifier was able to decode intended goal arm for participant 5 and remembered start arm for participant 4, but found no evidence of either prospective or retrospective coding for any other participants.

Classification of change type in PFC

Trial phase	dlPFC		OFC		ACC	
	Accuracy	p	Accuracy	p	Accuracy	p
Pre-decision	.52	.311	.48	.825	.53	.513
	.69	.222	.19	.999	.41	.393
	.41	.556	.35	.659	.36	.825
	.56	.336	.43	.416	.43	.828
	.41	.715	.47	.399	.53	.724
	.35	.992	.47	.932	.49	.688
	.37	.822	.40	.942	.36	.907
Post-decision	.63	**.003**	.53	.647	.44	.912
	.58	**.041**	.58	.623	.58	**.028**
	.35	.996	.38	.997	.35	.499
	.46	.834	.49	.698	.46	.377
	.56	.846	.48	.861	.41	.697
	.40	.789	.50	.604	.57	.637
	.53	.569	.46	.681	.49	.273
Outcome	.50	.541	.65	.751	.58	.352
	.86	.442	.64	.242	.69	**.039**
	.51	.803	.29	.621	.67	**.059**
	.51	.068	.57	.344	.43	.207
	.60	.191	.52	.999	.49	.151
	.40	.867	.40	.978	.48	.502
	.43	.861	.43	.417	.60	.266

Table 6.7 Classification of change type in PFC. Switch/reversal decoding accuracies and associated p values are included for each ROI, for each trial phase and for each participant. Bold font represents classification performance significantly better than chance (p<.05, uncorrected).

6.2.4 Discussion

Summary of findings

Behavioural results indicated that participants performed above chance level and similarly to each other at the VPM. Performance was also comparable to that of participants in studies using the VPM presented in previous chapters. Participants performed worse following a switch than following a reversal, particularly following a switch to the response strategy. Second level gLM analyses of fMRI data revealed a significant activation difference between switching and stable strategy periods during the outcome trial phase in an area of left ACC, as well as some differences close to achieving significance within right OFC during the same trial phase, and within right

Classification of strategy in hippocampus and caudate

Trial phase	Hippocampus		Caudate	
	Accuracy	p	Accuracy	p
Pre-decision	.50	.338	.43	.938
	.48	.999	.48	.999
	.56	**.006**	.53	.216
	.46	.761	.48	.694
	.48	.845	.53	.519
	.56	.067	.49	.655
	.47	.667	.50	.823
Post-decision	.49	.926	.51	.451
	.48	.999	.38	.975
	.54	**.007**	.52	.471
	.45	.829	.51	.856
	.50	.999	.49	.671
	.49	.801	.49	.633
	.53	.263	.48	.999
Outcome	.50	.498	.48	.766
	.48	.999	.48	.999
	.44	.683	.54	.735
	.48	.483	.47	.849
	.48	.834	.47	.535
	.45	.849	.54	.327
	.51	.387	.48	.493

Table 6.8 Classification of strategy in hippocampus and caudate. Place/response decoding accuracies and associated p values are included for each ROI, for each trial phase and for each participant. Bold font represents classification performance significantly better than chance ($p<.05$, uncorrected).

dlPFC during the pre-decision phase. However, there were no activation differences between place and response stable strategy periods within hippocampus or caudate nucleus. MVPA was also largely unsuccessful in decoding strategy switching, change type and strategy from the same ROIs. In each case there were classification accuracies that were significantly greater than expected by chance, but only for some ROIs during specific trial phases for particular participants. No effects were particularly strong or consistent across participants. In assessing prospective and retrospective coding, I was able to decode future and past locations from hippocampus each for only one participant. In contrast, using the same regressors and MVPA parameters, the classifier successfully decoded forward and rotational movement from V1 data for all participants.

Prospective and retrospective coding in hippocampus

Participant	1	2	3	4	5	6	7
Prospective	.51	.51	.49	.52	.57	.52	.44
	.789	.585	.762	.109	**.005**	.106	.859
Retrospective	.49	.49	.51	.57	.48	.57	.53
	.668	.892	.408	**.018**	.847	.124	.329

Table 6.9 Prospective and retrospective coding in hippocampus. Goal arm and start arm decoding accuracies and associated p values are included for the first movement and second movement phases, respectively, for each participant.

Interpretation of findings

The main findings of this study were the switching-related activation differences within dlPFC, OFC and ACC. Although these effects were weak, they are consistent with my original hypotheses, and provide some evidence in support of the role of dlPFC in strategy switching (Manes et al., 2002; Mansouri et al., 2006; Moore et al., 2009), as well as those of OFC and ACC in the related processes of reward processing (Tremblay & Schultz, 1999; Schultz et al., 2000; Rolls, 2000) and error detection (Carter et al., 1998; Botvinick et al., 2004; Carter & van Veen, 2007). This is in turn consistent with Aston-Jones and Cohen's (2005) model of the neural network underlying switching behaviour, and with previous work demonstrating that mPFC is responsible for navigational strategy switching in rodents (Ragozzino et al., 1999; Rich & Shapiro, 2007; Young & Shapiro, 2009). However, as above, the effects were not large, and, using MVPA, I was not consistently able to decode switching status or change type from the same ROIs. It may be that other areas of the brain are more important in navigational strategy switching, but considering the many other studies that have associated switching behaviour with PFC function (Dove et al., 2000; Monchi et al., 2001; Moll et al., 2002; Hampshire & Owen, 2006; Nyhus & Barceló, 2009), it seems more likely that the relative weakness of my findings can be attributed to methodological flaws, which I will discuss later.

I was unsuccessful in detecting consistent activation differences between place and

response strategy blocks, as well as in decoding strategy, within both the hippocampus and the caudate nucleus. These findings do not support my hypothesis and are at odds with previous research demonstrating changes in activity in hippocampus and caudate nucleus during allocentric and egocentric navigation. However, Hartley, Maguire, Spiers and Burgess (2003), for example, used a more complex task, which involved navigating a virtual town environment, either using an allocentric wayfinding strategy or an egocentric route-following strategy. It may be that the simpler allocentric and egocentric strategies used to complete the VPM are not specifically dependent on the hippocampus and caudate nucleus in the same way. On the other hand, Iaria, Petrides, Dagher et al. (2003) used a radial arm maze, which, while still slightly more complex than the VPM, involved similar place and response strategies, which they were able to associate with activity in the right hippocampus and caudate nucleus. One problem that is unlikely to have affected their task may have affected the VPM – in fact the variant of the VPM used in this study in particular. In this incarnation of the VPM, participants only ever started from one of two start arms, which means it would be quite easy for them to use two separate egocentric strategies during a place strategy block, with the view at the beginning of each trial serving as a visual cue for which strategy to use. In this event, participants may have relied more heavily upon the caudate nucleus to perform the task throughout the experiment, accounting for the lack of differences in activation. The additional visual cueing aspect of the task during place strategy blocks may well have caused a change in activation somewhere in the brain, just not in the hippocampus or caudate. Alternatively, the results could also be due to other methodological problems, discussed below.

I also found limited evidence of hippocampal prospective or retrospective coding, with the MVPA classifier performing significantly better than chance for only one participant in each case. These findings provide little support for my hypothesis that future and past locations could be decoded from hippocampal activity before and after making a response, and do not fully complement previous work on hippocampal prospective and retrospective coding (Ferbinteanu & Shapiro, 2003; Shapiro et al., 2006). While the limited results discussed above may be attributable to an unsuitable

task design, it seems less sensible to account for these results in the same way, as Ferbinteanu, Shirvalkar and Shapiro (2011) have previously demonstrated prospective and retrospective coding in the hippocampus using a plus maze task. However, this work was conducted in rodent subjects using electrophysiological techniques, which have much higher temporal resolution than fMRI, and detect signals from very small numbers of cells. According to Johnson and Redish (2007), prospective coding describes a very short signal, observed only during a very quick decision making process, which BOLD fMRI, due to masking by the HRF, may be unable to detect. Similarly, using fMRI to monitor activation of the millions of neurons in the hippocampus (West & Gundersen, 1990), it may not be possible to detect prospective or retrospective coding in a relatively small proportion of these cells.

The MVPA of movement type does not provide any insight into the neural mechanisms underlying navigational strategy switching, as the purpose of this analysis was merely to verify the findings of other analyses. The analysis served its purpose well because, as I used the same procedural code, the same MPVA parameters and the same trial phase regressors, the success in classification of forward and rotational movement confirms that the limited success in other analyses was not likely to have resulted from an error in choice or application of analytical procedure. Similarly, the typical behavioural findings confirm that participants performed normally at the VPM, remaining engaged with the task throughout the experiment (with the exception of one participant, whose fMRI data from the final session were excluded from analyses), suggesting that neural activity related to task performance should have been detectable.

Limitations

Second level gLM analyses revealed only a few effects of switching and none of using either strategy on activation within ROIs. A problem for second level analyses was of course the low number of participants, but then again, MVPA focuses on individual participants and still did not produce any consistent results. One other

major problem may have been the use of an event-related design, particularly because the early version of the VPM used in this study was too slow. Each trial involved a long period of movement to the central junction, a pause at the junction, and another long movement to the goal location, so that the trial took a total of 17s. During this time, participants only really had to engage in the task for a few brief moments. The most important of these was when they decided which direction to turn, which was arguably the only time they would have actually been using a strategy, or trying to engage a new one. This event could have happened in a fraction of a second, and at any time during the pre-decision trial phase, which was up to 8s long. It may be that any fleeting effects of switching or strategy use on activation in PFC, hippocampus or caudate were simply lost within this much longer time of disengagement from the task. Later variants of the VPM were improved in this respect by drastically reducing the amount of disengaged time during each trial, as described in Chapter Two (section 2.3.3) and in section 6.3.2.

Conclusion

Participants performed the VPM as expected, and second level gLM analysis of fMRI data revealed a significant overall activation difference within left ACC during the outcome phase, as well some slightly weaker differences in right dlPFC during the pre-decision phase and in right OFC during the outcome phase. These findings do provide some evidence to support that these regions are involved in navigational strategy switching, although I was unable to confirm this using MVPA. Similarly, I was unable to confirm that the allocentric place strategy is dependent upon the hippocampus, or that the egocentric response strategy is dependent upon the caudate nucleus. I successfully decoded future and past location from hippocampus each in only one case, providing limited evidence of prospective or retrospective coding. However, considering previous work demonstrating associations between various regions of PFC and strategy switching, as well as between hippocampus/caudate and allocentric/egocentric navigation, I think it is fair to attribute the limitations of my findings to methodological issues. In particular, I believe the temporal parameters of the VPM variant used in this study may have masked events of interest. One of the

important aspects of these findings is therefore that they highlight this problem, which helped me to improve the VPM for use in other studies, including a second planned fMRI study, as discussed in the next section of this chapter.

6.3 Study 8: Piloting a revised VPM for use with fMRI

6.3.1 Introduction

fMRI study designs

fMRI studies typically use either an event-related design or a block design. Event-related designs assess brief signal changes in response to individual trial events, whereas block designs explore activation differences throughout longer blocks of multiple consecutive trials of the same type (Gore, 2003; Aguirre, 2010). Event-related designs do not restrict the organisation of stimuli, which is important if trials have to be presented in a random order, or if they are retrospectively categorised according to the participant's response (Aguirre, 2010), making them useful for a wider variety of experimental paradigms (Gore, 2003). On the other hand, block designs have greater statistical power (Aguirre, 2010), meaning that, as long as stimuli can be organised in a block design, it should make it easier to detect an effect. Although the VPM uses blocks of place and response trials, in Study 7 it was organised in an event-related design, as I assessed activation changes in response to events that occurred at points during trial phases that were not grouped together but separated by other trial phases, as well as during trials that were later categorised based on participants' strategy learning performance. In this study I piloted a variation of the VPM organised in a block design.

Cued switching

In typical strategy switching tasks, including conceptual set-shifting tasks such as the Wisconsin Card Sorting Test (WCST; Berg, 1948), attentional set-shifting tasks (e.g.

Birrell & Brown, 2000), and the plus maze task (e.g. Ragozzino, 2007; Rich & Shapiro, 2007), participants change strategy in response to changes in reward, without being explicitly informed to perform a switch or reversal. However, task switching has been studied using cues to indicate when a switch is required, demonstrating that switch costs are still apparent (Kray et al., 2002; Arrington et al., 2007; Eppinger et al., 2007), and that older people are still impaired (Wasylyshyn et al., 2011). In Study 7, participants were only prompted to switch or reverse strategy if and when they noticed the change in reward. As described below, the VPM variant used in this pilot study utilised a block design, as well as specific instructions, explicitly indicating when participants were required to change strategy. While cueing strategy changes reduces the importance of reward monitoring in task performance, it still leaves participants to determine and engage the appropriate strategy in much the same way.

Current study

Despite the limited success of Study 7, I intended to complete a second fMRI study using both young and older participants. I planned to use a 7T scanner with higher spatial resolution in order to explore age differences in signal change within the LC, as well as in PFC, during navigational strategy switching. However, I first had to adapt the VPM to resolve the problems with it that became apparent following Study 7. The aim of this pilot study was to ensure that a new version of the VPM – organised in a block design, with much shorter trials and further changes, detailed below – was better suited to studying activity associated with navigational strategy switching using fMRI. With trial blocks divided into three sub-blocks, and specific instructions provided between sub-blocks, I expected that participants would learn the appropriate strategy during the middle sub-block. This would mean that they would be learning throughout the whole of the first sub-block and stably using the correct strategy throughout all of the last, allowing me to explore the effect of switching simply by comparing activity during the first and last sub-blocks.

6.3.2 Methods

Participants

Four (two female) Edinburgh and Magedeburg students were recruited as young participants (aged 23-30, M=25.5), and six (four female) research volunteers from the PPLS database were recruited as older participants (aged 63-78, M=70.3). Some of these participants did have previous experience of the VPM, but had not been tested on it for some time. All participants reported normal or corrected-to-normal vision and no known neurological disorders or cognitive deficits. They were reimbursed for their participation at a rate of £7 per hour.

Procedure

This study simply involved piloting a new version of the VPM, described below. The main task was also preceded by a VE familiarisation task, during which participants were allowed to visit each of the four goal arm locations until they felt that they knew where they were in relation to each other. Before beginning, participants provided informed consent and received instructions on completing the VPM. At the end of the experiment I also briefly discussed the purpose of the task with participants, including their perceptions of how their strategy learning related to the three sub-blocks.

VPM

The variation of the VPM used in this pilot study was one of the latest versions that I used throughout my doctoral studies, and differed substantially from the variant used in Study 7. The VE still consisted of a plus-shaped kerbed pathway on a grass-textured plain surrounded by mountain scenery, although there were no longer transparent walls around the pathway. The reward wells had also been removed from the original two goal arms (as all maze arms now served as both start arms and goal arms, as described below), with the reward signals simply appearing upon reaching

the correct goal arm. As in Study 5, I also placed landmarks at the end of maze arms; a log cabin, a playground, a small wood of trees and a car park.

As described in Chapter Two (section 2.3.3), I noticed two problems with the original plus maze paradigm, which I resolved by altering the VPM for my later studies. Firstly, in the original plus maze task, and in my earliest version of the VPM, following a reversal, participants were never rewarded for continuing to use the same strategy, whereas after a strategy switch, if they persevere with the previous strategy, they were still rewarded on 50% of trials. Secondly, only two start arms and two goal arms were used in the original task, which makes it possible to use two visually-cued response strategies instead of a place strategy during place trial blocks. By allowing participants a three-way choice at the junction, including the option to continue straight ahead, and by using two adjacent – rather than opposite – start arms during each trial block, I was able to ensure that participants were never rewarded for using the previous strategy following a switch, just as after a reversal (*figure 2.5*). I also used different start arms during each block, which meant that, while participants could still use two visually-cued response strategies during each block, they would at least be different across blocks, decreasing the likelihood of participants completing the task in this way. I decreased the likelihood further by facilitating the encoding of an allocentric representation of the VE in two ways; by introducing landmarks in addition to the mountain scenery, and by allowing participants time to explore the VE before completing the task.

Following on from the failure of Study 7, which I attributed largely to the excessively long trials with lengthy periods during which participants may have been disengaged from the task, I drastically reduced the length of trials in later versions of the VPM, particularly in the one piloted in this study. As shown in *figure 6.6*, trials were three times shorter, with much less time devoted to movement. The first movement and decision phases combined lasted only 2.5s, so participants likely used a much greater proportion of this time to decide on a response for that trial. Similarly, the outcome phase of the trial lasted only 1s, most of which would have been devoted to processing the appearance or absence of a reward signal.

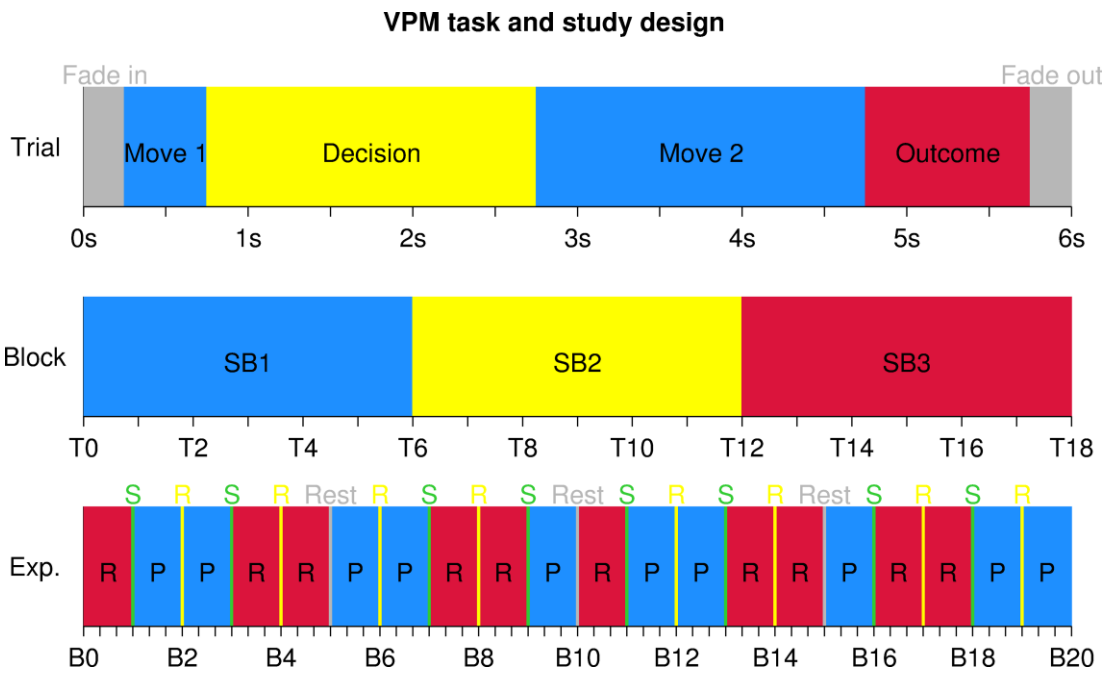

Figure 6.6 VPM task and study design. Timescales of a single trial in seconds (*top*), showing the four trial phases; of a block in trials (*centre*), incorporating the three sub-blocks; and of the experiment in blocks (*bottom*), comprising four sessions, 20 blocks and 16 changes.

I also used a block design in this pilot study. Between strategy switches and reversals I used blocks of 18 trials, divided into sub-blocks of six. At the beginning of the block, participants were instructed via an on-screen message to change strategy. At the beginning of the second sub-block, they were told which strategy they should be using, e.g. “turn left” or “go to the log cabin”. At the beginning of the third sub-block they were simply instructed to keep using the same strategy. I anticipated that participants would spend the entirety of the first sub-block switching or reversing strategy, would begin stably using the correct strategy at some point during the second sub-block, and would then continue to stably use the same strategy throughout the entirety of the last sub-block. The short trials and block design should have allowed me to explore the neural processes involved in navigational strategy switching simply by comparing activity during the first and third sub-blocks.

Data analysis

I used participants' responses to assess strategy learning throughout each block of 18 trials with the same Bayesian learning analysis used in Study 7 and described in Chapter Two (section 2.5.3). I recorded whether participants learned the strategy within the first, second or third sub-block, or whether they never learned the strategy, and reviewed how often each of these possibilities occurred, on average, for young and old participants. Initially, the most important thing to assess in this pilot study was whether or not the new block design worked, and I did not perform any further analyses into strategy, change type or group differences at this stage.

6.3.3 Results and discussion

Preliminary results

As above, it was important that participants consistently spent the entirety of the first six-trial sub-block switching or reversing strategy, and consistently spent the entirety of the last six-trial sub-block stably using the appropriate strategy. Therefore, for each block they were required to learn the strategy during the middle sub-block. As shown in *figure 6.7*, young participants acquired the appropriate strategy during the first sub-block most of the time (M=81.25%, SD=13.77%), as did older participants almost half of the time (M=45.00%, SD=6.32%). For the majority of remaining blocks, both young (M=15.00%, SD=15.81%) and old (M=31.67%, SD=12.91%) learned the strategy during sub-block two. Participants never (young: M=0%, SD=0%) or almost never (old: M=1.67%, SD=2.58%) learned the strategy during the final sub-block, and young participants rarely failed to learn the strategy at all (M=3.75%, SD=2.50%). However, older participants never learned the appropriate strategy for a relatively large proportion of blocks (M=21.67%, SD=8.17%).

Conclusion

The main finding of this pilot study was that, during the majority of trial blocks,

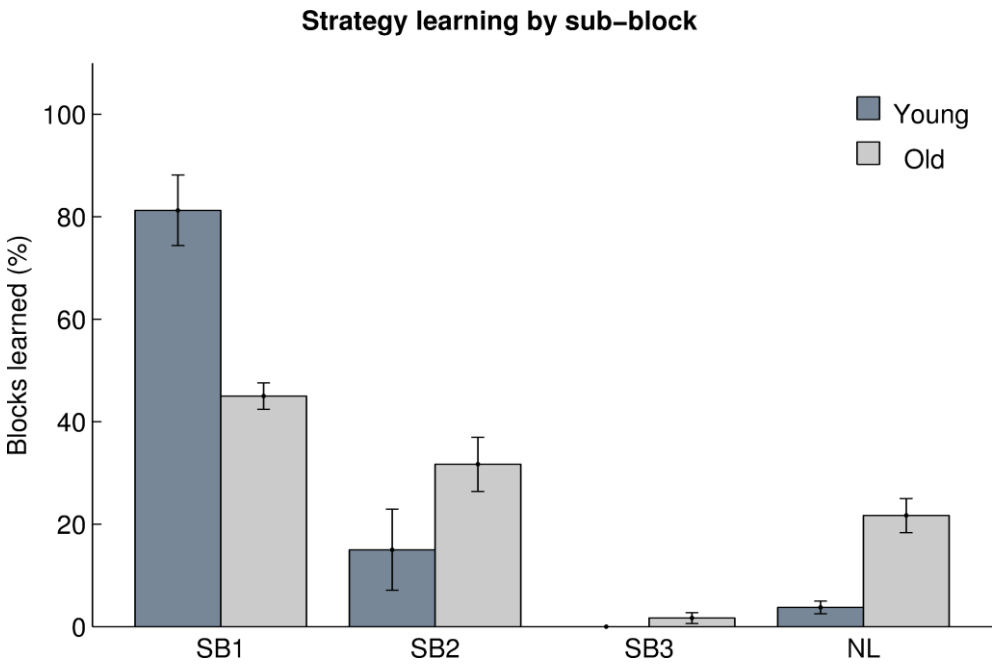

Figure 6.7 Strategy learning by sub-block. Mean proportion of blocks during which young and old participants learned the appropriate strategy during the first (SB1), second (SB2) or third (SB3) sub-block, or never learned the strategy (NL). Error bars represent SEM.

participants learned the correct strategy within the first sub-block. For the task to be useful in an fMRI study, it was critical that participants consistently learn the strategy during the second sub-block. In contrast to the original VPM, the variant used in this study avoided rewarding the previous strategy 50% of the time, provided additional landmark information, and even explicitly indicated when a strategy switch was required. While all of these changes served to ensure that participants were switching between allocentric and egocentric strategies when expected to, they also all made the task less difficult, and these preliminary findings suggest that it may have been too easy. It may be possible to increase the complexity of the task, by adjusting reward contingencies for example, in order to shift the point at which participants usually learned the strategy into the second sub-block, ensuring that participants consistently spent the entirety of the first sub-block switching or reversing strategy. However, it was also important that participants spent the third sub-block using the correct strategy, and on almost a quarter of blocks, older participants did not. While this may be consistent with a deficit in strategy switching, it is problematic for the

use of this task design in an fMRI study. Furthermore, increasing task difficulty in order to ensure that participants learned the strategy within the first sub-block less often would also probably increase the frequency with which older participants – and perhaps also younger participants – failed to learn the strategy before the last sub-block. I was forced to conclude that the revised VPM was unsuitable for use in a further fMRI study.

6.4 Chapter conclusion

In this chapter I presented an fMRI study of navigational strategy switching in young participants and a subsequent behavioural pilot study of a revised variation of the same task for use in a later fMRI study. In Study 7, I analysed fMRI data collected from young participants performing the original VPM. I explored the effects of strategy switching on activation within prefrontal regions thought to be responsible – together with the LC-NA system – for coordinating strategy switching, as well as the effects of strategy on activation within supporting structures, the hippocampus and caudate nucleus. Using MVPA, I attempted to decode strategy switching, strategy and change type in PFC, hippocampus and caudate, and also investigated hippocampal prospective and retrospective coding. Second level gLM analyses revealed a significant effect of switching on activation of an area within left ACC during the outcome phase, and weaker effects within right OFC, also during the outcome phase, and in right dlPFC during the pre-decision phase. These results are concordant with the role of these regions in component processes of navigational strategy switching; error detection, reward processing and decision making, respectively. However, the only other consistent results I found were in decoding forward and rotational movement from V1 data, which served only to verify my analytical procedures. My limited findings do support a prefrontal model of navigational strategy switching, but also draw attention to some issues with the original VPM regarding its suitability for fMRI experimentation.

I planned to conduct a second fMRI study, using both young and older participants,

in order to assess age differences in brain activity associated with strategy switching. I also intended to use a higher resolution 7T MRI scanner in Magdeburg to explore activation of LC, in addition to prefrontal regions. In Study 8, I piloted a variation of the VPM that I had adapted in numerous ways in order to circumvent the limitations of the original design identified in Study 7. The redesigned task used a block design, with each trial block split into three sub-blocks. It was important that participants spent the first sub-block learning the new strategy, successfully learned it at some point during the middle sub-block, and then spent the final sub-block stably using the correct strategy. Unfortunately, participants usually learned the strategy too early, during the first-sub block, suggesting that the task was too easy. However, older participants also failed to learn the strategy at all for many blocks, precluding any adjustment of the task designed to increase its difficulty. I had to conclude that the revised VPM was also unsuitable for fMRI experimentation, and I did not complete any further fMRI studies using the task.

In conclusion, my initial fMRI study provided some evidence in support of the involvement of the PFC-LC network in navigational strategy switching, although effects were weak, which I attribute to task design flaws. I redesigned the VPM for use in a second fMRI study, but pilot testing suggested that this version was also unsuitable. I was therefore unable to explore the contribution of age-related changes in functionality of the PFC-LC network to deficits in navigational strategy switching using fMRI. While I am sure it is possible to do so, it would require extensive further adaptation and fine-tuning of the VPM, or development of an entirely new task, which, regrettably, I was unable to incorporate into my PhD.

Chapter Seven
Noradrenergic Activity During Navigational Strategy Switching in Ageing

7.1 Chapter overview

In Chapters Four and Five, I reported several studies demonstrating an age-related deficit in switching to an allocentric navigational strategy. I have discussed this in terms of Aston-Jones and Cohen's (2005) model of switching behaviour, suggesting that dysfunction of the locus coeruleus-noradrenergic (LC-NA) system and/or prefrontal cortex (PFC) may underlie age-related navigational strategy switching impairments. As described in Chapter 6, I found some evidence in support of PFC's involvement in navigational strategy switching using functional neuroimaging, but I did not assess age differences in activation of PFC and LC. Study 5 did provide some evidence that navigational strategy switching deficits are at least partly attributable to prefrontal dysfunction, but, up until now, I have not addressed age differences in LC-NA function and their potential contribution.

In section 7.2, I present Study 9, in which I assessed the role of the LC-NA system in navigational strategy switching, and the contribution of LC-NA dysfunction to impairments in ageing. Using the virtual plus maze (VPM) to measure navigational strategy switching in young and old participants, I expected to replicate the findings of the behavioural studies presented in previous chapters. In order to assess LC-NA function throughout the task, I measured pupil size (PS), using eye-tracking equipment, and heart rate (HR), using a portable electrocardiographic device, or holter monitor. Changes in both PS and HR have been associated with LC-NA activity, so can be expected to respond to cognitive processes dependent upon LC-NA function. I hoped to confirm that these measures are useful proxy measures of LC-NA activity, and that the LC-NA system is involved in navigational strategy switching. Furthermore, I expected to see age differences in apparent LC-NA activity that related to navigational strategy switching impairments. For this study I received

assistance in use of eye-tracking equipment from Robin Hill, in use of electrocardiographic equipment from Dr Jeremy Langrish, and in data collection from Richard West.

Study 9 was the fifth study presented in this thesis that used the VPM to assess age differences in navigational strategy switching. To make use of the combined power of these five datasets, I have included a small meta-analysis as a final study in section 7.3. I assessed VPM performance in terms of trials correct, blocks learned and stable trials by age group and change type, exploring both the combined raw data and standardised effect sizes from the five studies. I hoped that this analysis would clarify the effects of ageing on navigational strategy switching and help to explain the discrepancies between the results of prior studies. I reconsider the findings of the original five studies in terms of the results.

7.2 Study 9: Noradrenergic activity during navigational strategy switching in ageing

7.2.1 Introduction

Recapitulation

In Studies 3, 5 and 6, using the VPM, I demonstrated a specific deficit in switching from an egocentric response strategy to an allocentric place strategy among older people. I have discussed this in terms of the noradrenergic model of switching behaviour (Aston-Jones & Cohen, 2005), which suggests that orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) monitor rewards, signalling to locus coeruleus (LC) when a behaviour becomes less profitable, which in turn changes its mode of output of noradrenaline (NA) to many brain regions, including prefrontal cortex (PFC). During the stable performance of a particular behaviour, the LC operates in a high-phasic low-tonic mode of NA output, promoting focused attention and task performance (Rajkowski et al., 1993, 1994; Minzenberg et al., 2008), while

the opposite high-tonic low-phasic mode promotes disengagement from a particular behaviour and the sampling of alternative strategies (Aston-Jones & Cohen, 2005). A subsequent shift back to the high-phasic mode is responsible for the activation of new functional networks (Bouret & Sara, 2005), and thus the engagement of a new strategy. During navigational strategy switching, this relates to the reweighting of inputs to PFC from the hippocampus and caudate nucleus (Doeller et al., 2008). The results of Study 6 were consistent with a prefrontal model of navigational strategy switching, and Study 5 provided some evidence of prefrontal dysfunction as the underlying cause of age-related deficits in switching to an allocentric strategy. However, I have not yet addressed the possibility that noradrenergic dysfunction also contributes.

Indirect assessment of locus coeruleus activity

The LC-NA system is also involved in coordination of the autonomic nervous system (ANS), particularly the sympathetic nervous system (SNS), associated with stress response and arousal (Samuels & Szabadi, 2008a, 2008b). SNS activity effects a variety of physiological changes, including pupil dilation and pulse elevation (Steinhauer et al., 2004; Bradley et al., 2008). Such physiological changes may therefore reflect changes in LC-NA activity. Indeed, artificial stimulation of LC does produce increases in pupil size (PS; Yu et al., 2004; Hou et al., 2005) and heart rate (HR; Berecek et al., 1984; Sved & Felsten, 1987), and several studies have also associated natural changes in LC activity with a pupillary response (Rajkowski et al., 1993; Gilzenrat et al., 2003; Kuipers & Thierry, 2013). These externally observable physiological changes may therefore serve as useful non-invasive proxy measures of LC-NA activity. In fact, pupil dilation has already been used to assess the role of NA in orienting attention (Gabay et al., 2011) and reward evaluation (Preuschoff et al., 2011), as well as disengagement of a behaviour and exploration (Gilzenrat et al., 2010; Jepma & Nieuwenhuis, 2011; Jepma et al., 2011); all involved in navigational strategy switching. However, this technique has not yet been used to investigate age differences in switching-related LC-NA function.

Current study

In Study 9, based on the above principles, I aimed to assess the role of NA in navigational strategy switching by measuring PS and HR as correlates of LC activity. I tested young and old participants on the VPM, using eye-tracking and electrocardiographic equipment to monitor PS and HR throughout. My hypotheses were that older participants would again demonstrate a specific deficit in switching to the allocentric place strategy, that both PS and HR would increase in response to changes in strategy, and, importantly, that the pupillary and cardiac responses of older participants to strategy changes, particularly to switches to the place strategy, would be lesser than those of young participants.

7.2.2 Methods

Participants

Twenty-eight (15 female) young (aged 19-30, M=22.6) and 28 (15 female) older (aged 60-79, M=70.2) were recruited from the university's student population, the local community and the existing PPLS database of research volunteers. Each was paid £7 for their participation, lasting approximately 1h. Many had previous experience of participating in research, none were known to suffer from any cognitive or neurological disorders, and all had normal or corrected-to-normal vision. One 69-year-old female withdrew from the experiment before completion and was therefore excluded from all analyses.

Procedure

All participants were fully informed about the details of the study and their rights as participants, and provided written consent before taking part. They then began by completing the MoCA to screen for MCI, but none were excluded on this basis. Following this, participants were fitted with eye-tracking and HR monitoring equipment, before completing the VPM. After completing the task, participants were

free to remove the eye-tracking and HR monitoring equipment. They were then asked to complete a two-item questionnaire on how difficult they found the task. Participants simply rated, on a scale of 0 to 10, how much mental effort they felt they had to apply throughout the task in general, and more specifically after a change in reward.

Equipment

Participants completed the VPM on a standard desktop computer, providing input via a standard keyboard, but, in contrast to previous studies, the task was displayed on a 21" standard aspect ratio (4:3) CRT monitor. As in previous studies, but of particular importance to this study, the experiment was conducted in an isolated, dimly lit room. PS was monitored throughout using the EyeLink II eye-tracking system, fitted and calibrated at the beginning of the experiment. PS was recorded in relative, arbitrary units (reflecting the number of pixels within the camera image covered by the pupil) at 500Hz. Cardiac activity was also monitored throughout the experiment by a Lifecard CF 3-channel holter monitor, also fitted and tested at the beginning of the experiment. The precise times at which heart beats occurred were logged, from which HR data could later be calculated. The system times of these pieces of equipment were synchronised at the beginning of every testing session.

Virtual plus maze

The VPM used in this study was set in the same VE as in other studies, featuring a plus-shaped pathway on a grassy plain, surrounded by mountain scenery. There were no transparent walls around the pathway and no reward wells at the end of goal arms. Participants were free to move straight ahead at the central junction, and started from two adjacent start arms, but always the same two. There were no landmarks at the end of goal arms, and no instructions signalling when to change strategy. Each trial lasted 5-8s, including a maximum decision time of 3s. The task included 13 blocks of 20, 25 or 30 trials, in a pseudorandomised order, producing a total of 320 trials, incorporating six strategy switches and six reversals. In this version of the VPM, the

reward for each trial was £0.02, so that the amount participants earned throughout the experiment approximated the actual reimbursement they received. This was intended to increase participants' motivation to perform well. However, at the end of the experiment, their virtual earnings were rounded up, so that all participants were paid the same amount.

Data analysis

VPM performance was represented in terms of trials correct, as well as stable trials, derived using the Bayesian learning analysis described in Chapter Two (section 2.5.3). A 24-year-old male and a 74-year-old female were identified as outliers, each performing more than 2.5 standard deviations below their respective group mean in terms of overall trials correct, and were therefore excluded from all further analyses. Increase in perceived mental effort (PME) during change periods was represented by a single figure, calculated as the difference between responses to the two questionnaire items.

PS data were preprocessed to remove and interpolate blink periods before analysis. A 22-year-old female participant's data included excessively long and numerous gaps, and were therefore excluded from all PS analyses. Following group comparisons of raw PS mean and variance, PS data were also z-scored by participant. HR data was calculated as the inverse of the intervals between individually recorded heart beats, then interpolated and resampled at a constant rate of 10Hz. A 22-year-old female, a 66-year-old male and a 74-year-old male exhibited abnormally high variability in HR (attributable to recording error, most likely due to poor connectivity), and were therefore excluded from all HR analyses. Again, data were z-scored by participant following initial group comparisons of HR mean and variance.

Following data preprocessing, I assessed the effects of age and task-related factors on measures of VPM performance, PS and HR, using mixed model ANOVAs and post-hoc t-tests with Holm-Bonferroni correction for multiple comparisons. I also explored relationships between behavioural and physiological variables by

calculating Pearson's correlation coefficient. Specific measures of pupillary and cardiac response are described in more detail in the following section.

7.2.3 Results

Behavioural performance

I first assessed behavioural performance, in terms of both trials correct and stable trials, across switch-to-place (S-P), switch-to-response (S-R), reverse-place (R-P) and reverse-response (R-R) change types. *Figure 7.1* represents mean trials correct (*top*) and stable trials (*bottom*) for young (red) and older (blue) participants for each of the four change types. As indicated by both charts, and as found in previous studies, older participants were impaired at switching to the place strategy. However, there were also similar, but slightly smaller, age differences in switching to the response strategy and in reversing the place strategy. The two age groups performed more similarly during reverse-response blocks.

A mixed model ANOVA, with age group and change type as factors, provided support for these findings. For trials correct, there were significant main effects of age ($F_{1,138}=14.91$, $p<.001$) and change type ($F_{3,138}=6.36$, $p<.001$) on trials correct, with a tendency towards a significant interaction between the two ($F_{3,138}=2.37$, $p=.073$). Post-hoc t-tests confirmed that these results were primarily due to the poorer performance of older participants during S-P ($t_{51}=4.33$, $pHB<.001$) and S-R ($t_{47}=4.79$, $pHB<.001$) blocks. The similar difference in performance throughout R-P blocks did not quite achieve significance ($t_{48}=2.31$, $pHB=.051$), although, surprisingly, older participants did perform significantly worse throughout R-R blocks ($t_{50}=2.17$, $pHB=.035$). I investigated whether these performance differences related to an age difference in perseverance with the previous strategy, but, as a percentage of all error trials, old ($M=58.18$, $SD=8.18$) actually made fewer perseverative errors than young ($M=67.43$, $SD=8.46$; $t_{51}=4.13$, $p<.001$).

A second mixed model ANOVA also revealed significant main effects of age

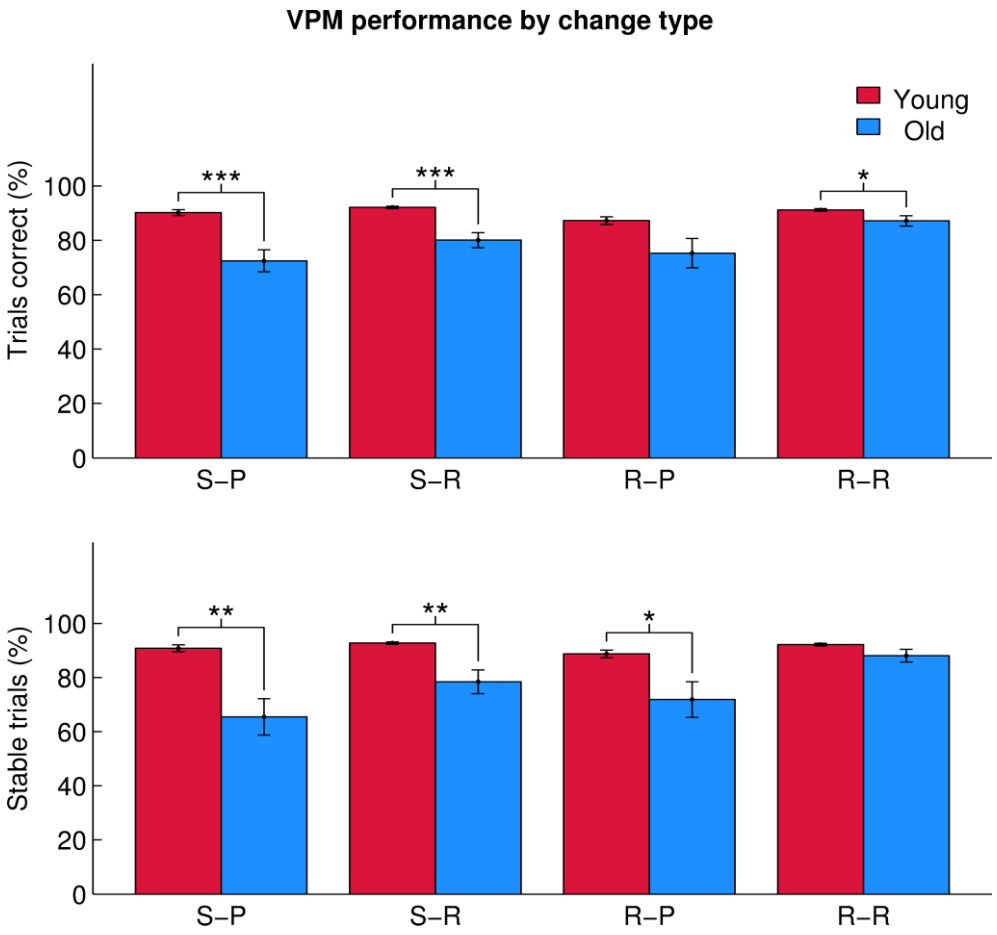

Figure 7.1 VPM performance by change type (switch-to-place, switch-to-response, reverse-place and reverse-response) in terms of percentage of trials correct (*top*) and stable trials (*bottom*) for young (red) and older (blue) participants. Error bars represent SEM. *, ** and *** represent significant age differences at p<.05, p<.01 and p<.001.

($F_{1,138}$=12.17, p<.001) and change type ($F_{3,138}$=5.38, p=.002) on stable trials, as well as a significant interaction ($F_{3,138}$=2.22, p=.008). Post-hoc t-tests confirmed that these results were due to the older group's impaired performance during S-P (t_{51}=3.77, p_{HB}=.002), S-R (t_{47}=3.61, p_{HB}=.002) and R-P (t_{48}=2.70, p_{HB}=.019) blocks, but not R-R blocks (t_{50}=1.77, p_{HB}=.083).

Pupil size

PS data were z-scored for each participant, so that I could average data across participants. *Figure 7.2* presents group timecourses for four-trial periods spanning

change points, averaged across all changes and participants. The illustrated time period runs from the onset of the outcome phase of the penultimate trial in each block preceding a change to the same point of the second trial of each subsequent block, marking the first movement (M1), decision (D), second movement (M2) and outcome (O) phases of the four trials in between. The change point, marked by the vertical dashed line, was defined as the beginning of the outcome phase of the first trial of each block, as the first indication to participants that the strategy had changed would have been the absence of the reward signal within this trial phase. The thick red and blue lines, representing mean PS, are surrounded by filled areas, representing two standard deviations either side of the mean. The thin horizontal red and blue lines represent mean PS throughout the two-trial periods before and after each change point. These lines, and *figure 7.3*, show that both groups exhibited an increase in PS in response to a strategy change, while *figure 7.4* represents this increase by change type, showing that PS increased in response to all change types. *Figure 7.5* summarises PS for young and older participants by trial phase, showing that PS was much higher throughout decision and outcome phases for both groups. As shown in *figure 7.6*, PS was highest during decision (*left*) and outcome (*right*) phases when the previous or current trial was not rewarded, but, during the decision phase, this effect was smaller for older participants. *Figure 7.7* illustrates that the strategy change-related increase in PS was not specific to the decision and outcome trial phases.

I performed numerous statistical analyses to corroborate these findings. Firstly, following preprocessing of PS data, but before z-scoring by participant, I found no significant age differences in mean PS (t_{50}=1.61, p=.114) or variance in PS (t_{50}=.70, p=.487). PS data were then z-scored for each participant before producing the averaged timecourses, *shown in figure 7.2*, and before performing any further analyses. I compared PS in the two-trial period following a change to the two-trial period immediately before, firstly across all changes, for each age group. A mixed model ANOVA with age group and change stage (before/after) as factors revealed a significant main effect of change stage ($F_{1,50}$=129.63, p<.001), but no significant effect of age ($F_{1,50}$=.56, p=.459) or interaction ($F_{1,50}$=.58, p=.451). Post-hoc tests confirmed that PS was significantly greater right after a change than just before, for

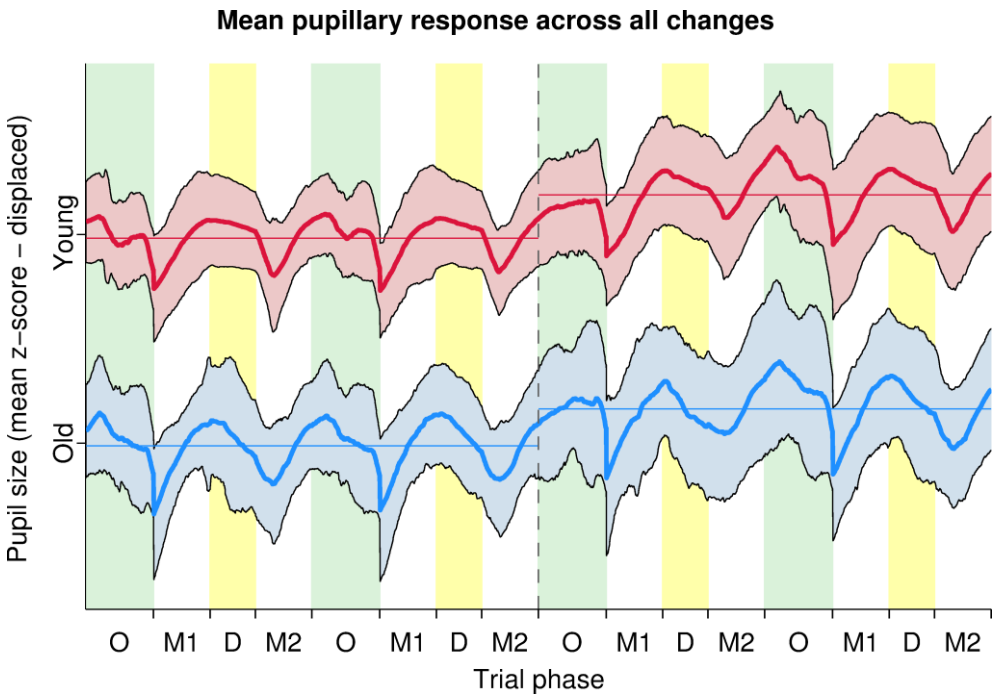

Figure 7.2 Mean pupillary response across all changes. Thick red and blue lines represent mean PS (z-scored) for each age group throughout the four-trial periods surrounding change points, resampled at 100Hz and averaged across all changes and participants. Surrounding filled areas represent all data within 2 SDs of the mean. Thin horizontal red and blue lines represent mean PS for the two trials immediately before and immediately after the change point, marked by a vertical dashed line. Trial phases (move 1, decision, move 2 and outcome) are also marked by background shading.

both young (t_{50}=9.40, p_{HB}<.001) and old (t_{50}=8.46, p_{HB}<.001) participants (*figure 7.3*).

To explore the effect of change type on this increase in PS, I then assessed differences in the mean increase in PS from the two trials immediately before each change to the two trials immediately after the change, relative to variability throughout the whole four-trial period. However, a two-way ANOVA revealed no significant main effect of age ($F_{1,43}$=.49, p=.487) or change type ($F_{3,129}$=.24, p=.869), nor a significant interaction between the two ($F_{3,129}$=1.22, p=.307), as, for both young and old groups, all change types were associated with a similar increase in PS (figure 7.4). I attempted to relate changes in PS to the behavioural data by assessing the correlation between relative mean PS increase (over all change types)

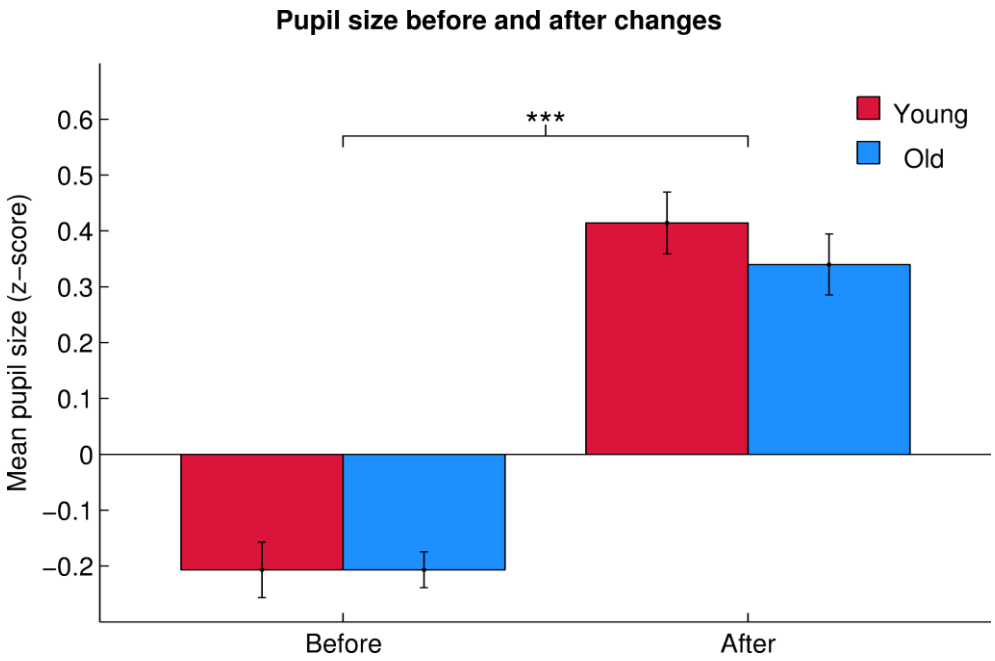

Figure 7.3 Pupil size before and after changes for young (red) and older (blue) participants. Error bars represent SEM. *** represents a significant difference at p<.001.

and overall VPM performance (in terms of trials correct). The two did not significantly correlate within either the young group (r=.319, p=.224) or the old group (r=.210, p=.304). I also assessed the relationship between relative mean increase in PS and change-related PME, but again found no significant correlation within the young (r=-.014, pHB=.946) or old (r=-.028, pHB=1.781) groups.

While PS increased in response to strategy changes, there were also more substantial fluctuations in PS throughout each trial (*figure 7.2*). I explored these fluctuations by splitting trials into four phases; the first movement to the central junction (M1), the decision at the central junction (D), the second movement to the goal location (M2), and the outcome at the goal location (O). A mixed model ANOVA demonstrated a significant main effect of trial phase ($F_{3,150}$=55.23, p<.001), but not of age ($F_{1,50}$=.012, p=.913), nor a significant interaction ($F_{3,150}$=.89, p=.448). This effect was due to significantly greater PS during decision and outcome phases than in movement phases (M1vD: t_{51}=10.03, p_{HB}<.001; M1vM2: t_{51}=1.28, $p_{HB=}$=.206; M1vO: t_{51}=6.36, p_{HB}<.001; DvM2: t_{51}=10.11, p_{HB}<.001; DvO: t_{51}=2.20, p_{HB}=.066;

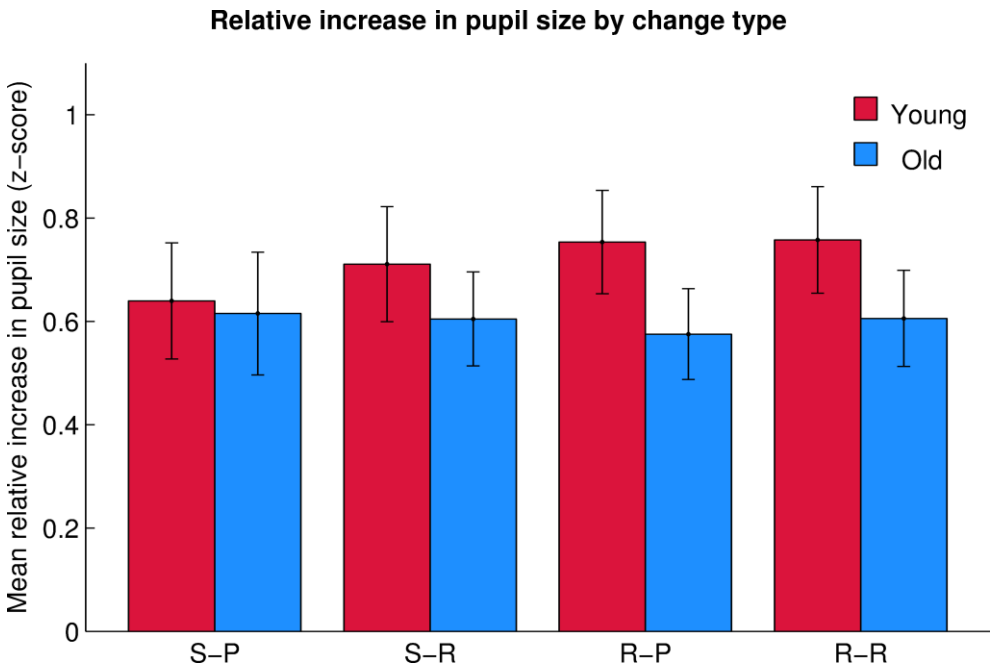

Figure 7.4 Relative increase in pupil size by change type (switch-to-place, switch-to-response, reverse-place and reverse-response) for young (red) and older (blue) participants. Error bars represent SEM. There were no significant age differences.

M2vO: t_{51}=10.18, p_{HB}<.001; *figure 7.5*) Further, I investigated how this effect related to reward, firstly assessing the effects of age and previous trial outcome (rewarded/not rewarded) on PS during the decision phase. There were significant main effects of both age ($F_{1,50}$=5.33, p=.025) and reward ($F_{1,50}$=90.99, p<.001), as well as a significant interaction ($F_{1,50}$=5.69, p=.021). PS during this phase was significantly greater among the young group than the old when the previous trial was not rewarded (t_{50}=2.69, p_{HB}=.020) but not when it was rewarded (t_{50}=.73, p_{HB}=.470). It was also significantly greater following an unrewarded trial than after a rewarded trial for both young (t_{25}=7.67, p_{HB}<.001) and old (t_{25}=5.69, p_{HB}<.001; *figure 7.6 left*). Similarly, I explored the effects of age and reward during the outcome phase of each trial, finding an effect of reward ($F_{1,50}$=212.15, p<.001), but no significant effect of age ($F_{1,50}$=.06, p=.815) or interaction ($F_{1,50}$=.31, p=.578). This effect was also due to significantly greater PS during the outcome phase of unrewarded trials compared to that of rewarded trials, again for both young (t_{25}=13.47, p_{HB}<.001) and old (t_{25}=8.46, p_{HB}<.001; *figure 7.6 right*).

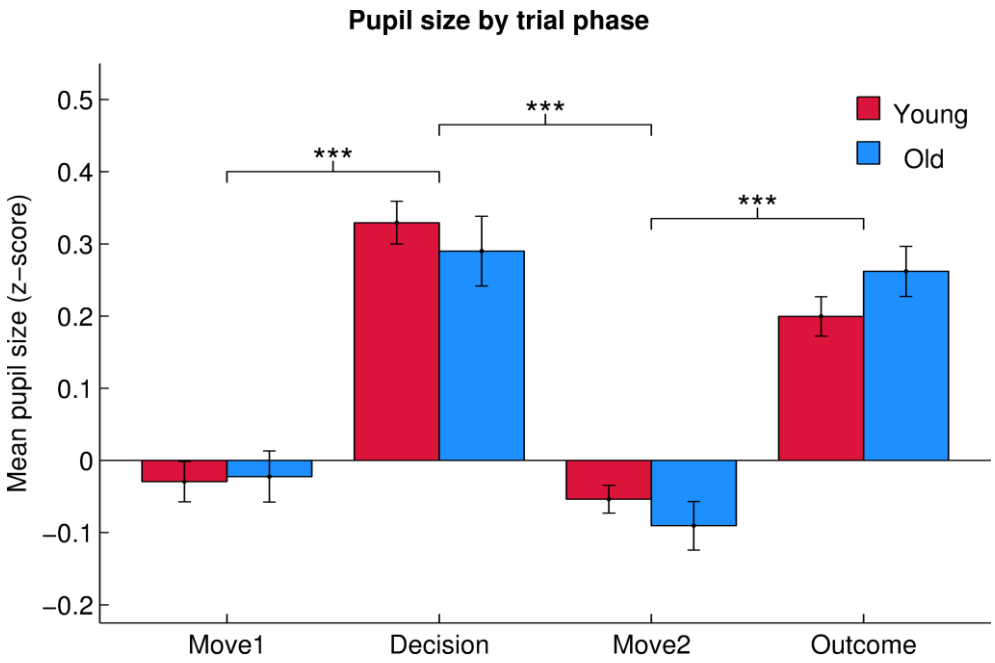

Figure 7.5 Pupil size by trial phase (move 1, decision, move 2 and outcome) for young (red) and older (blue) participants. Error bars represent SEM. *** represents significant trial phase differences at p<.001.

Having demonstrating that trial phase had a substantial effect on PS, I investigated how this related to strategy change-related increases in PS by assessing the effect of trial phase on relative increase in PS. A further two-way mixed model ANOVA again showed no significant effect of age ($F_{1,50}$=.13, p=.721), but also no significant effect of trial phase ($F_{3,150}$=1.21, p=.308) and no significant interaction ($F_{3,150}$=.74, p=.528). This indicates that the increase in PS induced by strategy changes was consistent throughout the trial (*figure 7.7*). Overall, PS increased in response to strategy changes, decision and outcome trial phases, and the absence of a reward signal, with an age difference in the effect that reward absence had upon PS during the following decision phase.

Heart rate

HR data are summarised in figure 7.8, showing group timecourses around change points, averaged across all changes and participants, as for PS data. However, as

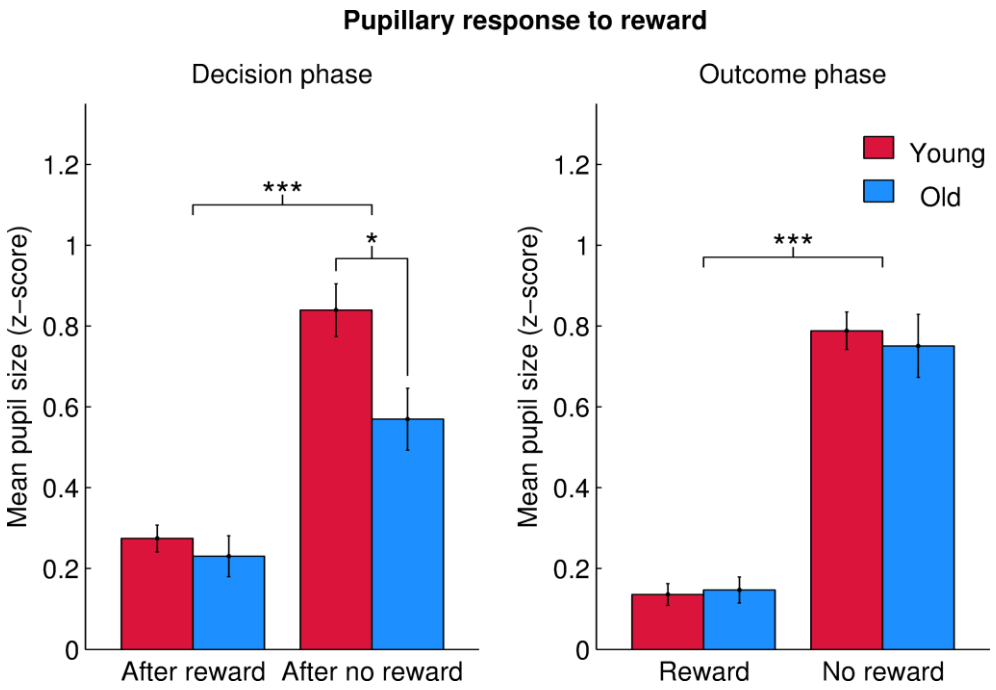

Figure 7.6 Pupillary response to reward during decision and outcome phases for young (red) and older (blue) participants. *Left:* PS during the decision phase following rewarded and unrewarded preceding trials. *Right:* PS during the outcome phase of rewarded and unrewarded trials. Error bars represent SEM. ** and *** represent significant age differences at p<.01 and p<.001.

shown, HR was relatively stable throughout trials and in response to strategy changes. I interpolated HR data before analysis, resampling at a rate of 10Hz, so that higher rates were not over-represented. Following this, there was no significant difference in mean HR ($t_{48}=1.18$, $p=.243$), but the older group did show significantly less variance in HR ($t_{48}=2.18$, $p=.034$). I therefore z-scored HR data before performing further analyses, as for PS data. Although HR timecourses did not seem to illustrate any response to either trial events or strategy changes, a mixed model ANOVA suggested a significant main effect of change stage ($F_{1,48}=7.17$, $p=.010$), but not of age ($F_{1,48}=2.87$, $p=.097$), nor a significant interaction ($F_{1,48}=.81$, $p=.372$). HR tended to be lower after a change within the young group ($t_{25}=2.32$, $p_{HB}=.058$), but not the older group ($t_{23}=1.44$, $p_{HB}=.164$). A second ANOVA indicated that there were no significant effects of age ($F_{1,44}=2.67$, $p=.110$) or change type ($F_{3,132}=.70$, $p=.557$) on relative mean increase, nor a significant interaction ($F_{3,132}=2.31$, $p=.079$). As for PS, there were no significant correlations between

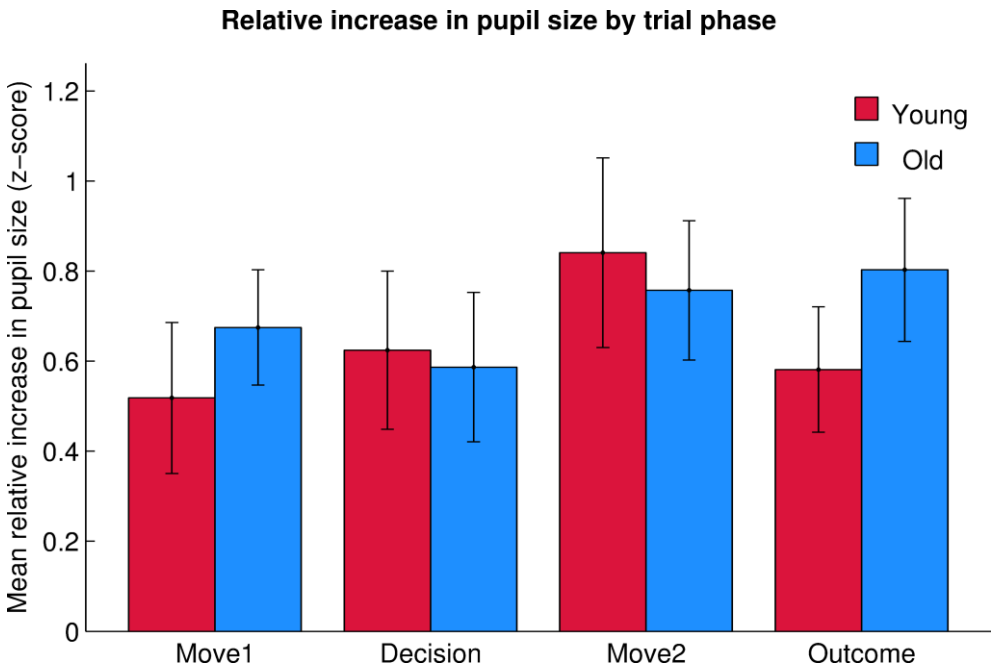

Figure 7.7 Relative increase in pupil size by trial phase (move 1, decision, move 2 and outcome) for young (red) and older (blue) participants. Error bars represent SEM. There were no significant age or trial phase differences.

relative mean increase in HR and overall VPM trials correct (young: r=-.381, pHB=.121; old: r=-.325, pHB=.139) or increase in PME (young: r=-.124, pHB=.556; old: r=.366, pHB=.248).

7.2.4 Discussion

Summary of findings

Older participants were impaired at switching to an allocentric strategy, and, although switches in the opposite direction – and, to a lesser extent, reversals – were also affected, switches to the allocentric strategy were most severely impaired. This did not relate to increased perseverance with a preceding strategy following a switch. In both groups, PS was significantly greater immediately after a change than immediately before, with no age differences within either period. Relative increase in PS was relatively consistent across all change types, and again showed no significant age differences. PS also significantly increased during decision and outcome trial

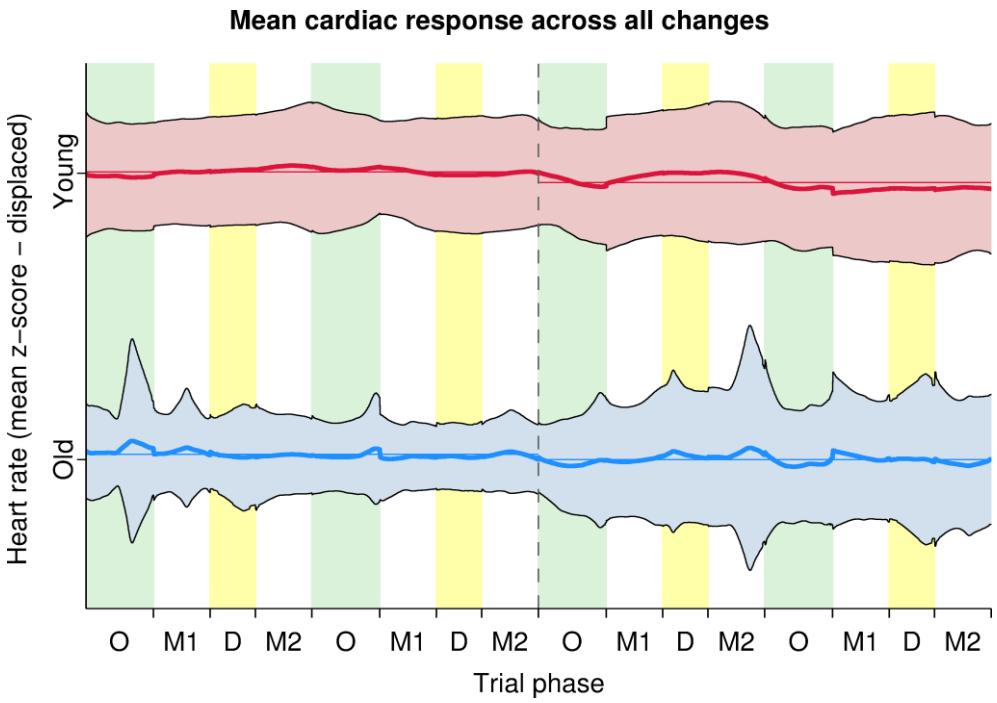

Figure 7.8 Mean cardiac response across all changes. Thick red and blue lines represent mean HR (z-scored) for each age group throughout the four-trial periods surrounding change points, resampled at 100Hz and averaged across all changes and participants. Surrounding filled areas represent all data within 2 SDs of the mean. Thin horizontal red and blue lines represent mean HR for the two trials immediately before and immediately after the change point, marked by a vertical dashed line. Trial phases (move 1, decision, move 2 and outcome) are also marked by background shading.

phases by comparison to movement phases, and this increase was significantly greater when the preceding/same trial was not rewarded. Absence of reward had a significantly smaller impact on the increase in PS during the decision phase of the following trial within the older group. HR seemed to show little response to trial events or strategy changes, although it did tend to be slightly lower after a change. Pupillary and cardiac responses to strategy changes did not correlate with either VPM performance or PME during strategy changes.

Interpretation of findings

The behavioural results of this study indicate that older people are impaired at switching to the place strategy, in concordance with the findings of several studies

presented in earlier chapters. However, in this study, switching to the response strategy, as well as reversals of one strategy or the other (depending on the measure of performance), were affected as well. In terms of trials correct, older people were impaired at switching to the place strategy and to the response strategy, as well as, to a lesser extent, reversing the response strategy. The significant difference in performance during reverse-response blocks may have been attributable to a ceiling effect, which reduced variance in both young and old groups. Aside from the lesser reverse-response deficit, these results indicate a general strategy switching deficit, rather than the more specific deficit observed in Studies 3, 5 and 6, although the age difference in switch-to-place performance was slightly greater than for switch-to-response. While this does not strictly adhere to my hypothesis, it is still in line with other previous work on age-related set shifting deficits (Moore et al., 2003; Ashendorf & McCaffrey, 2008; Young et al., 2010), and could still be explained in terms of the noradrenergic model of strategy switching (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005) and age-related dysfunction of the noradrenergic system (Manaye et al., 1995; Grudzien et al., 2007). The stable trials measure demonstrated impairments in switching to the place strategy, switching to the response strategy and reversing the place strategy, although switching to the place strategy still showed the greatest age difference. These results might be explained in terms of an allocentric processing deficit (Begega et al., 2001; Moffat et al., 2006; Antonova et al., 2009; Iaria et al., 2009) caused by hippocampal atrophy (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009), in addition to a general strategy switching deficit. The combined effect of these two impairments could account for the greater deficit in switching to the place strategy, and, reconsidering the results of Studies 5 and 6 in particular, perhaps even the apparent specific switch-to-place deficit. Although these behavioural results suggest a different effect of ageing on navigational strategy switching, they still confirm that it is impaired in ageing, and that switching to an allocentric strategy is most affected.

PS increased in response to strategy changes, as hypothesised, providing support for models suggesting the LC-NA system is involved in coordinating switching behaviour. In response to a change in reward, the LC is thought to switch to a high-

tonic mode of NA output (Aston-Jones & Cohen, 2005), promoting disengagement and the subsequent functional reorganisation of frontal neural networks (Bouret & Sara, 2005), but also producing autonomic effects, such as increased PS (Yu et al., 2004; Hou et al., 2005). The current results therefore further demonstrate the efficacy of measuring PS as an index of LC-NA activity (Sterpenich et al, 2006; Gilzenrat et al., 2010; Gabay et al., 2011). PS showed similar increases for switches in either direction, as well as for reversals of either strategy, suggesting that NA mediates reversals as well as strategy switches. This is consistent with previous work demonstrating that these two aspects of behavioural flexibility are closely related but differentiated within PFC (Rich & Shapiro, 2007; Young & Shapiro, 2009), as this suggests that the same upstream changes in LC's mode of NA output occur for each change type. It does seem inconsistent with previous studies showing that prefrontal NA depletion does not affect reversals (Tait et al., 2007; McGaughy et al., 2008), but, as these studies used the attentional set-shifting task (ASST) this may be attributable to a distinction between spatial and non-spatial reversals. In contrast to the behavioural results, there were no significant age differences in PS before or after a change, nor in relative increase for any of the four change types.

I also found that PS was significantly higher during the decision and outcome phases than throughout the movement phases of each trial. Considering that NA is also involved in decision making (Rogers et al., 2004; Doya, 2008; Baarendse et al., 2013), an increase in NA activity should be expected during the decision phase; therefore the observed increase in PS during this phase reaffirms that the change-related increases in PS did reflect increased NA activity. Similarly, reward processing is associated with changes in noradrenergic activity (Rogers et al., 2004; Aston-Jones & Cohen, 2005; Preuschoff et al., 2011), accounting for the pupil dilation during the outcome phase. However, while ageing has been associated with deficits in decision making (Denburg et al., 2005; Fein et al., 2007; Brown & Ridderinkhof, 2009; Eppinger et al., 2011) and reward processing (Marschner et al., 2005; Mell et al., 2005), there was no significant effect of age on PS during these trial phases. I also discovered that PS was significantly higher during decision and outcome phases when the previous or same trial was not rewarded than when it was, signalling that

the absence of reward was unexpected (Dayan & Yu, 2006; Preuschoff et al., 2011). However, during the decision phase following an unrewarded trial, older participants' PS was significantly lower, which may suggest that lack of reward had less bearing on older participants' next decision than on that of young participants. This might have affected the efficiency of their exploratory behaviour throughout LC high-tonic periods, perhaps contributing to a decrease in overall performance. However, it still does not explain the pattern of age differences in performance across the four change types.

Overall, the PS results are consistent with theory on (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005) and existing evidence for (Lapiz & Morilak, 2006; Tait et al., 2007; McGaughy et al., 2008; Snyder et al., 2012) the role of NA in strategy switching, thereby providing further support for the efficacy of PS as an indirect measure of LC-NA activity (Gilzenrat et al., 2010; Jepma & Nieuwenhuis, 2011; Preuschoff et al., 2011). However, as PS increases indicated that the LC-NA system was similarly involved in switches to and reversals of both strategies, and that there were no age differences in its response to any of the four change types, these data do not reflect my behavioural findings. I therefore argue that the navigational strategy switching impairments observed in this study and those presented earlier are not primarily attributable to LC-NA dysfunction. The results of this study indicate that, in ageing, the LC-NA system still functions to facilitate a change in behavioural strategy, when necessary, by innervating certain PFC regions, and therefore that it still receives the appropriate input from OFC and ACC in response to changes in reward. This suggests that brain regions involved in the switching process further downstream must be responsible for switching deficits. For example, prefrontal dysfunction, as observed in ageing (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011), might impair older people's ability to determine the most appropriate strategy to use. Alternatively, or additionally, reduced connectivity between PFC and other regions, such as hippocampus (Grady et al., 2003), may render older people less able to engage the appropriate strategy. However, as discussed above, the age difference in response to absence of reward within the decision phase of the following trial may reflect a subtle contribution of changes in

LC-NA function to deficits in deciding which strategy to engage.

Although HR was much less responsive to changes and trial events than PS, there was a subtle decrease in HR following a change. While this effect was in the opposite direction to that expected and demonstrated previously (Berecek et al., 1984; Sved & Felston, 1987), other work has suggested that LC innervation reduces HR (Stock et al., 1981; Miyawaki et al., 1991; Yao et al., 1999), so this result may still provide further evidence that NA is involved in mediating strategy changes. However, the effect was small and did not correspond to any significant post-hoc results, nor were there any differences in decrease between age groups or change types. It may be that the effects of task-related changes in LC-NA activity were masked by random variability, due to uncontrolled factors such as movement, or by greater individual differences in overall HR variance. Alternatively, changes in LC output mode may actually have less of an effect on HR than on PS. According to Samuels and Szabadi (2008b), increased LC output does increase HR, but this effect is compensated for by inhibition of the rostral ventrolateral medulla, producing a relatively small net effect in one direction or the other. Therefore, even though the current results do suggest that HR also responds to strategy changes, it may not be the most useful proxy measure of LC-NA activity.

Limitations

The most important limitation of this study was of course that PS and HR are only potential correlates of LC-NA activity. Following a change in strategy, PS did increase, and HR seemed to show a slight decrease, and I have reasonably inferred here that these effects reflected a change in LC's NA output mode from high-phasic to high-tonic. However, I cannot conclusively state that this change in LC output mode occurred during navigational strategy switching without having directly monitored LC activity. Unfortunately, due to the poor results of the pilot study presented in the previous chapter, I never did directly assess LC activity.

In summary, the behavioural results of this study provide further evidence that the ability to switch between navigational strategies – particularly (but not specifically) switching to an allocentric place strategy – is impaired among older people, contributing to widely reported age-related navigational deficits. The PS and HR data reaffirm that both measures – particularly PS – can be used to indirectly assess LC-NA activity, and confirm that the LC-NA system is involved in both switching and reversing strategies. However, age-related deficits in navigational strategy switching do not seem to be attributable to LC-NA dysfunction. Changes in PS reflecting decision making and reward processing further demonstrate the utility of PS as an indirect measure of LC activity, as well as the role of NA in these processes. Finally, a slight age difference in pupillary response to absence of reward suggests that subtle changes in LC-NA function may contribute to strategy switching deficits among older people by affecting their ability to correctly determine the optimal strategy to use. However, I conclude that age-related switching deficits must be more closely linked to reduced PFC functionality or connectivity than to LC-NA dysfunction.

7.3 Study 10: Virtual plus maze meta-analysis

7.3.1 Introduction

Study 9, presented in the previous section, was the seventh study included in this thesis that used a form of the VPM. Five of these studies (excluding those presented in Chapter Six) used comparable versions of the task to assess age differences in navigational strategy switching. I decided to make use of the combined power of these data sets by performing a meta-analysis on the findings. In this study, I therefore assessed the effect of change type on the size of age effects observed throughout the five studies. Of course, I had access to the raw data from each of these studies, which I was able to compile into a single data set. This final study

therefore also included a mega-analysis, directly assessing the effects of age and change type within the compiled data set. I expected both analyses to show a large effect of age on switch-to-place performance, perhaps with smaller effects for the other change types, but overall confirming a specific switch-to-place deficit among older people.

7.3.2 Methods

Data collation

I collated data from five of the preceding seven studies that utilised the VPM. Data from Study 7 were not included as there were no older participants involved in this study. Data from Study 8 were not included as the design of the VPM used in this study differed substantially from that used in other studies, and as some of the participants had already participated in one of the VPM studies. For Study 5, I used data collected using the standard version of the VPM only. For Study 6, data from young and old control participants were included, but data from orienteers were not. As studies differed in terms of the number of trials per block, I included data from only the first 15 trials in each block. Based on these data, for each participant, I calculated the percentage of trials correct, blocks learned and stable trials for each of the four change types. Participants for whom any information was unavailable were excluded. I also excluded a further seven participants (two old) as outliers, performing over 2.5 SDs beyond their respective group mean in terms of overall trials correct. Information on the inclusion and exclusion of participants from each of the five studies is presented in *table 7.1*. Those included were 97 (52 female) young (aged 18-30, M=22.1) and 66 (34 female) old (aged 60-80, M=69.7) participants.

Mega-analysis

Having collated the data from the five studies being assessed, I was able to perform a mega-analysis, as if the data had been collected in a single experiment. I assessed performance on each of the four change types in terms of trials correct, blocks

Participant information

Study	Original		Removed		Retained	
	Young	Old	Excluded	Outliers	Young	Old
3	18	20	14	1	14	9
4	24	12	8	2	18	8
5	27	23	12	1	23	14
6	18	19	7	0	15	15
9	28	28	6	3	27	20
Total	115	102	47	7	97	66

Table 7.1 Participant information. Details on the number of participants included in this study from each of the five original studies.

learned and stable trials. For each measure I ran a mixed model ANOVA, with age and change type as factors, followed by post-hoc t-tests, correcting for multiple comparisons according to the Holm-Bonferroni method.

Meta-analysis

I also ran a meta-analysis to explore the combined findings of the five studies by assessing effect sizes. For each study, for each performance measure and for each change type, I calculated the standardised mean difference (Hedge's g) between age groups. I then averaged effect sizes across data sets in order to easily compare age effects by change type for each measure of performance. This method has been deemed suitable for meta-analyses incorporating a small number of studies (Van Den Noortgate & Onghena, 2003).

7.3.3 Results

Mega-analysis

Older participants generally performed similarly to young during reverse-response blocks, but worse during reverse-place, switch-to-response and particularly

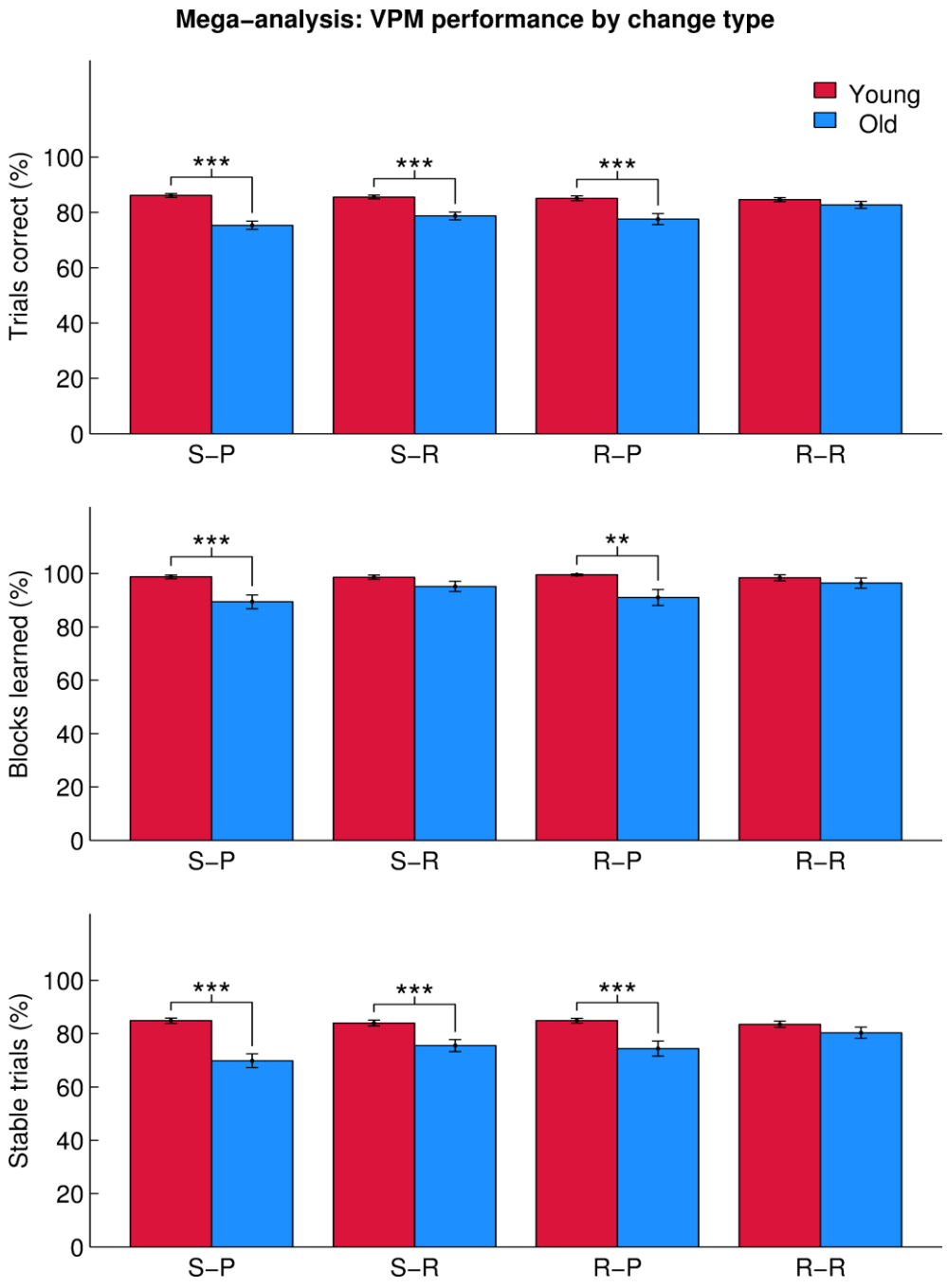

Figure 7.9 Mega-analysis: VPM performance by change type (switch-to-place, switch-to-response, reverse-place and reverse-response) in terms of percentage of trials correct (*top*), blocks learned (*centre*) and stable trials (*bottom*) for young (red) and older (blue) participants selected from the five collated data sets. Error bars represent SEM. ** and *** represent significant age differences at p<.01 and p<.001.

switch-to-place blocks (*figure 7.9*). In terms of trials correct, there were significant main effects of both age ($F_{1,161}$=43.38, p<.001) and change type ($F_{3,483}$=3.36,

p=.019), as well as a significant interaction between the two ($F_{3,483}$=7.05, p<.001). Post-hoc tests revealed that this was due to significant age differences in S-P (t_{161}=7.19, p_{HB}<.001), S-R (t_{161}=4.78, p_{HB}<.001), R-P (t_{161}=3.92, p_{HB}<.001), but not R-R (t_{161}=1.35, p_{HB}=.181) performance.

For blocks learned, there were also significant main effects of age ($F_{1,161}$=15.69, p<.001) and change type ($F_{3,483}$=2.74, p=.042) and a significant interactive effect ($F_{3,483}$=3.91, p=.009). These effects were due to significant age differences in performance during S-P (t_{161}=4.17, p_{HB}<.001) and R-P (t_{161}=3.44, p_{HB}=.002) blocks, but not S-R (t_{161}=1.86 p_{HB}=.129) or R-R (t_{161}=.94, p_{HB}=.345) blocks. Stable trials performance again showed main effects of age ($F_{1,161}$=31.38, p<.001) and change type ($F_{3,483}$=3.70, p=.012) and a significant interaction between the two ($F_{3,483}$=6.38, p<.001). As for trials correct, these effects were due to significant age differences in S-P (t_{161}=6.25, p_{HB}<.001), S-R (t_{161}=3.78, p_{HB}<.001), R-P (t_{161}=4.12, p_{HB}<.001), but not R-R (t_{161}=1.42, p_{HB}=.157) performance.

Meta-analysis

Mean effect sizes for each change type and for each measure of performance are shown in *figure 7.10*. For trials correct and stable trials, effect sizes were large for S-P performance (TC: M=1.09, SD=.51; ST: M=1.01, SD=.35), similarly moderate for S-R (TC: M=.66, SD=31; ST: M=.55, SD=.30) and R-P (TC: M=.59, SD=.17; ST: M=.61, SD=.13) performance, and relatively small for R-R performance (TC: M=.20, SD=.36; ST: M=.24, SD=.38). For blocks learned, effect sizes for reversals showed a similar pattern to the other two measures (R-P: M=.54, SD=.16; R-R: M=.17, SD=.33). On the other hand, effect sizes for switches were considerably smaller (S-P: M=.67, SD=.15; S-R: M=.32, SD=.27), although S-P still showed the largest average effect.

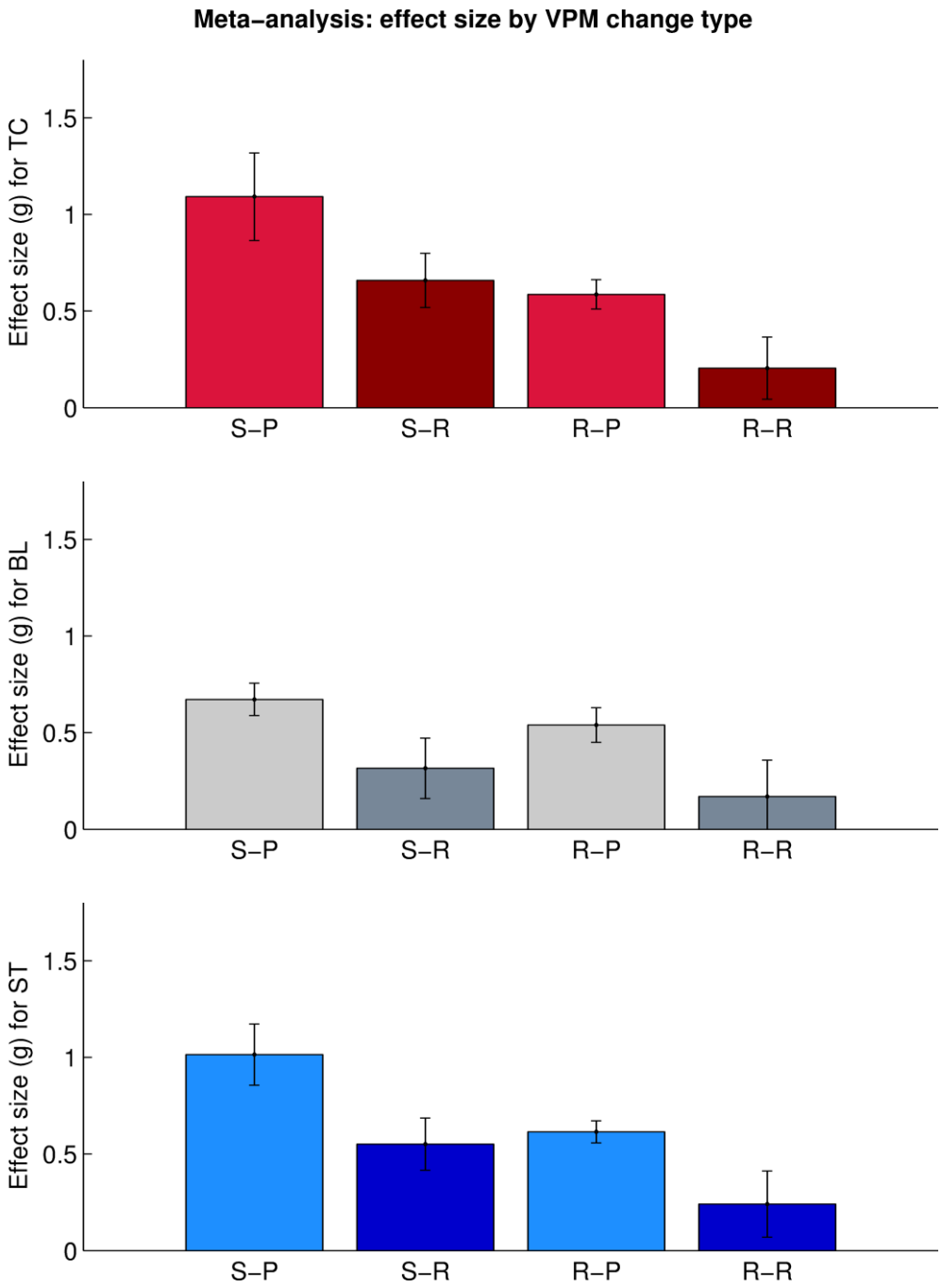

Figure 7.10 Meta-analysis: effect size by VPM change type (S-P, S-R, R-P, R-R) for trials correct (*top*), blocks learned (*centre*) and stable trials (*bottom*). For each measure, the standardised mean difference (g) in performance between young and old participants was calculated for each change type and then averaged across the five data sets. Error bars represent SEM.

4.3.4 Discussion

Summary of findings

The mega-analysis indicated that, in terms of both trials correct and stable trials, older participants performed significantly worse on all change types except reverse-place, with the largest difference in switch-to-place performance. In terms of blocks learned, there was no significant difference in switch-to-response performance, but this measure was susceptible to a ceiling effect, which may have masked age differences. The results of the meta-analysis reflect this, as effects on S-P and S-R blocks learned were smaller than for other measures. Due to the ceiling effect, blocks learned may not have been the most reliable measure of performance. Trials correct and stable trials both showed similar patterns of effect size across change types, with large effects on S-P performance, moderate effects on S-R and R-P performance and small effects on R-R performance. Reviewing the results of both analyses together for both trials correct and stable trials, it seems that R-R performance was affected by age very little, R-P and S-R performance was similarly impaired, and S-P performance was affected most of all.

Interpretation of findings

The fact that even this study, using multiple data sets, revealed little or no effect of age on R-R performance indicates that both performance of reversals and use of an egocentric response strategy are relatively unimpaired in ageing. This suggests that the effect on R-P was due solely to an impaired ability to engage or use the allocentric place strategy, most likely due to allocentric processing deficits (Moffat et al., 2006; Antonova et al., 2009; Iaria et al., 2009) related to hippocampal degeneration (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009), although possibly attributable to reduced functional connectivity between hippocampus and PFC (Grady et al., 2003; Wang et al., 2006; Bai et al., 2009). It also suggests that age differences in S-R performance reflect a general strategy switching deficit (Ashendorf & McCaffrey, 2008; Gamboz et al., 2009), associated

with dysfunction of PFC (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011) or the LC-NA system (Manaye et al., 1995; Grudzien et al., 2007). Although allocentric and switching deficits may not necessarily combine additively, it seems likely that the greater effect of age on S-P presented here – and reported as a specific S-P deficit in earlier chapters – is simply produced by the combined effects of a general strategy switching deficit and an allocentric deficit.

There was a difference in effect size between measures. Trials correct, which reflected performance throughout trial blocks, and stable trials, which reflected strategy stability throughout blocks, showed quite similar results. However, results were slightly different in terms of blocks learned, which only represented whether participants had learned the appropriate strategy by the end of each block. This measure therefore did not take into account whether participants had learned the strategy early on and performed well throughout the rest of the trial block, or had performed poorly but eventually learned the strategy near the end of the block. Effect sizes were smaller for S-P and S-R performance in terms of blocks learned compared to the other two measures, although they were similar for R-P and R-R performance. This demonstrates how the underlying switching and allocentric processing deficits may contribute to the apparent switch-to-place deficit in different ways. As might be expected, it seems that switching impairments only affect performance following a strategy switch, whereas allocentric impairments continue to affect performance throughout the block. This seems more consistent with an impairment in using an allocentric strategy, associated with hippocampal degradation (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009), rather than in engaging an allocentric strategy, which may relate to reduced connectivity between PFC and hippocampus (Grady et al., 2003; Wang et al., 2006; Bai et al., 2009). However, as above, due to a ceiling effect, interpretation of blocks learned data may be less reliable.

The inference that separate switching and allocentric deficits combine to produce a larger impairment in switching to an allocentric strategy is consistent with the findings of Study 9, in which older participants performed worse than young during S-R, R-P and particularly S-P blocks, and simply restates my interpretation of those

findings included in section 7.2.4. It is also consistent with the results of Study 5 and Study 6, even though in each case they were interpreted as evidence of a more specific switch-to-place deficit. While both of these studies demonstrated a significant age difference only in S-P performance, non-significant differences in both S-R and R-P performance were apparent. In light of the results of the present analyses, it seems reasonable to infer that the apparent switch-to-place deficits could have been produced by the combination of subtler impairments in strategy switching and allocentric processing. In reporting Study 4, I concluded that older participants were less able to switch to an allocentric wayfinding strategy primarily due to a switching deficit (whether general or specific), but also in part due to allocentric impairments. Again the results of this study are consistent with this interpretation.

However, the results of the mega-analysis and meta-analysis seem to disagree with the first behavioural findings I made using the VPM. In Study 3, as in both studies presented in Chapter Five, I found evidence of a specific switch-to-place deficit. But in Study 3, young and old participants performed much more similarly in terms of S-R and R-P performance, suggesting that the older participants' general strategy switching and allocentric processing abilities were relatively unimpaired. As this study was the only one demonstrating such similar performance of young and old on these two change types, I believe that general strategy switching and allocentric processing impairments may still have affected the older participants, but that they were simply not detected for some reason. In other words, although these deficits were not observed, they may still have contributed to the switch-to-place deficit. However, the size of the age difference in S-P performance seems to suggest that other factors must also play a role. I have previously suggested that a specific switch-to-place deficit can be explained by reduced functional connectivity between PFC and hippocampus, or by a decision making bias against using an allocentric strategy due to reduced prefrontal signal-to-noise and a pre-existing discrepancy between the two types of strategy in terms of difficulty. Such age-related changes may contribute to older people's particularly impaired ability to switch to an allocentric strategy, in addition to the effects of general switching and allocentric processing deficits.

Taken together, the results of the mega-analysis and meta-analysis suggest that older people are generally impaired at switching between navigational strategies, as well as at using an allocentric strategy, and that these impairments underlie the larger deficit in switching specifically to an allocentric strategy. This conclusion is concordant with the results of most of the studies presented in prior chapters, although it led me to revise some of my previous interpretations of these results. It does not seem consistent with my original VPM results, which may suggest that other factors also contribute to the switch-to-place deficit; for example, prefrontal dysfunction may have more of an effect on switching to a more complex strategy, or reduced prefrontal-hippocampal connectivity may have a specific effect on switching to a hippocampal-dependent strategy. Overall, it seems that multiple effects arising from dysfunction of hippocampus and the prefrontal-noradrenergic switching network are responsible for the substantial deficit in switching to an allocentric strategy observed in ageing.

7.4 Chapter conclusion

This chapter covered the final experimental study to be included in this thesis, followed by a short meta-analysis of the five preceding studies that used the virtual plus maze to assess age differences in navigational strategy switching. Study 9 focused on the role of noradrenergic dysfunction in age-related navigational strategy switching deficits, monitoring changes in pupil size and heart rate throughout VPM performance. As in several other studies, older participants performed worse at switching to the place strategy, but in this study, they also performed worse at switching to the response strategy and, to a lesser extent, reversing the place strategy. These behavioural results seemed to reflect separate impairments in switching between navigational strategies and using or engaging an allocentric strategy, combining to produce a larger switch-to-place deficit. PS increased in response to all strategy changes, consistent with the idea that the LC was in high-tonic mode when

switching or reversing strategies. PS also increased during decision and outcome trial phases, and in response to an absence of reward. However, the only age difference in pupillary response was in the PS increase after no reward during the decision phase of the subsequent trial. This may indicate that subtle LC-NA dysfunction has some effect on older people's choice of strategy during switches, but, overall, age-related navigational strategy switching deficits do not seem to be attributable to LC-NA dysfunction. HR showed some response to strategy changes, but was not as variable as PS, and therefore may not be such a useful proxy measure of LC-NA activity.

This final experimental study was the fifth complete study to test both young and old participants on the VPM. I therefore performed a small meta-analysis, presented as Study 10, on the data and results of these five studies. The first part of this analysis was actually a mega-analysis, using a selection of the pooled raw data from the five studies. It showed significant age differences in trials correct and stable trials during switch-to-place, switch-to-response and reverse-place blocks, but not reverse-response blocks. The largest differences appeared to be in S-P performance. The second part of the analysis assessed average effect sizes across the five studies for each change type. In terms of trials correct and stable trials, there were small effect sizes for R-R, medium effect sizes for S-R and R-P, and large effect sizes for S-P. Together, the results are indicative of separate strategy switching and allocentric processing deficits, combining to produce the largest impairment in switching to an allocentric strategy, as found in Study 9. Age differences and effect sizes were lesser for S-P and S-R blocks learned, reflecting that the general strategy switching deficit only affected performance while switching, whereas the allocentric deficit affected performance throughout place blocks.

The results of these two studies, particularly the meta-analysis, led me to reinterpret some of my findings presented in earlier chapters. Two of the three studies that seemed to demonstrate a specific switch-to-place deficit also showed some difference (although not significant) between young and old groups in terms of S-R and R-P performance. This pattern of results could also be accounted for by separate switching and allocentric deficits combining to produce a large effect on S-P

performance – sometimes even the only effect large enough to achieve statistical significance. On the other hand, Study 3 showed very little difference between age groups in S-R and R-P performance, perhaps indicating that the switch-to-place deficit is more than just a sum of switching and allocentric impairments. Factors that uniquely affect S-P performance, such as reduced prefrontal-hippocampal connectivity, may also contribute. My final conclusion will be discussed in more detail in the following chapter.

Chapter Eight – Discussion

8.1 Summary of findings

8.1.1 Chapter Three

Before addressing navigational strategy switching, I presented two studies of navigational strategy use in young and older people. Study 1 used the alternative approach task (AAT) to assess the ability to rejoin a learned route from a novel direction, demonstrating an age-related impairment. Specific test trials revealed whether participants were using an allocentric configuration strategy, an egocentric associative cue strategy or an egocentric beacon strategy. All participants used mainly egocentric strategies at the beginning of the task, but young participants gradually shifted to the allocentric configuration strategy throughout the experiment. On the other hand, older participants continued to use mainly egocentric strategies, showing a specific preference for the beacon strategy. The following Study 2 was designed to assess whether this specific preference was attributable to an impaired ability to use the associative cue strategy. Young and old participants completed one of two versions of a route learning task (RLT); one that facilitated use of the beacon strategy and one that restricted participants to using the associative cue strategy. Unexpectedly, there were no age differences in performance, although participants performed slightly better in the beacon condition.

8.1.2 Chapter Four

I first assessed navigational strategy switching using the virtual plus maze (VPM) in Study 3. As detailed in previous chapters, the VPM involved using either an allocentric place or an egocentric response strategy to navigate a plus-shaped maze, and periodically switching or reversing strategies. Older participants performed worse throughout place but not response trial blocks, and following switches but not reversals. Further analysis revealed that these effects were due to a specific deficit in switching to the place strategy. In Study 4, I attempted to assess switching from an

egocentric to an allocentric strategy using a more realistic task. Young and old participants were repeatedly trained on long routes to four goal locations in a virtual town environment, then asked to find the shortest way to each goal location during testing. While young participants switched to an allocentric wayfinding strategy by using available shortcuts, older participants instead continued to use a route-following strategy. Shortcut use was predicted by performance on a short version of the VPM, but not on a cognitive mapping test (CMT).

8.1.3 Chapter Five

Study 5 was intended to assess the contribution of decision making deficits to impairments in navigational strategy switching. Participants completed two versions of the VPM, one of which did not depend on decision making, as well as a navigational gambling task (NGT), as a measure of decision making. Older participants were again impaired at switching to the place strategy on the standard VPM, but this deficit was alleviated by removing the decision making aspect of the task. This effect was related to NGT performance, which also revealed decision making deficits among older participants and predicted performance on the standard VPM. Study 6 explored the effect of practice on ageing-related decline in navigational strategy switching abilities. Young and old orienteers and controls completed the VPM, as well as Raven's Standard Progressive Matrices (RSPM) as a test of general fluid intelligence. Older controls were again significantly impaired at switching to the place strategy, and orienteers did not perform significantly better. However, while older controls were also significantly impaired at the RSPM, older orienteers performed significantly better, and not significantly worse than young participants.

8.1.4 Chapter Six

In Study 7, I used functional magnetic resonance imaging (fMRI) to explore the neural mechanisms underlying navigational strategy switching in a small sample of young participants, who performed the original VPM. Second level gLM analyses

revealed some effects of strategy switching on activation of prefrontal regions of interest (ROIs) – specifically dorsolateral PFC (dlPFC), orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC). However, these effects were weak, and I did not find support for them using multi-voxel pattern analysis (MVPA). I attributed the limitations of my findings to the design of the VPM, and developed a very different version for use in a second fMRI study, in which I planned to use both young and old participants and a higher resolution scanner. The new VPM split each trial block into three sub-blocks, and participants were expected to learn each new strategy within the second sub-block. Pilot testing of this new design, in Study 8, indicated that participants usually learnt the strategy too early, while some older participants still failed to learn it at all. Consequently, I did not complete the second fMRI study.

8.1.5 Chapter Seven

In Study 9, I used changes in pupil size (PS) and heart rate (HR) to indirectly assess activity of the locus coeruleus-noradrenergic (LC-NA) system during VPM performance. Behavioural data demonstrated a more general strategy switching deficit than in previous studies. PS varied substantially in response to trial events, and also increased during performance of strategy switches and reversals, but, in contrast to my expectations, there were no age or change type differences in PS increase. However, PS was much higher in decision and outcome trial phases when participants did not receive a reward, and this effect was significantly greater in young participants than old. HR was much more stable, although it did tend to decrease during switches and reversals in the young group. Finally, a brief meta-analysis of five of the preceding VPM studies was presented as Study 10. This also incorporated a mega-analysis of all of the data from each set (adjusted in order to achieve greater equivalence), which revealed significant age differences in performance throughout reverse-place, switch-to-response and particularly switch-to-place blocks. The actual meta-analysis of weighted effect sizes from the five studies revealed large effects of age on S-P trials correct and stable trials, with lesser but still substantial effects on S-R and R-P performance.

8.2 Interpretation of findings

8.2.1 Navigational strategy preferences in ageing

In Study 1, older participants exhibited a preference for egocentric navigational strategies, or a bias against using an allocentric strategy. This result was consistent with our original hypotheses, and with previous work demonstrating a similar preference in aged animals and humans. For example, Nicolle, Prescott and Bizon (2003) trained 12 and 23 month old rats on the Morris water maze using an egocentric visual cue-based strategy (or beacon strategy), as well as the allocentric place strategy typically used on this task. On probe trials, the 23 month old rats exhibited a preference for the egocentric beacon strategy. In humans, Rodgers, Sindone and Moffat (2012) assessed navigational strategy preferences using a virtual Y-maze. In each block of trials, participants always started from the same arm of the maze, and the reward was always at the same one of the other two arms, so that the task could be solved using either an allocentric place strategy or an egocentric response strategy. On probe trials, where participants started from the third maze arm, the two strategies predicted different responses, and older participants used the egocentric response strategy much more frequently. It is important to note that the animals and human participants in these previous studies were not required to use an allocentric strategy, but were just as free to use, and had previously been rewarded for using, an egocentric strategy. These studies demonstrate a spontaneous strategy preference, but do not show whether it affects navigational performance when an allocentric strategy is required. The advantage of our study was that it demonstrated that the preference for egocentric strategies among older people persists even when use of an allocentric strategy is more appropriate, and use of an egocentric strategy is detrimental to navigational performance.

A preference for egocentric strategies could be explained by an improvement in egocentric navigation abilities with ageing. However, evidence suggests that this does not occur, and instead that egocentric abilities decline with age (Wilkniss et al., 1997; Head & Isom, 2010) due to degeneration of caudate nucleus (Raz et al., 2005;

Hasan et al., 2008). However, decline in allocentric abilities has been much more widely observed (Moffat & Resnick, 2002; Driscoll et al., 2003; Antonova et al., 2009; Iaria et al., 2009), as has associated degeneration of hippocampus (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009; Nedelska et al., 2012), which could certainly account for a bias against allocentric strategy use. Importantly, several studies have demonstrated that egocentric processing is less impaired by ageing than allocentric (Begega et al., 2001; Jansen et al., 2010; Wiener et al., 2012), so the observed egocentric strategy preference among older people may reflect their reliance on the most intact navigational system, following greater dysfunction of brain regions responsible for allocentric processing (Jernigan et al., 2001; Fjell et al., 2009; Raz et al., 2010). The alternative, discussed below, is that older participants were impaired at switching to the allocentric configuration strategy. However, older participants exhibited a greater preference for egocentric strategies even in the first testing repetition, which suggests that differences in allocentric abilities do at least contribute to this preference. The role of allocentric deficits is discussed further in section 8.2.3.

However, some evidence argues against this explanation. For example, the results of Study 2 demonstrated that older people's specific preference for the beacon strategy over the associative cue strategy does not relate to an impaired ability to use the associative cue strategy. Similarly, Nicolle et al. (2003) demonstrated an age difference in preference for a beacon strategy over an allocentric place strategy in rats, despite no age differences in performance of a place strategy, nor any correlation between place strategy performance and beacon strategy preference within the older group. The egocentric strategy preference may instead reflect an impaired ability to switch between strategies. During navigation, the ability to flexibly switch between navigational strategies allows people to select whichever strategy is most appropriate for a particular situation (Foo et al., 2005; Wolbers & Hegarty, 2010), suggesting that they do not exhibit a preference for any particular strategy. However, if this ability is impaired – and previous work suggests that strategy switching is impaired in ageing (Rodríguez-Aranda & Sundet, 2006; Ashendorf & McCaffrey, 2008; Hampshire et al., 2008; Gamboz et al., 2009;

Maintenant et al., 2011) – then people may be more reluctant to switch between strategies at all, and thus more likely to stick to just one strategy. The fact that the older participants in Study 1, in contrast to young participants, did not show any change in strategy use across testing repetitions seems consistent with this explanation. The reason for relying on an egocentric strategy, and on a beacon strategy in particular, may simply be that it is less cognitively demanding.

Of course, it is likely that impairments in allocentric processing and strategy switching both contribute to the egocentric strategy preference observed in ageing. It is also likely that this preference in turn affects performance on tasks that depend on allocentric navigation or navigational strategy switching. In fact, the relationship between these three factors remains unclear. It may be that allocentric impairments produce the egocentric strategy preference, which in turn affects navigational strategy switching. Or allocentric deficits may be the reason why navigational strategy switching impairments produce a preference for egocentric strategies in particular. It is also possible that deficits in strategy switching produce the strategy preference, which then impairs allocentric navigation. I would argue that the egocentric strategy preference is caused by underlying deficits in both allocentric navigation and navigational strategy switching, but also subsequently exacerbates impairments in both of these areas, as shown later in *figure 8.1*.

8.2.2 Navigational strategy switching in ageing

A specific deficit in switching to an allocentric place strategy

I first used the VPM to assess navigational strategy switching in Study 3. Older people responded correctly to fewer trials, learned the correct strategy in fewer trial blocks, and stably used the correct strategy for fewer trials, specifically when using the allocentric place strategy following a strategy switch. They did not show any impairment during response strategy blocks that followed a switch, nor in place or response blocks after reversals, but appeared to be specifically impaired at switching to the allocentric place strategy. This finding partly supported my original

hypothesis, in demonstrating an age-related navigational strategy switching impairment, but the deficit was more specific than expected. The specific switch-to-place deficit could be attributable to the combined effects of a general impairment in switching between navigational strategies, as I had expected based on previous findings of strategy switching deficits in other contexts (Rodríguez-Aranda & Sundet, 2006; Ashendorf & McCaffrey, 2008; Hampshire et al., 2008; Gamboz et al., 2009), and deficits in allocentric navigation, which have also been demonstrated previously (Moffat & Resnick, 2002; Driscoll et al., 2003; Antonova et al., 2009; Iaria et al., 2009). However, the observation that older participants performed very similarly to young throughout switch-to-response blocks argues against a general strategy switching deficit, while performance during reverse-place blocks also suggests that older participants were not impaired by allocentric processing deficits.

Some previous studies have also demonstrated impairments in switching strategies in only one direction. For example, Maintenant, Blaye and Paour (2011) found that, when performing a semantic categorisation task, older participants were equally able to switch from a taxonomic to a thematic categorisation strategy, but were impaired at switching to the taxonomic strategy. Floresco, Block and Tse (2008) trained rats to press levers using either a response-based strategy or a visual cue-based strategy. Inactivation of medial PFC (mPFC) impaired switching from the visual cue to the response strategy, but not switching in the opposite direction. Floresco et al. suggest that the specificity of this impairment related to the response strategy being more difficult than the visual cue strategy. This may also explain the specificity of the switch-to-place deficit, as the place strategy was more cognitively demanding than the response strategy. Switching to the place strategy was therefore the most difficult change type, as the only one associated with an increase in cognitive load. Allocentric deficits, although not apparent during reverse-place blocks, may have made switching to the place strategy even more difficult, thereby contributing to the poorer performance specifically during S-P blocks. An egocentric strategy preference – as demonstrated in Study 1 and other studies (Nicolle et al., 2003; Rodgers et al., 2012; Konishi et al., 2013) and discussed in the previous section – could have discouraged older people from switching to an allocentric strategy, also affecting S-P

performance.

The switch-to-place deficit may also relate to a specific aspect of neurodegeneration. While PFC (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011) and hippocampus (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009) are known to degenerate with ageing, unimpaired performance during switch-to-response and reverse-place blocks indicates that they are still sound enough to support navigational strategy switching and simple allocentric navigation, respectively. However, in coordinating a switch to the place strategy, these two regions must interact, and some previous evidence suggests that deterioration of the connections between the two occurs in normal ageing and mild dementia (Grady et al., 2003; Wang et al., 2006; Bai et al., 2009). Reduced prefrontal-hippocampal connectivity could account for the switch-to-place deficit, and particularly for its specificity. It could also explain the bias against using an allocentric strategy, and may therefore be an important contributing factor in the emergence of impairments in allocentric processing, and navigation in general, with advancing age.

Studies 5 and 6 provided further evidence of a specific switch-to-place deficit among older people using the VPM. In Study 4, I used a more realistic task to assess switching from an egocentric route-following strategy to an allocentric wayfinding strategy. Older participants were also impaired on this task, providing further evidence in support of an age-related deficit in switching to an allocentric strategy, and in fact, the effect was even more pronounced. While, on the VPM, older participants switched to the place strategy less often and more slowly, on the shortcutting task, none of the older participants stably switched to a wayfinding strategy. The results of this study in particular demonstrate just how much of an impact a deficit in switching to an allocentric strategy may have on real-world navigational performance.

A general deficit in switching between navigational strategies

The final VPM study presented in this thesis produced some different results. In

Study 9, older participants were again impaired at switching to the place strategy, but also performed worse than young participants throughout switch-to-response blocks. This finding is more consistent with a general strategy switching deficit, as I originally expected to find. It is also more consistent with previous studies that have used set-shifting tasks to demonstrate switching impairments in aged rodents (Barense et al., 2002; Young et al., 2010; Tanaka et al., 2011), primates (Moore et al., 2003; Picq, 2007; Hara et al., 2011) and humans (Rodríguez-Aranda & Sundet, 2006; Ashendorf & McCaffrey, 2008; Gamboz et al., 2009). More generally, it illustrates the contribution of executive dysfunction to the navigational difficulties experienced by older people. In terms of the stable trials measure, the older participants of Study 9 also performed worse than young participants during reverse-place blocks. Just as the observed poorer performance during both switch-to-place and switch-to-response blocks indicates a general switching impairment, the poorer performance in both S-P and R-P blocks is indicative of deficient allocentric processing. This is consistent with a large number of previous studies demonstrating impairments in allocentric navigation among older animals (Gage et al., 1984; Begega et al., 2001; Wilson et al., 2003) and humans (Moffat & Resnick, 2002; Driscoll et al., 2003; Antonova et al., 2009; Iaria et al., 2009). Furthermore, the age difference in performance was greatest for S-P blocks, as would be expected from the combined effect of deficits in both strategy switching and allocentric navigation.

These results reintroduce the idea that the specific impairments in switching to an allocentric strategy that were apparent in other studies were actually produced by a combination of switching and allocentric deficits. Although I dismissed this explanation when discussing the results of my first VPM study, it does seem to account for the results of most of the VPM studies. For example, in Studies 5 and 6, there were significant age differences in VPM performance only during S-P blocks. However, in both studies, older participants also seemed to perform slightly worse during S-R and R-P blocks. It may be that these participants were impaired in terms of strategy switching and allocentric processing, but that these deficits were too subtle to produce statistically significant effects on S-R and R-P performance. In combination, these subtle deficits produced greater effects on S-P performance,

which were significant. In Study 4, older participants performed significantly worse only during S-R blocks, which certainly does not relate to a specific S-P deficit. However, there was a non-significant difference in S-P performance, which suggests that it does reflect a general navigational strategy switching deficit. In the same study, older participants were unable to switch from an egocentric route-following strategy to an allocentric wayfinding strategy, which is evidence of an impairment in switching to an allocentric strategy, but, as the shortcutting task did not assess switching in the opposite direction, this finding could equally reflect a more general strategy switching deficit. The meta-analysis of data from five VPM studies, presented as Study 10, provides stronger evidence in favour of a general impairment in navigational strategy switching, combining with allocentric deficits to produce a greater effect on switching to an allocentric strategy. The results of Study 3 still seem discordant with this account, and may indicate that other factors, as discussed in the previous section, further exacerbate the effect of ageing on switch-to-place performance.

The navigational strategy switching deficits that I have observed in older people relate not only to previous findings of age-related strategy switching deficits in other contexts, but also to navigational strategy switching deficits produced by prefrontal lesions in rodents. For example, Ragozzino, Wilcox, Raso et al. (1999) tested rats on a version of the plus maze using response and visual cue strategies. Following inactivation of mPFC by infusion of a potent anaesthetic, rats were impaired at switching between these strategies. Similar studies using a place and response strategy plus maze also suggest the mPFC is involved in navigational strategy switching (Rich & Shapiro, 2007; Young & Shapiro, 2009). This suggests that my behavioural findings may reflect ageing-related degeneration of dlPFC – the primate analogue of rodent mPFC (DeVito et al., 2010) – which is consistent with the prefrontal degeneration that is observed in ageing (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011), and particularly previous work suggesting a key role for dlPFC in ageing (MacPherson et al., 2002). It is also consistent with Aston-Jones and Cohen's (2005) model of switching behaviour, which implicates regions of PFC in strategy switching. However, this model suggests that deficient

navigational strategy switching could instead reflect dysfunction of the LC-NA system, which is also evident in ageing (Manaye et al., 1995; Grudzien et al., 2007). I will discuss these potential underlying neural mechanisms in further detail in section 8.2.5.

Optimal navigation depends heavily on the ability to switch between navigational strategies (Foo et al., 2005; Wolbers & Hegarty, 2010). As we move around our environment, the availability of particular cues changes, we often encounter obstacles, and we sometimes have to revise our navigational goals. Due to these factors and others, which navigational strategy is most appropriate also changes frequently. Impaired navigational strategy switching may therefore have a severe effect on navigation in ageing, and could have contributed to previous findings on navigational impairments in older animals (Gage et al., 1984; Begega et al., 2001; Wilson et al., 2003) and humans (Moffat & Resnick, 2002; Driscoll et al., 2003; Antonova et al., 2009; Iaria et al., 2009). As discussed above, the performance of older participants on the shortcutting task used in Study 4 demonstrates the profound effect that strategy switching impairments can have on real-world navigation. Furthermore, due to the everyday importance of navigation abilities, navigational strategy switching impairments may have a substantial impact on the lives of older people.

Other factors affecting navigational strategy switching

In several studies, I assessed the contributions of factors other than age to navigational strategy switching performance. For instance, I measured spatial working memory using the Corsi blocks task and a custom spatial working memory task (SWMT). In terms of each of these measures, spatial working memory did not predict performance on the VPM. However, the Corsi blocks task in particular may have measured an irrelevant aspect of spatial working memory, as it assesses memory for sequences in small-scale space, which is not important in the VPM. Then again, the SWMT did measure relevant aspects of spatial working memory in large-scale virtual space, and still did not relate to VPM performance. This suggests

that navigational strategy switching does not depend heavily enough on spatial working memory for any between-subjects variability to directly translate into variability in VPM performance. VPM performance may instead have been more closely related to another measure of cognitive flexibility.

Some previous studies have demonstrated gender differences in aspects of navigational ability, with men performing better than women in most cases (Harrell et al., 2000; Wolbers & Hegarty, 2010; Liu et al., 2011). However, throughout all of my studies, I only found evidence of an effect of gender in one, and this effect was very small and did not produce a significant gender difference in performance. I would therefore infer that there are no gender differences in navigational strategy switching abilities. This may be because, as above, navigational strategy switching does not depend heavily on those aspects of navigational ability that show gender differences, and is instead more strongly influenced by executive functioning.

In Study 6, I used a group of orienteers to explore the effect of navigational strategy switching practice on performance. There was no significant difference between the older orienteering and control groups in VPM performance, suggesting that practice does not alleviate decline in navigational strategy switching abilities. Older orienteers did perform better on the RSPM, a measure of general fluid intelligence, suggesting that orienteering may mediate cognitive decline in general. This may simply reflect an effect of regular exercise, which has previously been shown to reduce cognitive decline in ageing (Yaffe et al., 2001; Kramer et al., 2004; Sofi et al., 2011). The observation that VPM performance was not improved in older orienteers may indicate that decline in navigational strategy switching is particularly resistant to treatment. However, Study 6 used small samples of orienteers and controls, so this would require much further investigation.

8.2.3 Impaired allocentric navigation

As above, several VPM studies and the meta-analysis demonstrated greater age differences in VPM performance throughout S-P and R-P blocks than S-R and R-R

blocks, respectively. This most likely reflects deficits in allocentric processing. Also as discussed earlier, the egocentric strategy preference exhibited by older participants in Study 1 may be caused by impairments in both navigational strategy switching and allocentric navigation. In Study 4, I used other tasks that were dependent on allocentric abilities and, although I found that the age difference in switching to a wayfinding strategy was more closely related to switching performance on the VPM, other aspects of Study 4 produced further evidence of impaired allocentric navigation in ageing.

Firstly, during the training phase of the shortcutting task, participants learned the four routes and were periodically tested on their knowledge of the routes, but also on their knowledge of the spatial relations between landmarks in the virtual environments (VEs). On route probe trials, participants were simply asked to follow the same routes they were being trained on, but without directions. On mapping probe trials, participants were positioned in one of the VEs facing a particular landmark and asked to turn until they were facing another specified landmark. Participants were identified as having learned each route when they could follow it without directions and without making errors, and as having learned each VE when they could respond correctly to all three of a set of mapping probe trials for that VE. Although older participants learned all of the routes almost as quickly as young participants, many failed to learn the spatial relations between landmarks. This may relate to impaired navigational strategy switching, as the training mainly involved egocentric route navigation, with only the mapping probe trials dependent on allocentric processing. Similarly, it could relate to the bias against using an allocentric strategy. However, it may also indicate that the older participants were unable to encode allocentric information about the environment during the training session.

A clearer indication of this is that older participants performed much worse on the CMT, which they completed at the end of the experiment. As above, this could relate to older participants persisting with an egocentric strategy throughout training and testing, due either to their egocentric strategy preference or impaired ability to switch between navigational strategies, but people generally form an allocentric

representation of the environment automatically, even during route navigation (O'Keefe & Nadel, 1978; Montello, 1998). This finding also relates to previous studies that have asked participants to draw or label a map of an experienced environment as a test of cognitive mapping. These studies have demonstrated that the ability to produce a two-dimensional representation of an environment does relate to allocentric navigational performance (Gillner & Mallot, 1998; Liu et al., 2011). However, this ability is dependent on specifically focusing on the layout of the environment during exploration (Wolbers & Büchel, 2005), which older people may be less inclined to do. Still, the large age difference in CMT scores provides at least some indication of impaired allocentric navigation in ageing. Importantly, switching to the wayfinding strategy on the shortcutting task was predicted by VPM but not CMT performance.

Evidence of impairments in allocentric navigation among the older people that took part in my studies is consistent with previous findings of allocentric deficits in older animals (Gage et al., 1984; Begega et al., 2001; Wilson et al., 2003) and humans (Moffat & Resnick, 2002; Driscoll et al., 2003; Antonova et al., 2009; Iaria et al., 2009). It is therefore also consistent with evidence of degeneration of hippocampus (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009) and its relation to decline in allocentric processing abilities (Driscoll et al., 2003; Moffat et al., 2006; Antonova et al., 2009; Nedelska et al., 2012). As discussed in previous sections, allocentric impairments may explain why older people exhibit a preference specifically for egocentric strategies, and why switching to an allocentric strategy is more severely impaired than switching in the opposite direction. However, it is of course important to remember that allocentric processing deficits also have a direct impact on navigational performance.

8.2.4 Deficits in navigational decision making

Navigational strategy switching involves several stages, the first of which is detecting that a change in strategy is required, based on changes in reward, or the utility of the current strategy. This is monitored by OFC and ACC (Rolls, 2000;

Botvinick et al., 2004; Kennerley et al., 2011), which are thought to then signal to LC that a strategy change is required (Aston-Jones & Cohen, 2005). In response, LC coordinates the second step in the process, disengaging from the current strategy, by changing to a tonic mode of NA output. The final step is engaging the new strategy, which depends on the LC switching back into phasic mode in order to activate a new functional network (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005). However, before this, the new strategy to engage must be determined through the sampling of alternative behaviours. This exploratory period is facilitated by tonic LC-NA activity, but may also depend upon decision making, which is coordinated by regions of PFC (Bechara et al., 1994; Manes et al., 2002; Denburg et al., 2007; Doya, 2008). Others have previously suggested that age-related deficits in switching may relate to deterioration of decision making abilities (Marschner et al., 2005; Eppinger et al., 2007).

In Study 5, I used a navigational adaptation of the Iowa Gambling Task (IGT; Bechara et al., 1994) to demonstrate impairments among older participants in navigational decision making. This is consistent with previous findings that older people show impairments on the IGT (Denburg et al., 2005; Fein et al., 2007; Bauer et al., 2013) and other measures of decision making (Brown & Ridderinkhof, 2009; Eppinger et al., 2011). As IGT performance has also been demonstrated to depend heavily on PFC, specifically ventromedial PFC (vmPFC) and dlPFC (Bechara et al., 1994; Manes et al., 2002; Denburg et al., 2007; MacPherson et al., 2009), and as PFC is known to degenerate with ageing (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011), this impairment in navigational decision making likely reflects prefrontal dysfunction. In the same study, I confirmed that impairments in navigational strategy switching do relate to deficits in decision making. On an altered version of the VPM that did not depend on decision making, older people were less impaired at switching to the place strategy. Furthermore, the older group's poorer S-P performance on the standard VPM related to impairments in decision making, as measured by the NGT.

The critical implication of these findings is that age-related navigational strategy

switching deficits can be attributed to prefrontal dysfunction. As described in further detail in Chapter Five (section 5.4.2), the effects of prefrontal dysfunction on navigational strategy switching can be understood in terms of the Diffusion Drift Model (Ratcliff & Rouder, 1998). Briefly, this model suggests that decision making can be represented by a decision signal drifting between response-associated thresholds as new information is integrated. Due to age-related degeneration and reduced signal-to-noise in PFC, it may take more information for the decision signal to cross a response threshold. Pre-existing differences between change types in terms of difficulty, represented within the model by higher thresholds, may explain why strategy switching, particularly to the place strategy, is more impaired in ageing. The role of prefrontal dysfunction in navigational strategy switching impairments in ageing is discussed further in the following section.

8.2.5 Neural mechanisms

As outlined above, in previous chapters and in *figure 1.7*, strategy switching is thought to be coordinated by a functional network comprising OFC, ACC and other regions of PFC, as well as the LC-NA system. OFC and ACC are involved in reward processing and error detection (Rolls, 2000; Botvinick et al., 2004; Kennerley et al., 2011), while tonic and phasic LC-NA activity facilitate the disengagement and engagement, respectively, of behavioural strategies (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005). Those regions of PFC involved in selecting a new behavioural strategy may involve mPFC in rodents (Ragozzino et al., 1999; Lapiz & Morilak, 2006; Rich & Shapiro, 2007; McGaughy et al., 2008), or corresponding dlPFC in primates (Li & Mei, 1994; Mansouri et al., 2006; Moore et al., 2009) and humans (Hampshire & Owen, 2006).

In Study 7, I used fMRI data collected from young participants during VPM performance to confirm that dlPFC, OFC, ACC are involved in navigational strategy switching. Specifically, there was a significant activation difference between periods of strategy switching and stable strategy use in an area of left ACC, and a slightly smaller difference in an area of right OFC. These activation differences were

apparent during the outcome trial phase, in concordance with the roles of these regions in reward processing and error detection. There was also an activation difference within right dlPFC that was close to achieving significance during the pre-decision phase, providing some evidence that dlPFC is involved in selecting which strategy to use. Unfortunately, these effects were relatively weak, and were not supported by pattern classification results. I believe this was due to limitations of the original task's design.

However, as discussed in the previous section, I did find some further evidence in support of PFC's involvement in navigational strategy switching, also suggesting that prefrontal dysfunction is responsible for age-related deficits. The association between VPM and NGT performance identified in Study 5 indicates that navigational strategy switching is dependent upon decision making, and that a particular aspect of neural dysfunction accounts for age-related impairments in both. Strategy switching (Rolls, 2000; Carter & van Veen, 2007; Gläscher et al., 2012) and decision making (Marschner et al., 2005; Botvinick, 2007; Doya, 2008) have both been associated with OFC and ACC, but as they are involved in reward processing and error detection, any dysfunction would be expected to affect switches and reversals equally by causing perseverative errors. On the VPM, performance of reversals was relatively unimpaired, and, as shown in Study 3, the errors made by older participants were not usually perseverative. Furthermore, older participants were still impaired on the standard VPM used in Study 5, which relied much less heavily on reward processing and error detection. It is therefore unlikely that navigational strategy switching impairments in ageing reflect degeneration of OFC or ACC. The other prefrontal region that has been implicated in both strategy switching (Li & Mei, 1994; Hampshire & Owen, 2006; Mansouri et al., 2006; Moore et al., 2009) and decision making (Kim & Shadlen, 1999; Manes et al., 2002; Heekeren et al., 2006; MacPherson et al., 2009) is dlPFC. I therefore argue that Study 5 provides evidence that degeneration or dysfunction of dlPFC is responsible for ageing-related impairments in navigational strategy switching. The same study indicated that factors other than deficient decision making also contribute, which may relate to other effects of prefrontal dysfunction, or to LC-NA dysfunction.

In Study 9, I assessed age differences in LC-NA function during navigational strategy switching using pupil size and heart rate as indirect measures of activity. PS proved particularly useful as such, as in previous studies that have also used it as a proxy measure of LC-NA function (Gilzenrat et al., 2010; Gabay et al., 2011; Jepma & Nieuwenhuis, 2011; Jepma et al., 2011; Preuschoff et al., 2011). PS increased during strategy changes, as well as during decision and outcome phases of each trial, and in response to the absence of a reward. However, there were no age differences in pupillary response to strategy changes. There was also no association between navigational strategy switching performance and pupillary response. Furthermore, there was no difference between change types in terms of pupillary response, suggesting that LC-NA dysfunction would impair performance of reversals as well as strategy switches. These findings all suggest that ageing-related navigational strategy switching deficits are not caused by LC-NA dysfunction.

Previous studies have demonstrated that prefrontal NA depletion does impair strategy switching (Tait et al., 2007; McGaughy et al., 2008). In fact, Caetano, Jin, Harenberg et al. (2013) recently demonstrated this using a navigational task that involved switching between memory- and stimulus-based strategies. Considered in terms of these previous findings, my results indicate that the older participants in Study 9 were not affected by prefrontal noradrenergic dysfunction, and therefore that LC-NA function is relatively unaffected by ageing. This, of course, stands in contrast with previous evidence of LC atrophy in ageing (Manaye et al., 1995; Grudzien et al., 2007). However, Palmer and DeKosky (1993) suggest that LC atrophy may not necessarily affect NA levels in other brain regions, which may explain why ageing did not affect noradrenergic activity – or pupillary response – during navigational strategy switching.

On the other hand, PS data did show one slight age difference in LC-NA activity. The absence of a reward for a particular trial produced an increase in PS during the outcome phase of that trial and the decision phase of the subsequent trial. However, the increase in the subsequent decision phase was significantly smaller among older participants. This may indicate that ageing reduces the duration of the noradrenergic

response, and therefore its influence. On the VPM, older participants' decision making during strategy switches may have been impaired as a result. Overall, the results of Study 5 and Study 9 indicate that navigational strategy switching impairments in ageing are caused primarily by degradation of PFC, but that less severe dysfunction of the LC-NA system also has a minor contribution.

8.2.6 Navigation in ageing: interaction between multiple deficits

Most of the studies presented in previous chapters produced results indicative of navigational strategy switching impairments among older people. As discussed above, these impairments seem to relate to the prefrontal dysfunction observed in ageing (West, 1996; Pfefferbaum et al., 2005; Raz et al., 2005; Kaup et al., 2011), partly through ageing-related deficits in decision making (Fein et al., 2007; Brown & Ridderinkhof, 2009; Eppinger et al., 2011; Bauer et al., 2013). Although I demonstrated that LC-NA dysfunction does not account for the marked age differences in navigational strategy switching ability, it does appear to make a minor contribution. My findings, in accordance with those of many previous studies, also provide some evidence of impairments in allocentric processing, which are generally associated with degeneration of hippocampus (Jack et al., 1997; Driscoll et al., 2003; Lister & Barnes, 2009; Nedelska et al., 2012). Impairments in navigational strategy switching and allocentric processing are both likely to have direct effects on navigational performance, with significant implications. However, they may also interact to produce specific effects, for example, on switching to an allocentric strategy, thereby having an even greater impact on real-world navigation. A model of how impairments in navigational strategy switching and allocentric processing interact to effect the navigational difficulties experienced in ageing is illustrated in *figure 8.1*.

As shown, the egocentric strategy preference identified in Study 1 is a good example of how strategy switching and allocentric processing deficits interact. A diminished capacity to switch between strategies naturally leads to a reduction in switching between strategies, which makes older people more likely to use a single strategy,

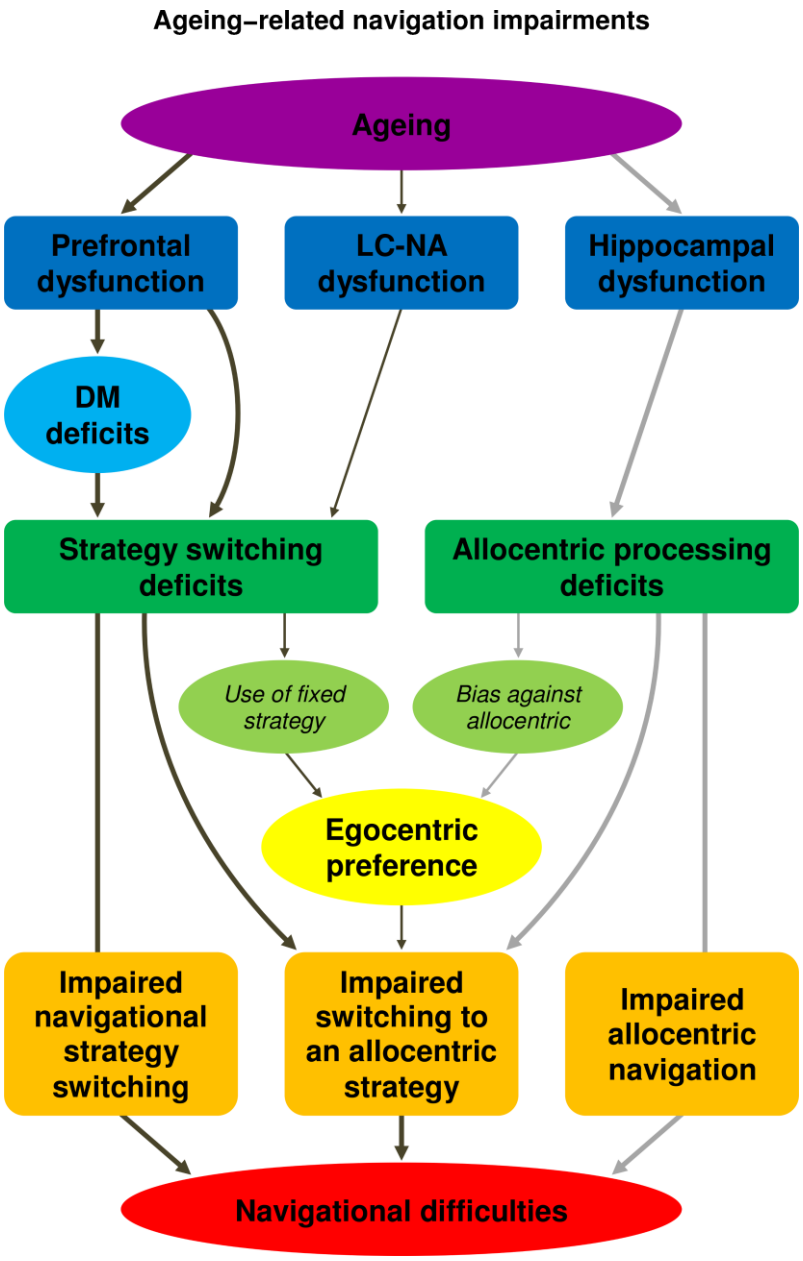

Figure 8.1 Ageing-related navigation impairments. Model of how ageing leads to navigational difficulties in terms of multiple deficits. Darker arrows highlight aspects of the model specifically relevant to navigational strategy switching. DM = decision making.

rather than to flexibly switch between strategies as required during navigation. However, it is deficits in allocentric processing that bias older people against using an allocentric strategy. As allocentric and egocentric systems compete to guide navigation (Bohbot et al., 2007; Doeller et al., 2008), a bias against allocentric

navigation thus determines that the fixed strategy used is an egocentric strategy. This preference may in turn exacerbate deficits in both navigational strategy switching and allocentric processing, specifically by contributing to the impairment in switching to an allocentric strategy.

I have left some aspects out of the model presented above. For instance, even before ageing, there is an existing difference between allocentric and egocentric strategies in terms of difficulty. This may play a role in the aetiology of navigational impairments in ageing, particularly by influencing the egocentric strategy preference. An additional aspect of neurodegeneration that I mentioned earlier, but have also excluded from the model, is the reduction in functional connectivity between PFC and hippocampus seen in ageing and mild dementia (Grady et al., 2003; Wang et al., 2006; Bai et al., 2009), which may also contribute to impairments in switching to an allocentric strategy. As discussed in the next section, there are also other brain regions and neurotransmitters that I have not studied or included in this model, but that have previously been associated with strategy switching. Finally, I have previously insinuated that strategy switching impairments may affect allocentric navigation, but the model does not appear to show this. I must clarify that navigational strategy switching will not actually impair allocentric navigation, but by affecting the ability to switch to an allocentric strategy when required, it will impair performance on tasks dependent on allocentric navigation.

This model places as much emphasis on ageing-related allocentric navigation impairments as on those in navigational strategy switching. This is because allocentric processing deficits are undeniably important to the emergence of navigational difficulties in ageing, and I do not by any means intend to refute the wealth of evidence supporting their existence (e.g. Moffat & Resnick, 2002; Driscoll et al., 2003; Antonova et al., 2009; Iaria et al., 2009). However, the value of this model and of my findings is in their drawing attention to the importance of strategy switching in navigation, and of executive and prefrontal dysfunction in ageing-related decline in navigation abilities.

8.3 Limitations and future directions

One of the original objectives of my research was to identify the neural mechanisms underlying navigational strategy switching abilities and their decline in ageing. While the results of Study 5 indicate that deficits relate to degeneration or dysfunction within PFC, these behavioural results did not provide direct evidence of this. Study 9 also found that LC-NA function was relatively unaffected by ageing, and may only play a minor role in ageing-related navigational strategy switching deficits, but again, the physiological measures used in this study were only correlates of LC-NA activity. I used fMRI to directly assess activation of dlPFC, OFC and ACC during VPM performance in Study 7, providing some evidence that these regions are involved in navigational strategy switching, but this study did not address the effects of ageing. I had also planned a second fMRI study that would have assessed age differences in neural activation during navigational strategy switching, but after piloting (Study 8), I did not complete this study. Evidence in support of the role of PFC and LC-NA dysfunction in navigational strategy switching impairments in ageing was therefore relatively limited. Furthermore, previous work also suggests that other regions, such as the striatum (Ragozzino et al., 2002; Daw et al., 2006; Monchi et al., 2006), and other neurotransmitters, such as dopamine (DA; Ragozzino, 2002; Floresco et al., 2006; Darvas & Palmiter, 2011), are involved in decision making and cognitive flexibility, but, having chosen to focus on the prefrontal-noradrenergic model of switching behaviour, I did not investigate these other factors. Future neuroimaging studies should focus on directly assessing the involvement of degeneration within PFC and LC – as well as the striatum and dopaminergic regions, such as the ventral tegmental area – in ageing-related decline in navigational strategy switching.

Although my research was primarily concerned with investigating ageing-related impairments in navigational strategy switching, as well as their underlying mechanisms, the overall purpose of ageing research is to develop ways of preventing, reducing or reversing decline. In Study 6, I assessed the effect of involvement in orienteering on VPM performance, exploring the utility of practice as a protective

intervention against decline in navigational strategy switching abilities. Orienteering did not significantly benefit navigational strategy switching, although it did seem to have a positive effect on general fluid intelligence, perhaps by involving regular physical exercise. This may indicate that navigational strategy switching deficits are more resistant to exercise interventions, but, as this study used small samples of participants who were non-randomly pre-assigned to conditions, I cannot say so with any certainty. A more extensive assessment of factors that could mediate decline in navigational strategy switching abilities was beyond the scope of my doctoral research, and I did not contribute directly to the development of any potential interventions. However, highlighting the role of strategy switching impairments in navigational decline in ageing could have an important effect on future developments. Future work could also aim to directly assess the effects of practice, exercise and other potential interventions on decline in navigational strategy switching abilities through more controlled longitudinal studies.

Perhaps the most notable limitation of my research is that all experiments were conducted within virtual reality (VR). Using VR tasks allowed me to assess navigational strategy switching during fMRI and eye-tracking, as well as to collect behavioural data much more quickly and easily, and therefore to conduct more experiments within the available time. However, navigation in VR is a much less active process, which limits self-motion cues to optic flow only. It is possible that the performance deficits I observed in the older people that took part in my VR studies are not actually representative of navigational impairments experienced in real-world environments. On the other hand, virtual navigation tasks have previously been validated as measures of real-world navigation abilities. For example, Cushman, Stein and Duffy (2008) demonstrated that performance on a real-world navigation task correlated closely with performance on an equivalent virtual navigation task in ageing and dementia. Scores on the Santa Barbara Sense of Direction Scale (Hegarty et al., 2002), a self-report measure of real-world navigation abilities, have also been shown to correlate with navigational performance in VR (Halko et al., 2013). Furthermore, as already discussed, my findings are consistent with previous work on navigation, navigational strategy preferences and strategy switching in ageing, as

well as navigational strategy switching in rodents. It therefore seems most reasonable to infer that my findings do relate to real-world navigational strategy switching in ageing, although their basis in VR is still an important consideration.

Future studies could therefore assess navigational strategy switching in real-world environments, although this would be much more complex to coordinate. Even a relatively simple navigational strategy switching task, such as the plus maze, would be associated with problems, such as with moving participants from a goal location to the start arm of the next trial. This could be avoided if participants simply started the next trial from whichever goal location they chose to visit, but this would mean a place strategy could not be used. However, a response and beacon strategy plus maze could work this way, and would actually enable the assessment of navigational strategy switching deficits without being influenced by impairments in allocentric navigation. A shortcutting task in a real town environment would not be practical, as it would be extremely difficult to adequately restrict participants' exposure to the environment throughout what would most likely be a lengthy training phase. An alternative to using real-world environments would be to use head-mounted displays (HMDs). Although participants would still navigate a VE, the HMD would allow them to do so by walking around, providing proprioceptive and vestibular cues, and thereby creating an experience and measure of something much closer to real-world navigation.

My research focused on the group differences between young and old people in navigational strategy switching abilities, but there was of course variability in performance within each group, especially older groups. A further consideration for future work is individual differences between older people in navigational strategy switching performance. Assessing individual differences in decline may provide further insight into underlying neural mechanisms, and could identify mediating factors, perhaps leading to the development of effective interventions. Finally, I believe that in demonstrating that strategy switching impairments are important to navigation in ageing, I have simply provided an example of how executive dysfunction can affect the everyday lives of older people. Future work could further

explore the wider implications of this interpretation by examining the effects of ageing-related deterioration of other executive processes in other important aspects of everyday behaviour.

8.4 Conclusions

Throughout the studies presented in previous chapters, I have demonstrated that older people prefer to use an egocentric strategy even when an allocentric strategy is required, and that they are less able than young people to switch to an allocentric strategy on the VPM, and even less so on a more realistic task. Switching in the opposite direction was also affected, but to a lesser extent, and use of an allocentric strategy and performance on other allocentric tasks was also impaired. fMRI results provided some support for a prefrontal model of navigational strategy switching. Furthermore, evidence of an association between deficits in navigational strategy switching and decision making is consistent with a neurophysiological explanation of navigational strategy switching deficits based on prefrontal dysfunction. On the other hand, pupillary response data confirmed that the LC-NA system is involved in navigational strategy switching, but plays only a minor role in age-related impairments. My main conclusions are therefore that navigational strategy switching is impaired in ageing; that this impairment reflects dysfunction of PFC and, to a lesser extent, the LC-NA system; that, due to an interaction between impairments in navigational strategy switching and allocentric navigation – as well as other factors, including the egocentric strategy preference – switching to an allocentric strategy is particularly impaired; and that navigational strategy switching deficits can have a substantial effect on navigation in general.

A large proportion of previous work on navigation has focused on allocentric processing and the hippocampus. My findings demonstrate that strategy switching and PFC may be critically involved as well, and may even have contributed to navigational difficulties that have been previously attributed to hippocampal allocentric deficits. At least, they highlight the importance of other processes and

brain regions, which I hope will be taken into consideration in future studies of navigation. Similarly, much cognitive ageing research has been based on measures of general intelligence and memory, whereas my research contributed to an understanding of the effects of ageing on a set of abilities of greater relevance to everyday life. Subsequent research into cognitive ageing should focus on exploring the effects of executive dysfunction on other important aspects of everyday behaviour. Following on from my work more specifically, any future research into ageing-related decline in navigational strategy switching should aim to more directly confirm the neural mechanisms responsible for this decline, and to identify potential interventions that could reduce it.

In summary, my research has demonstrated an important role for strategy switching deficits and underlying prefrontal dysfunction in ageing-related decline in navigation abilities. Older people are impaired at switching between navigational strategies, particularly to an allocentric strategy, and exhibit a preference for egocentric strategies, in addition to the more established age-related deficits in allocentric navigation. In combination, these impairments can have a profound effect on real-world navigation. More generally, this provides an example of the impact that executive dysfunction in ageing can have on aspects of behaviour of particular relevance to everyday life. Although not all of my work went according to plan, I am pleased to say that I have achieved my original objectives of investigating the effects of ageing on navigational strategy switching and its underlying mechanisms. Furthermore, while many questions surrounding navigational strategy switching in ageing remain to be answered, I feel I have made an important contribution to this area of research, as well as to the wider field of navigation in ageing.

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