Binding information in short-term memory: Evidence from healthy individuals, Alzheimer's Disease and other clinical populations

Mario Alfredo Parra Rodríguez

MD, MSc, Superior Institute of Medical Sciences, Cuba

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DECLARATION

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I declare that this thesis is of my own composition, and that the material contained within describes my own work.

It has not been submitted for any other degree or professional qualification.

All quotations have been distinguished by quotation marks and the sources of information acknowledged.

Mario Alfredo Parra Rodriguez

February, 2009

ABSTRACT

Memory binding is a cognitive process that enables complex objects to be stored or retrieved coherently during perception, learning, or action. Binding functions are aimed at reducing the misattribution of the features of objects in crowded and changing sensory contexts, ensuring accurate representation in visual working memory. Binding is a relatively new concept in working memory research. However, as an integrative function it provides a rich context in which to investigate the mechanisms underlying memory deterioration. In this PhD project, a range of experimental temporary binding paradigms were used to investigate whether some of the memory impairments observed in patients with Alzheimer's Disease could be accounted for by deficits in this memory function. A set of neuropsychological tasks were used to investigate binding operations across memory domains (i.e., verbal and nonverbal), sensory modalities (i.e., visual and auditory), types of information (e.g., objects and colours), and retrieval processes (i.e., recognition and recall) in healthy individuals, Alzheimer's Disease patients and other clinical populations. The results suggest that the efficiency of short-term memory to store bound complex events depends on the nature of the information presented (e.g., type of information bound into objects) (Chapter 2). Short-term memory seems to be equipped with relatively separate mechanisms to store integrated objects and individual features (Chapter 4). It was also observed that the binding properties of short-term memory apply to healthy young and older people, and are functions which are preserved in the elderly (Chapter 3). In two additional experimental chapters (5 and 6) the preserved binding abilities of older people were compared with temporary binding in Alzheimer's Disease. The latter group showed a very large impairment in binding that was distinct from their impairments in memory for individual features. These findings

suggest that memory binding tasks could reliably separate the cognitive changes in normal ageing from those linked with Alzheimer' Disease. Moreover, the results of Chapter 7 suggested that memory binding tasks may detect memory changes in people that will develop Alzheimer' Disease (i.e., asymptomatic carriers of the gene defect E280A of the Preseniline-1 gene) almost 10 years before the average age of onset. These results are relevant to our understanding of short-term memory and to the memory models currently available. Finally, it is suggested that the constructs of memory binding may increase the sensitivity of current assessment procedures for people at risk of developing Alzheimer's Disease.

CONTENT

CHAPTER 1

Part I - Binding information in the healthy brain: current perspectives

> When soldiers of the liberty army saw the flag heading the battalion, they saw in its colours … "*the aspiration for freedom that all men shared: red, white, and blue. Three blue stripes represented the states into which the island was divided at that time; two white stripes implied the force and dedication of the idealistic soldiers for independence; a red triangle for equality, fraternity and liberty, and the blood shed in the pursuit of freedom; a white five-sided star, inside the red triangle, as a symbol of freedom between nations*" (Sierra, 2008). All pieces came together into one meaningful concept, sovereignty.

1.1 The issue of binding in the human brain

1.1.1 What is binding?

In the earliest stages of central information processing, primary sensory cortices unpack sensory inputs to extract from them elementary attributes of stimuli such as luminance, contours, colours, frequency, intensity, motion, which at this level, are processed by separate networks (Denys et al., 2004; Kandel & Wurtz, 2000; Van & Drury, 1997). Later mechanisms should enable the recombination of these basic properties and allow stimuli to be represented coherently in subsequent and higher order steps along the functional brain hierarchy. The function underlying these combinatory processes is called binding and it operates at many neuronal levels ranging

from perception, memory, and action (Ecker, Zimmer, & Groh-Bordin, 2007; Ghose & Maunsell, 1999; Groh-Bordin, Zimmer, & Mecklinger, 2005; Roskies, 1999; von der Malsburg, 1995; von der Malsburg, 1999; Wolfe & Cave, 1999; Zimmer, Mecklinger, & Lindenberger, 2006). Binding is therefore the brain response that mediates the association of multiple sources of information to form coherent representations of the real world (Treisman, 1996; 1998; 1999; Treisman & Gelade, 1980; Zimmer et al., 2006).

1.1.2 Is binding a single issue?

Roskies (1999) suggests that the binding issue encompasses in reality numerous related issues. The logic behind this proposition is that binding occurs for visual information across the visual space and across different types of features, but it can also occur for other modalities such as auditory inputs (e.g., recognizing a voice in a crowd). To make this even more complicated, binding also occurs across sensory systems (e.g., identifying a dog by its bark), a process known as cross-modal binding. She argues that there are additionally cognitive binding problems such as associating objects with their semantic knowledge, or linking previous stored information with new information to form integrated representations.

In addition to these perceptual/cognitive binding issues, there are other problems that arise from the structure of the brain systems responsible for information processing. First, the human brain is equipped with systems with limited capacities. Therefore, how to accommodate coherently the flow of information that reaches these systems over a particular time period is indeed, a conundrum. Second, we still lack clear understanding of how, at neuronal level, the brain integrates this continuous flow of information without committing too many errors.

Different solutions have been proposed to solve the issue of binding information in the human brain. As Treisman (1999) suggested the most important issue in solving this problem is that whatever the processes responsible for integrating information, the output of those processes will be interpreted and used by later stages in cognitive processing regardless of whether they encode memories, determine choices, or select motor responses. For example, when neurons encoding information from the same event (e.g., colours, shapes, motion) synchronize their activity to identify this event as unique and different from other events, this integrated activity is read out by higher level operations as an integrated object with its own identity. This observation led to the proposal of the so called Neuronal Synchrony Hypothesis which will be reviewed in more detail in the next Section.

1.2 Neuronal mechanisms of binding

1.2.1 Is binding necessary?

Binding seems to be needed at both the levels of the phenomenological description of our experience (Cer & O'Reilly, 2006) and that of the neuronal mechanisms responsible for constructing these experiences (Ghose & Maunsell, 1999). Within the first level, binding can help to explain for instance how one can recognize a canary, as features distinguishing this particular bird are recorded into a unique representation. At the second level, binding may explain how the limited number of neurons available in the human brain can be efficiently used to represent the vast number of stimuli and stimuli dimensions that reach our sensory cortices. It is accepted that the number of objects that humans can distinguish is limited (perhaps around

100,000; Biederman, 1987). However, when the number of different dimensions for each object is considered, the outcome would be a combinatorial explosion which would override any processing capacity. Therefore, binding seems to be rather an intrinsic feature of the human brain; however, it does require solutions at different levels.

1.2.2 Neuronal Synchrony

One problem posited by Treisman (1977) and Treisman and Gelade (1980) is precisely how to encode bindings of information. That is, how different features that are bound together can be translated into neural codes so as to be accessible for further cognitive processes. One hypothesis (although subject to controversies) is that labelled "Neuronal Synchrony", "Temporal Synchrony", or "Temporal Correlation" (Gray, 1994; Shadlen & Movshon, 1999; Singer & Gray, 1995). According to this hypothesis, neurons coding features belonging to the same object will discharge with high synchronicity and with frequencies different from other neurons coding other objects. This process recruits extended populations of cells forming neuronal assemblies wherein objects are represented as a whole and are segregated from other objects, backgrounds, temporal concurrences, etc. There is evidence that the Temporal Synchrony Hypothesis has both strengths and limitations. I will briefly refer to some arguments supporting both perspectives.

1.2.3 Arguments in favour of the Temporal Synchrony Hypothesis

If we look at the functional sensory maps over the visual cortices presented by Van Essen and Drury (1997), one obvious question would be how distributed features are represented into emergent representations, and once this is done, how these representations are made different from one another.

The Temporal Synchrony Hypothesis does provide an attractive solution to both the binding and superposition problems (Gray, 1999). The superposition problem is that arising when multiple feature maps are activated concurrently due to several inputs hence features can be bound erroneously. Gray (1999) suggested that after the theoretical considerations by Miller in 1974 and by von der Malsburg in 1981 and 1985, which drew on the concept of Hebbian cell assemblies (Hebb, 1949); the Temporal Synchrony Hypothesis is the only one that has provided empirical evidence in an attempt to solve the binding problem.

1. Gray (1999) suggests that the very first evidence should be the occurrence of temporal synchrony in the nervous system. Now there is accrued evidence coming from animal studies suggesting that there is a great deal of synchronic oscillatory activity particularly in the visual cortex, a region wherein this phenomenon has been more thoroughly investigated (Gray, 1994; Singer & Gray, 1995).

2. The Temporal Synchrony Hypothesis offers an account to explain the required coarse coding within dimensions (Treisman, 1999). This is a great advantage of the hypothesis as it accounts for, e.g., small variations in colours hues which make objects perceptually different but which require fine tuning. Treisman (1999) suggested that coding different values within feature dimensions using ratios of activity (i.e., a different frequency for each intermediate value) in differently tuned populations of cells can maximize discriminability.

3. It also provides a plausible explanation for the limited capacity of cognitive systems to handle complex objects; it is claimed that attention has a capacity of around four objects (Treisman, 1999) and that visual working memory could process about the same number of

items at any one time (Luck & Vogel, 1997). Because perception and memory require a capacity to represent objects, both are subject to, as suggested by Hummel and Holyoak (1997), computational constraints. According to the authors, these constraints are imposed by the need for dynamic binding (i.e., binding by synchrony). The authors acknowledged that dynamic binding is a capacity limited mechanism. Therefore, one may infer that this binding by synchrony limitation (i.e., coding of a maximum of four to six concurrent objects as suggested by Hummel & Holyoak, 1997) would reflect upon both perception and memory.

4. The idea of the "labelled line coding", which stems from the existence of cardinal cells (i.e., cells able to code specific precepts such as faces, motion), allows for representing different object parts relying on the firing of different conjunction codes (Shadlen & Movshon, 1999). These cells will form assemblies which will eventually represent the structure of the external world.

5. Temporal synchrony reflects anatomical connection between cells. Studies carried out in the visual cortex of cats showed that there is a positive linear relation between the strength of anatomical connections between brain regions and the percentage of synchronized activity between these regions (Fries, Roelfsema, Engel, Konig, & Singer, 1997; Roelfsema, Lamme, & Spekreijse, 1998). Therefore, the Temporal Synchrony Hypothesis does offer an account for the functionality of short and long connecting pathways that allow establishing extended networks across brain regions.

6. There is empirical evidence suggesting that temporal synchrony accounts for the majority of the Gestalt grouping properties. In

intracellular recordings within retinotopically organized regions it has been found that neurons discharge synchronically when the distance between cells is approximately 10 mm. This distance typically corresponds to 5^{o} of visual field suggesting that proximity is a feature that elicits synchronic activity in the visual cortex (Gray, 1999). Continuity and segmentation, Gestalt attributes that provide important clues for grouping in perception, have been found to produce temporal synchrony of neural firing (Gray & Singer, 1989). Segmentation is one of the Gestalt principles that drew more attention from this movement (Rock & Palmer, 1990). While effort has been put into trying to identify the neural correlates of this sensory function, more empirical data is still required to elucidate what are the actual bases of this phenomenon (von der Malsburg, 1995).

7. One important prediction of the Temporal Synchrony Hypothesis is that if it does exist, it should correlate with performance on perceptual discrimination tasks. This is by far one of the least explored applications of the Temporal Synchrony Hypothesis. However, animal studies carried out in cats with strabismus have shed light into this potential relation. Fries et al. (1997) investigated the neuronal correlate of binocular rivalry in primary visual cortex of awake strabismic cats. They first presented stimuli monocularly and found that those stimuli readily perceived evoked synchronized discharges (within gamma-frequency range). When stimuli were presented binocularly, the stimulus that continued to be perceived increased the synchronicity of their oscillatory patterning while the reverse was true for neurons responding to the stimulus that was no longer perceived (i.e., due to the strabismus). The authors proposed that this differential change suggests that at early stages of visual processing the degree of

synchronicity seems to determine which signals are perceived and control behavioural responses.

1.2.4 Criticisms of the Temporal Synchrony Hypothesis

The limitations of this hypothesis arise from the fact that (1) our brain is composed of modular systems each with potentially limited capacity and (2) that the Temporal Synchrony Hypothesis proposes how binding is signalled however it leaves unanswered how binding is computed. That is, how the different systems accessing these neuronal outputs identify which features belong together and which are part of different objects (Shadlen & Movshon, 1999).

1. Treisman (1999) suggested that these neuronal assemblies would face a combinatorial explosion if all the possible discriminable arrangements of all objects were mapped onto unique cells. As mentioned before, the number of available neurones would not be sufficient to meet this demand (Ghose & Maunsell, 1999).

2. Treisman (1999) also pointed out that the concept of cell assemblies does not distinguish between "identifying" and "seeing" or between "types" and "tokens". These cardinal cells would encode feature bindings only by identifying pre-stored conjunctions leaving new or unexpected conjunctions unbound or unperceived.

3. Cardinal cells have no way of representing the hierarchical structure of the object: "*…the different momentary constellations of articulated parts in a given integrated item as seen on a particular occasion*" (Treisman, 1999). Ghose and Maunsell (1999) suggested that stimulus dimensions

(e.g., depth, size, rotation, colour hues) exponentially increase the number of neurons required to encode them. Hence, there would not be enough neurons to represent all possible combinations of stimulus attributes that determine the variations of these complex items.

4. The Temporal Synchrony Hypothesis has a limitation for decoding the information belonging to the same object (Cer & O'Reilly, 2006). The hypothesis assumes that features belonging to the same object would be encoded by cells within assemblies which synchronize their firing. However, these assemblies will receive inputs with relative phase lags as no all features belonging to the same objects are processed at the same speed (Arnold, Clifford, & Wenderoth, 2001; Hannus, van den, Bekkering, Roerdink, & Cornelissen, 2006). Therefore, the downstream neurons may receive inputs that actually characterize different objects. Moutoussis and Zeki (1997) suggest that the brain binds visual attributes that are perceived together, rather than ones that occur together in real time. The authors observed that subjects misbinded the colour and the direction of motion because colour and motion are perceived separately and at different times, with colour being perceived first.

5. Another limitation of the Temporal Synchrony Hypothesis is the fragility of bound information (Cer & O'Reilly, 2006). For cellular assemblies to be able to code features together, a precise timing of their firing rate is required. Fragility addresses the question of how this highly synchronized activity would be possible in a context whereby interference is so likely to occur or where a huge noisy activity underpins the different functional states in the human brain.

6. According to how the hypothesis is postulated, cells assemblies would synchronize their discharges as long as the stimuli to-be-encoded are within the perceptual space (e.g., visual or auditory fields). An explanation is needed for the fact that even when these stimuli are removed from the visual or auditory fields, they can still be vividly and accurately represented. Cer and O'Reilly (2006) called this limitation transience, and they also proposed a solution which they call conjunctive representations (this solution also tackles the limitations summarised in points 4 and 5).

7. Another set of limitations result from unsuccessful attempts to reproduce in animal models the synchronic oscillatory patterns (30 – 60 Hz) postulated by the hypothesis. However, given the dearth of any other more convincing solutions, it has been proposed that these limitations may have resulted from methodological problems (e.g., recording techniques), animal models used and compared (e.g., cats versus monkeys), or from the combination of different stimulus modalities (e.g., motion and direction) (Gray, 1999).

Even though the number of arguments presented in favour of the Temporal Synchrony Hypothesis equals the number of criticisms, Gray (1999) suggested that evidence favouring the rejection of the Temporal Synchrony Hypothesis is still more limited in scope than the supporting evidence. In a recent review Uhlhaas and Singer (2006) suggested that the Temporal Synchrony Hypothesis may help to explain some relevant cognitive impairments in diseases such as Schizophrenia, Epilepsy, Autism, and Alzheimer's Disease. In fact, more plausible propositions accounting for so many different edges of the binding problem are indeed not available. Perhaps, these limitations proposed for the theory are rather methodological or theoretical caveats of these studies discussed above. However,

discrepancies about whether or not temporal synchrony is required to form coherent representation of objects in the visual system are still unsettled (see Cheadle, Bauer, Parton, Müller, Bonneh, & Usher, 2008; Fujisaki & Nishida, 2005, for more recent results supporting the hypothesis and Dong, Mihalas, Qiu, von der Heydt, & Niebur, 2008; Farid, 2002; Farid & Adelson, 2001, for results disregarding the hypothesis).

The Temporal Synchrony Hypothesis focuses more on those neural mechanisms that are mainly driven by the physical attributes of sensory inputs. As such, it addresses the binding issues associated to bottom-up processes. At the cognitive level, different accounts have been proposed to address the binding issue. In the next Section some of these propositions will be reviewed.

1.3 Binding, perception, and attentional resources

The main problem for binding in perception concerns the issue of how features processed along different or distantly located sensory maps (as shown by Van Essen & Drury, 1997) could be bound together in such a way that objects reach perception.

1.3.1 The Feature Integration Theory of Attention

The binding problem in perception received a great deal of attention in the early 80's. Anne Treisman pioneered the studies on perceptual grouping with the aim of offering an account for the binding problem at a cognitive level. One of her important contributions (see e.g., Treisman & Gelade, 1980) was the proposition of the Feature Integration Theory. According to the Feature Integration Theory, the process of feature integration in perception

occurs in two stages. During the initial stage, considered pre-attentive, features are distributed onto maps that process distinctive aspects of sensory inputs (e.g., colours, shapes, motion, etc.). At this stage, features remain independent entities and feature maps are not aligned (or linked) in any particular order. Treisman (1982) and Treisman and Souther (1985) suggested that, in addition to these maps, there should be a master map of locations to which the individual feature maps are referred. In the second stage, a cross-dimensional processing takes place. During this stage attention is required. Attention will allow scanning and recovering the relation between features using the links outlined onto the master map. Therefore at this level of processing bottom-up processes would not suffice for the integration of information but top-down operations will be required (Treisman & Souther, 1985). Because attention plays a crucial role in the operational definition of the Feature Integration Theory, the theory was referred to as the Feature Integration Theory of Attention.

Further attempts showed that when attention is not available in the required amount, features may be conjoined at random, leading to illusory conjunctions (Treisman & Schmidt, 1982). These perceptual errors open up the field of binding to cognitive neuroscientists. Since its proposal, the Feature Integration Theory has been subject of continuous debate. The central focus of this debate stems from the actual involvement of attention in feature binding. Firstly, Treisman (1996) suggested that the Feature Integration Theory has offered an account to explain first the illusory conjunctions phenomenon, which is frequently observed when attention is diverted from to-be-perceived objects. Secondly, directing attention in advance to a target location improves target detection more for conjunctions than for individual features. Thirdly, visual search appears to be serial, as searching for a target in arrays of items defined by conjunction of features (e.g., letters and colours) tends to be slower and less accurate than searching

for targets when arrays consist of single-feature items (e.g., letters or colours only) .

Whether there is no binding at pre-attentive stages, the extent to which all types of features require the same attentional resources to-be-bound into integrated objects, or whether attention is required at all, are issues still under investigation (for a critical review of the Feature Integration Theory see Quinlan, 2003). However, as the Temporal Synchrony Hypothesis offers an account to explain how feature binding operates at cellular level, the Feature Integration Theory of Attention helps to understand, at least in part, how this process is carried out at a cognitive level. For example, using functional MRI, Shafritz, Gore, and Marois (2002) showed that regions of the parietal cortex involved in spatial attention are more engaged in feature conjunction tasks than in single feature tasks. This was true when multiple objects were shown simultaneously at different locations but not when they were shown sequentially at the same location. This suggest that at a cognitive level, at least for some types of features, attention is required in order to integrate them in perception (e.g., location).

The literature on binding in perception raises the following questions in relation to binding in memory:

1. If attention is required to form bound representations in perception, will attention also be required to bind information in memory?

2. Are those processes that keep features together in perception similar to the processes that keep features together in memory?

3. If the Feature Integration Theory of Attention proposes a mechanism by which the binding problem in perception can be partially solved, what account we do have to address the same problem in memory?

1.4 Binding in Memory

The binding problem in memory tackles the question of how those objects that are integrated in perception are held or represented in memory. One other relevant question is how memory ensures stable representations of features bound into objects across its different domains (i.e., verbal and visual, short-term and long-term stores).

1.4.1 Encoding bindings

There is compelling evidence suggesting that binding processes operating in perception are not isolated from those operating in memory (Chaumon, Drouet, & Tallon-Baudry, 2008; Elazary & Itti, 2008; von der Malsburg, 1995). For instance, it has been found that the complexity of visual objects affects the capacity of visual working memory: more complex objects (e.g., faces) are remembered less accurately than simple objects (e.g., colours) (Eng, Chen, & Jiang, 2005). This effect was found to be much stronger with shorter presentation times, suggesting that when the information to-be-encoded is more complex, memory capacity is more limited. Alternative views suggest that with experience (i.e., previous knowledge), the integration of detailed object information to form a simplified representation is facilitated. That is, memory capacity is affected by the existence of long-term representations of the to-be-encoded stimuli (Jackson & Raymond, 2005). Therefore, there seem to be interactive perceptual/memory operations that play a crucial role in how objects are integrated and represented at both levels.

In reviewing the topic, von der Malsburg (1995) suggested some criteria that highlight the interaction between perception and memory during the process of binding information. He maintained that there should be early mechanisms that guarantee the dynamic generation of binding. As discussed before, the number of possible representations that one object may have are countless and they could, by far, overflow our sensory, perceptual and memory capacities. Therefore, early in perception relevant aspects of these objects will be selected for further processing. Once selected, these attributes have to be implemented into individual entities. The author also suggested that those bound structures, once stored, will be used for future reference. There is evidence that this stored information can impact on both the very early stages of feature selection and feature binding and the way these bindings will be later represented in memory (Groh-Bordin et al., 2005; Woodman, Vecera, & Luck, 2003).

According to von der Malsburg (1995), these bound structures once stored will provide support to the early selection processes. This support would prevent, for instance, firing in response to illusory conjunctions. Therefore, previous experience will aid the process of early selection of features to-be-bound and in the later representations of these objects in perception and memory. One last criterion mentioned by von der Malsburg (1995) is the efficiency of learning by proper constraint of long-term synaptic plasticity. Through this binding process, new events will be firmly represented in a more durable format. Miyashita (1993) suggested that the inferior temporal cortex seems to be the place where perception meets memory. Therefore, this should be the locus where these operations are carried out. I will return to this point later in the chapter.

1.4.2 Maintaining bindings

The next step would be to consider how these perceptually integrated objects are represented in memory to be used to elicit and guide action. How is the information bridged from perception to memory? There are three propositions which try to explain how this connection is established. The early proposition made by Atkinson and Shiffrin (1971) posited that information coming from perception accesses long-term memory via short-term memory. In this way, short-term memory acts as a gateway to long-term memory. A second proposition suggests that information arriving from perception reaches short-term memory which in turn represents a temporary activated subset of long- term memory (Anderson, 1983; Cowan, 1988; 2008). A third proposition states that working memory is a separate system with its own properties. This proposition holds the idea that information can access short-term and long-term memory in parallel and that this information can be transferred in either direction between the two systems (Baddeley, 2007a; Baddeley & Hitch, 1974). These models of memory and their relation to binding processes will be discussed in more detail later in this chapter.

The rest of this Section will be spent reviewing how information is represented in short-term memory as this is the system at the core of my research thesis. However, I will also touch upon the current perspectives on the relation between short-term and long-term memory during the processing of bound information.

To offer an account for the storage of information in working memory (a short-term memory system conceived to manipulate information during action), Baddeley modified the initial three-component model (Baddeley & Hitch, 1974) by adding a fourth new component called the "Episodic Buffer" (Baddeley, 2000; Baddeley, 2007b). The logic behind this modification was

that the initial model did not support the storage of larger chunks of information. Hence, the question was raised as to how this complex information (e.g., long sentences) could be held and manipulated in memory for a short time. Evidence supporting the existence of a buffer with these functional properties came from studies in language processing (Baddeley, 2003; Baddeley, Gathercole, & Papagno, 1998; Collette, Van der, & Poncelet, 2000) whereby words grouped into sentences can be remembered easier than words presented as individual entities. More recent evidence suggests that the Episodic Buffer could also subserve the storage of visual objects (e.g., coloured shapes) (Allen, Baddeley, & Hitch, 2006). Baddeley suggested that equipped with a buffer like this, working memory may play an important role in solving the binding problem as multimodal information would converge into a system wherein it can be integrated into unified representations (Baddeley, 2000; 2007b).

The existence of an Episodic Buffer offers an account of how larger chunks of information can be held in working memory but it does not modify the capacity of this system which is set to be approximately four items (Jonides, Lewis, Nee, Lustig, Berman, & Moore, 2008). In an attempt to explore the unit of capacity of visual working memory, Luck and Vogel (1997) carried out an experiment in which they presented participants with increasing number of features bound into objects. They found that four was the number of items that participants could remember most effectively, which resembles the results found by other authors (Cowan, 2001; 2008; Cowan & Chen, 2009). However, they found that four objects were equally well remembered when each displayed one feature as when each displayed four features (sixteen features in total). The authors suggested that according to this evidence, visual working memory seems to store integrated objects. These initial findings were replicated by the same authors in a more extensive study a few years later (Vogel, Woodman, & Luck, 2001). Following these observations

Luck and Vogel (1997) and Vogel et al. (2001) proposed the hypothesis that visual working memory is object-based. This hypothesis proposes that as long as features belong to the same objects (i.e., they share the same visual space) they will be represented in visual working memory into unified representations.

Moreover, adding features to the same objects seems not to consume extra memory capacity (i.e., cost-free process). These objects will be accurately represented in memory whenever they do not exceed in number the capacity of short-term memory. Therefore, according to this hypothesis the capacity of visual working memory is determined by the number of objects that this memory system can hold and not by the number of features that are bound within these objects. By this mean, the hypothesis of an object-based attention (Duncan, 1984) is extended to visual working memory.

Wheeler and Treisman (2002) carried out a study in which they tried to replicate the initial findings by Luck and Vogel (1997) and Vogel et al. (2001). However, they came to diverging conclusions. Using a similar task, Wheeler and Treisman (2002) observed that remembering 3 objects composed of two colours each was more demanding than remembering three unicoloured objects. The authors concluded that remembering many colours is not a cost-free process. That is, the number of objects accurately remembered is determined by the number of colours composing these objects rather than by the number of objects *per se*. As a result, an alternative hypothesis was posited suggesting that visual working memory is feature-based.

This discrepancy has proved fruitful as both hypotheses have been fuelled by interesting findings. Table 1.1 summarizes some of these findings.

Table 1.1. Object-based versus feature-based visual working memory, evidence from the literature.

Authors	Stimuli	Paradigm	Results	Interpretation
Luck and Vogel, 1997; Vogel et al., 2001	Colours only or colours bound into bicoloured objects.	CDP, 50% chance, whole display. AS used. Change consisted of new features in the second display[1].	No cost for remembering bicoloured objects as compared to unicoloured object.	Binding is for free, visual working memory is object-based.
Walker and Cuthbert, 1998	Completed or degraded letters, nameable shapes, and nonsense shapes were presented individually or combined with colours.	Study cards presented for 5 sec followed by a recognition phase. AS was used in some experiments.	Verbal codes support shape-colour associations for bound and unbound features, visual integration only occurs when features are perceived together.	Visual representations are strictly object-based.
Wheeler and Treisman, 2002 [2]	Colours only or colours bound into bicoloured objects.	CDP, 50% chance, whole display. AS used. Change consisted of features swapping between objetcs in the second display.	Poorer memory performance for bicoloured objects than for unicoloured objects.	Colours are not integrated into unified objects. Visual working memory seems to be feature-based.

[1] One of the criticisms of this task is that for change trials new features replaced features previously presented, therefore actual binding of features was not required.
[2] Only one experiment from Wheeler and Treisman (2002) is presented in this table as it represents an unsuccessful attempt to replicate the results of the experiment presented by Luck and Vogel (1997) and Vogel et al. (2001) even though the authors used similar designs.

Table 1.1. Contd.

Authors	Stimuli	Paradigm	Results	Interpretation
Xu, 2002	Oriented bars, colours, math symbols, presented as individual features or as object parts	CDP, 50% chance, whole display. AS not used. Change consisted of new features in the second display.	Better memory performance for features that were parts of the same objects than for features presented as individual entities.	Visual short-term memory stores information about object parts in an object-based representation format.
Olson and Jiang, 2002	Colours only or colours bound into bicoloured objects. Size- or colour-orientation conjunctions.	CDP, 50% chance, single probe. AS used in one experiment only. Change consisted of new features in the second display.	Poorer memory performance for bound colours than for unbound colours. Conjunctions require less memory capacity but do not double it.	Conjunctions of features boost memory capacity but this depends on both the type of information and type of conjunction.[3]
Alvarez and Cavanagh, 2004	Snodgrass drawings, shaded cubes, random polygons, Chinese characters, letters, and colours	CDP, 50% chance, whole display. AS no used. Change consisted of one object changing identity.	Change detection was analyzed as a function of search times for each object. The type of item determined the capacity of memory.	Visual short-term memory capacity is not a fixed number of items. It depends on both the amount and type of information[4].

[3] Olson and Jiang (2002) suggest that the different pattern of results between labs may be due to using different methodologies such as blocked versus interleaved conditions, with and without concurrent verbal load tasks, whole display versus single probes, or different presentation times for memory displays.

[4] Similar findings were reported by Davis and Holmes (2005).

Table 1.1. Contd.

Authors	Stimuli	Paradigm	Results	Interpretation
Gajewski and Brockmole, 2006	Common shapes (e.g., star, square, etc.), colours, or shape-colour conjunctions	Cued-Recall. AS used. The retention interval was filled with an attentional load task.	Features of an item are remembered together or not remembered at all.	Visual short-term memory stores objects. This occurs without the need for attention[5].

AS: Articulatory suppression; CDP: Change detection paradigm

Some experiments summarised in Table 1.1 address the question of the representational format of visual working memory (Walker & Cuthbert, 1998; Xu, 2002), others investigate its capacity (Alvarez & Cavanagh, 2004), and others assessed both (Luck & Vogel, 1997; Olson & Jiang, 2002; Vogel et al., 2001; Wheeler & Treisman, 2002). In addition, the work by Gajewski and Brockmole (2006) assessed the extent to which attention may be required to hold bound information in visual working memory. I shall discuss the issue of the demand of cognitive resources and memory binding later in this chapter.

The evidence presented in Table 1.1 conveys some messages that may drive future research within the area of memory binding:

1. Binding information in visual short-term memory seems to reflect the activity of separate systems (e.g., visual information processed within the dorsal stream, or within the ventral stream, or across streams).

[5] This work was aimed at demonstrating the involvement of attention in binding information in visual short term memory. The lack of need for attention for holding bound items in memory observed by Gajewski and Brockmole (2006), has been also reported by Vogel et al. (2001), and by Johnson, Hollingworth, and Luck (2008) (but see Wheeler & Triesman, 2002 and Treisman, 2006 for a different view).

2. Somehow, this segregation should result in a coordinated activity of different systems (e.g., feature dimensions such as colour, shape, location, or memory domains such as verbal and nonverbal), each with its own functional principles. This coordinated activity will mediate the multimodal association.

3. The type of integration required (i.e., which features should be bound), the memory domains wherein these objects will be stored (i.e., verbal or visual), the process through which this bound information will be retrieved (i.e., recall or recognition), and retrieval cues (i.e., whole displays or single probes), all seem to determine the outcomes of these integration processes and how much resource will be required to carry them out.

As shown in Table 1.1, how bound information is retrieved from memory (i.e., recalled or recognized) seems to be an additional element to be considered when assessing binding in memory. There is evidence suggesting that recall and recognition are supported by separate processes (Kopelman et al., 2007; Mayes, Montaldi, & Migo, 2007; Milner, 2003). In the next Section I will briefly review the literature on retrieval processes and memory binding.

1.4.3 Retrieving bindings

Treisman (1977) suggested that conjunctions of features can be held in working memory through three mechanisms. First, forming higher level units wherein the formerly separate features are encoded. Second, she argued for the existence of spatial tags by which features sharing the same space are bound together. Third, she suggested that verbal labels could account for this integration. The use of verbal labels is a plausible and

accepted hypothesis of how bound information can be both kept active in and retrieved from working memory (Jonides et al., 2008; Smith & Jonides, 1997). Rehearsal has been the mechanism suggested as responsible for these operations. However, as Heathcote, Walker, and Graham (1994) remarked, this may not be the case for recovering information from visual working memory, as verbal codes are not available to this system.

Operations responsible for holding and retrieving bound information in and from visual working memory are less well understood (Baddeley, 2007c). The Feature Integration Theory of Attention (Treisman & Gelade, 1980) suggests the existence of a master map of locations through which features are kept together in perception aided by attention. Looking at the interpretation of the series of studies presented in Table 1.1, probably a map similar to this also exists in memory. This map would contain not only information about the location of items but also about the constituent features, temporal relation, contextual information, and all information that in turns defines episodes or past events. This may be thought of as an index map, and through these indices those aspects defining an episode would be retrieved (see Cer & O'Reilly, 2006). This map would account, for instance, for the observation that by retrieving specific features of one episode the remaining features defining this episode also could be accessed. This would also account for the object files proposed by Treisman (2006). However, an additional question emerges. How can one map like this subserve the retrieval of information from short-term and long-term memory? According to the model proposed by Cer and O'Reilly (2006) the hippocampus would play some role in indexing bound information. However, the hippocampus has been associated with long-term memory. This leaves the interpretation of how information is retrieved form visual short-term memory as a more challenging issue.

Bound information that is held in verbal short-term memory can be retrieved via the meaningful representations of the integrated items. This is supported by long-term memory. These meaningful links however, are not available to visual short-term memory. How is bound information accessed when it is held in visual short-term memory? Insights might be found by looking at the differences between performance in recall and recognition tasks. Little research has been published within the area of visual working memory and binding reporting the use of recall tasks. Most of the literature has focussed on the use of recognition tasks, particularly, change detection tasks. This point is highlighted from the summary of the available data in Table 1.1.

There is now compelling evidence suggesting that recall and recognition are processes meditated by separate mechanisms (Bastin et al., 2004; Delbecq-Derouesne, Beauvois, & Shallice, 1990; Kopelman et al., 2007). Recall is considered a more effortful process which relies on the working of the hippocampus while recognition requires less effort and seems to be supported by extra-hippocampal regions (i.e., perirhinal cortex) (Brown & Warburton, 2006). Furthermore, there is now evidence suggesting that recognition encompasses two distinct processes, recollection and familiarity (Daselaar, Fleck, & Cabeza, 2006; Davidson & Glisky, 2002; Opitz & Cornell, 2006; Quamme, Yonelinas, & Kroll, 2006; Rugg & Yonelinas, 2003).

Perhaps the greater use of recognition tasks over recall tasks to investigate the binding of information in visual working memory results from the fact that the separation of the contribution of recollection and familiarity to this retrieval process has provided a more precise account to explain how information is recovered from visual short-term memory. There is evidence suggesting that recollection might foster the recognition of relational bindings among items (Opitz & Cornell, 2006; Quamme et al., 2006). These

relational bindings may be formed over time probably through rehearsal or repetition of bound information. Therefore, this seems to be a process that involves the formation of long-term bindings. Familiarity, however, might support recognition of associative or conjoined components that are coherently encoded into bound representations (Haskins, Yonelinas, Quamme, & Ranganath, 2008; Opitz & Cornell, 2006; see also Moses & Ryan, 2006 for an up to date revision of the predictions made by the relational and conjunctive hypotheses of the hippocampal functions). By this means, familiarity may support the recognition of bound information that was once registered in a pure visual format. Evidence supporting this statement arises from the application of the Signal Detection Theory to recognition tasks. Memory tasks assessing the recognition of bound features elicit more biased responses than memory tasks assessing single features. This increased bias has been associated with a high sense of familiarity of the recombined features. In change detection tasks features in the study and test displays are the same but in the test display they are rearranged into different combinations 50% of times ("different trials"). This makes the probability of responding "same" more likely when the study and test arrays are actually different, suggesting that familiarity is affecting change detection (Cowan, Naveh-Benjamin, Kilb, & Saults, 2006). The likelihood of biased responses, hence the familiarity effect, has less impact if the study displays contain features that can be somehow encoded verbally or some kind of strategy is allowed to be used (e.g., mental imagery) (Hannula & Ranganath, 2008).

This evidence indicates that the contribution of familiarity and recollection to associative recognition depends on the types of binding operations required (Opitz & Cornell, 2006). Familiarity seems to be less resource demanding than recollection hence a question that arises is whether binding information in visual short-term memory is an active and resource demanding process or is rather automatic. In an attempt to provide answers to this question Allen

et al. (2006) carried out a series of experiments aimed at investigating the extent to which binding information in short-term memory occurs automatically or whether it relies on the functions of the central executive. Using dual-task methodology the authors demonstrated that concurrent tasks have no differential effects on visual short-term memory for bound information as compared to individual features. Therefore, they suggested that binding in visual short-term memory may occur automatically. Similar conclusions were reached by Treisman (2006).

In summary, there are some key issues to be taken from this literature:

1. Rehearsal can operate in verbal short-term memory to hold and retrieve bound information. We do not have a precise account for explaining how bound visual information is kept active in visual short-term memory.

2. Recall operates more effectively for retrieving well established associations from long-term memory while recognition seems to operate more effectively in visual short-term memory. Familiarity seems to provide the clues that aid this process.

3. Binding information in visual short-term memory seems to be an automatic process while binding in long-term memory requires more resources during both the consolidation and retrieval processes.

An important topic that follows on previous discussions of memory processes and binding functions is how this newly introduced concept of memory binding can help to understand (and eventually reconcile) the functional principles proposed for the models of human memory currently available that were briefly addressed in the Section 1.4.2. In the next Section I

shall review the available literature on this subject also stressing the relation between short-term and long-term memory for bound information.

1.5 The concept of binding and memory models

One controversial area within memory research concerns the definition of the boundaries between memory domains (long-term, short-term, and working memory) (Cowan, 2008). One first controversial point within this area has been the relationship between short-term memory and long-term memory, and different views have arisen. These propositions aimed to provide reliable accounts of memory operations concerning time scales, representational formats, unit of capacity, or the interrelatedness between systems. Noteworthy is the definition of long-term working memory (Ericsson & Kintsch, 1995) which represents a clear conceptual attempt of connecting two memory systems each of which has independent functional constructs.

A second controversial point has been defining the structure and operations of working memory and short-term memory, an area to which this thesis is relevant. There are reports in the literature addressing the capacity of working memory for objects and features (Luck & Vogel, 1997; Vogel et al., 2001). Working memory however, was conceived as an active memory system (Baddeley, 1992; Baddeley & Hitch, 1974) wherein information coming from different short-term memory components is manipulated during online processing or during decision making.

Therefore, what would determine the capacity of working memory would be the capacity of these subsidiary systems (short-term stores) from which it is fed and wherein information is passively kept.

1.5.1 Is binding important for short-term memory?

The three main models that have dominated the research into memory in the last decades were briefly mentioned in the Section dedicated to the maintenance of bindings in memory (1.4.2). In this Section I would like to focus on those aspects of these models that concern short-term and working memory binding.

1.5.1.1 Multicomponent model of Baddeley

The parallel model addresses working memory as a multi-component model (Allen et al., 2006; Baddeley, 2000; 2007a; Baddeley & Hitch, 1974). As was discussed earlier in this chapter, the initial model proposed in the 70s underwent substantial revision and the Episodic Buffer was added (Baddeley, 2000) as to accommodate those chunks of information described by Miller (1956) and Cowan (2001) which did not fit well in the former model. According to the operational rules of this working memory model, information coming from perception drains into working memory which in turn also draws information from long-term memory. Working memory hence acts a workspace within which new and old information can interact during action and learning. The Episodic Buffer was first thought of as a multimodal store where information coming from different domains (i.e., verbal and visual) converges (Baddeley, 2000). Research into language functions and verbal working memory extended this previous hypothesis adopting binding within the verbal domain as the process by which long segments of information coherently represented into meaningful units (i.e., sentences) would be stored with high efficiency and would boost memory capacity considerably (Baddeley, 2007d; Cowan & Chen, 2009). If the Episodic Buffer subserves the integration of verbal information, why not

think that visual information can also be integrated within the Episodic Buffer.

The work discussed above by Allen et al. (2006) addressed this issue and it led to two main suggestions. First, binding does occur within visual working memory and this process seems to rely on the function of the Episodic Buffer. Second, holding bound information in this buffer does not demand extra resources such as those administered by the central executive. The first conclusion fitted well into the previous ideas of the Episodic Buffer whereas the second one prompted a revision of the model and the way the buffer would be inserted into it. In his last book, Baddeley (2007b; e) himself acknowledged that the Episodic Buffer may involve the subsidiary slaves directly (e.g., visuo-spatial sketchpad) rather than been fed by the central executive as it was initially thought. Based on extensive evidence from neuropsychological and experimental data the other aspects of the model were left unmodified.

1.5.1.2 Workspace by Logie

One alternative view to this proposition of working memory as a workspace is proposed by Logie (2003). The author's view is that information flowing through the model may not exactly be as it is described by Baddeley et al.'s model. The fact that information held in working memory can become meaningful and it can also support the formation of new knowledge relying on previous experience suggests that inputs from perception may not drain straight into the slave systems as suggested by Baddeley et al.'s model, but they may first rely on long-term memory and from there, they would be fed into the workspace (i.e., working memory). As suggested by Logie (2003), the fact that dynamic visual noise impairs retrieval from long-term visual

memory but leaves intact visual short-term memory, suggests that visual inputs do not reach working memory directly but after they have activated long-term memory. Logie proposed that this model would offer a more creative and active space where the interaction between new and old information becomes a crucial feature of its functional properties.

One second addition to the initial multi-component model made by Logie is the definition of the visuospatial sketchpad as the integration of two fractionable components, the visual and the spatial. In this view, each component possesses its own functional properties (Logie, 2003; Logie & van der Meulen, 2009). These findings, which were based on both experimental and clinical evidence, have led the author to propose a new model of working memory which is still multi-component in nature but more dynamic in its interrelations with long-term memory. However, there are issues in which this model may encounter limitations. For instance, how abstract information would be represented in working memory if at its entrance to the system it will find no previous representations or reference patterns to match with in long-term memory? Moreover, how long-term memory would subserve the maintenance or use of this information in working memory if it holds no meaningful value? I shall come back to this point in the Section discussing the interaction between long and short-term memory in memory binding.

If perception drives the activation of long-term representations or the formation of new representations relying on working memory, and attention is thought to be a function important for carrying on these processes, would attention be required to represent bound information in working memory? The issue concerning resource demands and memory binding will be addressed later in this chapter. However, it leads straight to the model proposed by Cowan (1988) which will be discussed in the next Section.

1.5.1.3 Cowan's model

According to Cowan's view, there is no such distinction between short- and long-term memory nor is there a need for a multicomponent model to explain how the retention of information over short periods of times takes place. Simplifying his model, Cowan suggests that short-term memory should be seen as a subset of long-term memory which is activated (selected) by attention. In Cowan's model, attention is the core function and he describes the function of attention as pointers (i.e., similar to the central executive, or to the action of the Episodic Buffer) which indicate the section of these long-term records that will be selected and then used for action. Both Baddeley and Logie do not think of working memory in such a way. Their views were strongly influenced by neuropsychological data by which the different working memory components they proposed were found to be differentially impaired (Baddeley, 2007d; Della Sala & Logie, 2002) even in patients who exhibit no long-term memory deficits (which seems to be unaccounted by Cowan's model).

One other caveat of Cowan's model may stem from the observation of attentional demands during working memory binding tasks. If it is true that, as Cowan (2008) suggested, not all type of concurrent tasks draw equal amount of attention and not all would interference in the same way (e.g., during rehearsal), it leaves unexplained why even when attentional resources are depleted, bound information can be held in working memory no differently than unbound or unrelated information (Gajewski & Brockmole, 2006; Allen et al., 2006). I will review the issue of resource demands and memory binding in the next Sections aiming at finding insights into the involvement of attention in this memory function. However, before finishing this Section I would like to highlight that if a variety of arguments have been used in the past to criticize and reshape these models, those

arguments arising from binding processes seem to be promising approaches to keep refining the theoretical constructs of human memory. More precisely, I would like to propose that adopting binding as a theoretical perspective in future research may help to reconcile some of the discrepancies we still face when using these models to offer accounts of our data.

1.5.2 Binding in visual short-term memory and capacity issues

Visual short-term memory has been considered the least well investigated component of the Baddeley and Hitch's (1974) working memory model (Baddeley, 2007c; Pearson, 2001). There is little understanding of how the information that is bound into unified objects is held in this memory system. On the one hand evidence suggests that the unit of capacity of visual working memory depends on the number of objects to be stored (Gajewski & Brockmole, 2006; Luck & Vogel, 1997; Xu, 2002). On the other hand it has been suggested that the number of features composing these objects, the type of features, as well as the way these features are combined, may affect this capacity (Alvarez & Cavanagh, 2004; Davis & Holmes, 2005; Eng et al., 2005; Olson & Jiang, 2002; Xu, 2002) (Table 1.1 presents comprehensive evidence supporting these hypotheses of visual working memory).

Following on from this evidence, it has been proposed that the amount of information that can be effectively maintained in visual working memory may not be a fixed number of items. This raises the question of whether the unit of capacity of visual working memory for multi-feature objects may be affected by the type and the amount of information comprised by these complex objects. Evidence suggests that these factors do affect visual short-term memory.

The capacity of visual working memory has been set to be 4 objects (Cowan, 2001). That is, four objects will be stored in this memory system regardless the number of features they comprise (Luck & Vogel, 1997; Vogel et al., 2001). For a variety of features this has been found to be the case (see Luck & Vogel, 1997; Vogel et al., 2001). However, other types of features have shown to be less likely to be bound into unified representations (see Wheeler & Treisman, 2002 for a discussion on this issue) following the same functional principles. The Parallel Processing Hypothesis provides some accounts for this discrepancy. This hypothesis suggests that features are stored in separate unimodal dimensions each with its own capacity. According to this hypothesis, it is the capacity of each dimension that determines the capacity of visual working memory for multi-feature objects. If the assumption of this hypothesis is valid, it would be reasonable to expect that the type of information to-be-bound into single objects would affect the capacity of visual working memory, as remembering multi-feature objects composed of the same type of feature would result in a more demanding task (due to within dimension competition) than remembering objects defined by different types of features (due to shared capacities).

One reason for this discrepancy between binding same and different feature types may be that the processes responsible for integrating features compete for resources and this competition may result in interference. This interference has been found to be greater when features compete for the same resources (e.g., within the same feature dimension, for example binding colours into bicoloured objects; Wheeler & Treisman, 2002) than when different feature dimensions are involved (e.g., binding colours with locations). This suggests that the efficiency of binding information in visual short-term memory depends on both the amount of resources available within each feature dimension and the degree of interference that may arise from competition for these resources.

Furthermore, slight variations of experimental settings have removed the object-based representation proposed by Luck and Vogel (1997) (e.g., using single probes rather than whole displays, varying physical properties of colours, changing the way the verbal load task was carried out – e.g., rehearsing loudly versus rehearsing saliently) even when very similar designs have been used (Wheeler & Treisman, 2002; Xu, 2002). This suggests that binding information in visual short-term memory reflects the operation of fragile processes (see Allen et al., 2006 for a similar view) and that methodological changes may yield different results. Another important factor affecting the integration of features into objects is the amount of information to-be-bound. Olson and Jiang (2002) observed that the capacity of visual working memory depends on both the number of objects and the number of features that are bound into these single objects.

Alvarez and Cavanagh (2004) used a visual search task and measured the time taken to search for objects composed of different number of features (e.g., coloured squares, letters, Chinese characters, random polygons, line drawing). They plotted this time as a function of the estimated capacity of visual working memory. The authors founds that those objects comprising more features resulted in longer search time and they also limited the capacity of visual working memory to a greater extent. According to Alvarez and Cavanagh (2004), more complex objects would require more visual scanning time which in turn would reduce available capacity in visual working memory. This suggests that the time allotted to studying visual arrays would impact on the amount of information encoded and consequently transferred into visual short-term memory.

1.5.2.1 Binding in short-term memory: neuroimaging evidence

Prabhakaran, Narayanan, Zhao, and Gabrieli (2000) carried out a fMRI study aimed at investigating, in healthy young adults, the brains regions responsible for binding in working memory letters to locations. The authors found activation of the right prefrontal regions when participants remembered objects defined by the combination of these items. This activation was larger than when participants remembered letters only or locations only, stimuli that resulted in more processing in posterior regions. Moreover, the authors reported that holding integrated information in working memory recruited less brain volume in the prefrontal regions than the volume recruited in the posterior regions when single items where remembered. Prabhakaran et al. (2000) suggested that these findings point to the right prefrontal region as the neuroanatomical correlate of the Episodic Buffer proposed by Baddeley (2000). In a more recent neuroimaging study, Xu (2007) assessed the neuroanatomical correlates of memory binding when arbitrary shapes with colours were held in visual short-term memory. Xu (2007) suggested that posterior brain regions, more precisely the intraparietal sulcus, seem to represent the total amount of feature information retained in visual short-term memory but not the number of objects. Uncapher, Otten, and Rugg (2006) addressed similar questions as Xu (2007) but using different type of stimuli (words + colours or words + location). In this study the authors found that the intraparietal sulcus was the region with significant activation when they analyzed the multifeatural effects (i.e., integrated features).

In summary, neuroimaging studies seem to converge in that there are brain regions responsible for processing feature information while other regions are more involved in object processing (see Donner, Kettermann, Diesch, Ostendorf, Villringer, & Brandt, 2002 for additional evidence on the role of

prefrontal and parietal regions in attention, feature integration, and object identification). Which brain region is more engaged in one or another type of processing seems to depend on the nature of information that is being processed and the structure of this bound information. These factors have proved to affect both the pattern of brain activation (as shown by neuroimaging studies) as well as memory performance (as it was discussed through behavioural evidence presented above).

1.5.3 Resource demands and memory binding

As was discussed in Section 1.3, attention is important for perceptual grouping however less well understood is whether attention is also important for holding bound information in short-term memory. Concerning the functions of working memory, there is divergence across evidence addressing this issue. Experiments by Treisman and colleagues (Treisman, 2006; Wheeler & Treisman, 2002) and others (Cowan, 1988; 2008; Cowan & Chen, 2009; Cowan et al., 2006) have suggested that attention seems to be important for both binding in perception and in memory. However, Vogel et al., (2001), Gajewski and Brockmole (2006), and Allen et al. (2006), have suggested that attention is not required any more for retaining complex objects in working memory than it is for retaining single features. This last set of findings has led to the suggestion that binding in visual working memory should be seen as an automatic process demanding few cognitive resources.

However, there are still some outstanding issues in this area. First, the tasks that have been used to overload attention may not have done so as efficiently (e.g., demanding enough) as to elicit interference by depleting resources (see Cowan, 2008 for a similar view). Second, the nature of the information used

to overload attention may not be the most appropriate given the nature of the to-be-interfered tasks. For instance, when it comes to the retention of bound information in the verbal and visual memory systems as Figure 1.1 shows, the issue seems to be more complicated.

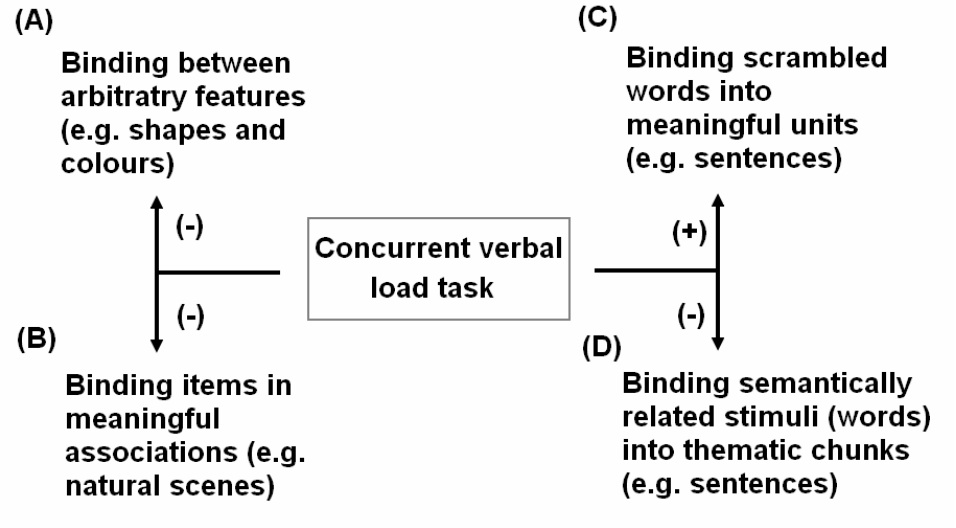

Figure 1.1. Diagrammatic example of the effect of concurrent verbal load task on binding information in short-term memory across visual and verbal domains. Reference to these effects can be found in (A) Allen et al. (2006), Vogel et al. (2001), Treisman (2006), Gajewski and Brockmole (2006); (B) Hollingworth (2005); (C and D) Baddeley, 2007 b; e; (-) no differential effects on binding; (+) effects on binding.

In the majority of these studies, the to-be-remembered materials were visually presented whereas the interfering tasks were verbal in nature (e.g., articulatory suppression by rehearsing vocally or subvocally letters or digits, n-back tasks, etc). As suggested by Cowan (2008), not all forms of concurrent verbal load tasks impose an equal amount of demand or exert equal amount of interference. For example, the author highlighted this point so as to stress why in Vogel et al.'s study (2001) the use of a verbal load task may have had no effect on visual short-term memory performance for colours bound into

objects. Cowan (2008) argued that when the interposed task is more automatic and does not require attention (as is the case for an articulatory suppression task), there is less effect of this interposed process. In line with this view, Logie (2003) suggested that people can use more than one form of coding when given, for instance, a verbal recall serial task. These suggestions convey the message that visual-to-verbal or verbal-to-visual bypass of information may occur and this in turn may aid performance during memory tasks by further reducing interference effects.

Going back to Figure 1.1, it might be suggested that when the information is verbal in nature (B, C and D), people seem to be more likely to form units by binding this information into meaningful larger chucks (e.g., in sentences as in C and D). The difficulties encountered in doing so (e.g., in C), will pull more resources out from the cognitive systems. This difficulty seems to be overridden when semantic clues are available during the encoding of to-be-bound information. For example, looking into the verbal domain, as long as letters can be grouped into words, words into sentences, or digits into telephone numbers or important dates (processes known as chunking) (Baddeley, 2000; Cowan, 2001; Cowan & Chen, 2009; Miller, 1956), the efficiency of memory is largely boosted while the consumption of resources drops considerably. Within the visual domain, when the binding of visual features results in integrated objects that lead to previous meaningful or semantic representations, these objects are held and used by short-term memory more efficiently than if they are composed of meaningless or randomly combined arbitrary features. Moreover, the way in which this information is available to make online decisions (i.e., impact of long-term on short-term memory performance) also varies depending on whether verbal coding of these bound features and/or their semantic relations with external clues is possible (for example natural scenes as shown by Hollingworth, 2005 versus random features as shown by Colzato, Raffone, & Hommel, 2006;

Logie, Brockmole, & Vandenbroucke, 2009; Treisman, 2006). I will come back to this issue in the Section discussing the interactions between short- and long-term memory. Other evidence backing up this observation comes from studies in which people are presented with letters of their own alphabet and are asked to remember their visual appearance. Logie (Logie, Della, Wynn, & Baddeley, 2000; Saito, Logie, Morita, & Law, 2008) suggested that people could swap from one form of representation to another one, e.g., remembering sequences of Kanji characters in Japanese speakers either as visual codes or as phonological codes.

Summing up, the efficiency of binding processes and the amount of resources required for these operations seem to vary depending on the nature of the information to-be-remembered. People seem to be able two swap from one form of representation to another one (i.e., verbal to visual or visual to verbal) depending on whether or not the to-be-remembered information holds semantic value. One may assume that the semantic value of these inputs may facilitate the access to long-term representations, and this would aid both the process of binding and memory maintenance. As shown in Figure 1.1., when the to-be-bound features are familiar items (i.e., words, objects within natural scenes), and the outcomes of their integration are meaningful units (i.e., sentences, familiar scenes), the binding of these items seems to happen effortlessly. However, when this integration cannot yield meaningful units (i.e., scrambled words), more resources are drawn from the central executive.

Some questions arising from the literature reviewed above are:

1) What is the role of long-term memory in verbal binding and visual binding?

2) Is the lack of effect of concurrent verbal load tasks used in the studies presented in Figure 1.1 A (arbitrary bindings of visual features) and B (natural scenes) attributable to similar mechanisms?

Answering these questions may help to fill in some gaps still nurturing the large body of works published in the area of memory binding. These answers will also help to improve our understanding of how short- and long-term memories are reciprocally bridged and what is the role of binding functions in this process. In the next two Sections I will review the available literature on binding and long-term memory.

1.5.4 Is binding important for long-term memory?

This research project investigated aspects related to short-term memory. In fact most of this review has addressed the literature on this theme. However, I will discuss some general aspects of long-term memory which may help to make the relational nature of human memory more evident. To do that, I will undertake a quick theoretical journey through the different long-term memory systems encompassed by the taxonomy of long-term memory described by Tulving & Donaldson (1972). In doing so, I will identify the extent to which the functional integrity of these systems may depend on binding processes.

1.5.4.1 Episodic memory

Episodic memory is the memory system responsible for storing and recollecting previous events and the location of these events in space and time (Tulving & Donaldson, 1972). From this definition it becomes clear why

Tulving proposes a relational nature for episodic memory. Tulving (2002) suggests that episodic memory may be thought of as a series of past experiences bound into complex events or more precisely as different forms of memory expressions bound across systems which process the different pieces of information encompassing these events (i.e., space-time, events-contexts, emotions-actions, and so forth).

Holding bound information in short-term memory seems to occur effortlessly (Allen et al., 2006). However, forming long lasting representations which could be later accessed explicitly, does require a great deal of cognitive resources (Tulving, 2002). To accomplish these binding functions the medial temporal lobe structures, and specifically the hippocampus, seem to be crucial. Moses and Ryan (2006) reviewed the literature on long-term memory and associative learning and suggested that two main predictions made by the hippocampal functions reflect the role of this structure in memory. These are the relational and conjunctive binding hypotheses which address how these medial temporal lobes regions mediate the formation of integrated representations in memory.

There is now accrued evidence in the literature on amnesia (Hannula & Ranganath, 2008; Hannula, Tranel, & Cohen, 2006; Mayes et al., 2004; Mayes, Holdstock, Isaac, Hunkin, & Roberts, 2002; Moses & Ryan, 2006), animal studies (Moses, Cole, Driscoll, & Ryan, 2005; Moses, Cole, & Ryan, 2005; Moses & Ryan, 2006), computational model (Cer & O'Reilly, 2006; O'Reilly, Busby, & Soto, 2003), and fMRI studies (Mitchell, Johnson, Raye, & D'Esposito, 2000; Mitchell, Johnson, Raye, Mather, & D'Esposito, 2000), which has consistently supported the role of these brain regions in memory binding as well as their role in learning and forming new episodic representations.

I will not describe in detail these studies in this Section as they will be addressed throughout the series of experiments carried out as part of this research project.

1.5.4.2 Semantic memory

The content of semantic memory is thought to comprise our knowledge of the world. For example, meaning of words, interpretations of events, etc. (Baddeley, 2001a; Hart, Jr. et al., 2007; Tulving & Donaldson, 1972). Semantic memory is linked to binding functions in that it has been considered the cognitive glue required to unitize features into single unified objects (Heathcote et al., 1994; Lloyd-Jones, 2005). As was discussed above, when lexical clues that can lead to word representation are available (e.g., phonemes that enable word formation), memory operates more efficiently by chunking these individual clues into lexical or semantic units (Cowan, 2001; Cowan & Chen, 2009; Miller, 1956).

Evidence about the contribution of binding functions to semantic memory mainly comes from studies of language formation and language acquisition (Baddeley, 1998; 2000; 2007e). In this context the working memory model proposed by Baddeley and Hitch (1974) and more specifically the phonological loop, has played a crucial role (Baddeley, 1998; 2007e). There is evidence that binding functions can operate across different memory domains (i.e., cross-modal binding) and the results of this integration yields to the representation of new semantic objects which are drawn from multimodal visual stimuli (e.g., picture of a candle and the word "icing" activate the internal representation of a "cake") (Kraut, Kremen, Moo, Segal, Calhoun, & Hart, Jr., 2002; Kraut, Kremen, Segal, Calhoun, Moo, & Hart, Jr., 2002) .

Additional evidence comes from the neuropsychology literature (Knott, Patterson, & Hodges, 1997) in which patients with Alzheimer's Disease (Buschke et al., 1999; Buschke, Sliwinski, Kuslansky, & Lipton, 1997; Kraut, Cherry, Pitcock, Vestal, Henderson, & Hart, Jr., 2006; Lloyd-Jones, 2005), Mild Cognitive Impairment (Kraut et al., 2007), or Semantic Dementia (Knott et al., 1997) have been found to be less able to use their binding abilities to aid semantic or lexical representations. For example, when patients with Alzheimer' Disease are given lists of word pairs which are associated following different semantic categories (i.e., country, food, etc.), they are less able to retrieve the missing words in the cued recall phase of the test either by using the cue or the category under which words were paired (Buschke et al., 1997).

Summarizing, there seems to be a bidirectional relation between memory binding and semantic representation. That is, binding operations subserve the representation of complex events into meaningful or semantic units, and these semantic units would then aid the process of holding or representing information about these complex events either in a transient (i.e., short-term memory) or in a more durable format (i.e., long-term memory). This proposal fits well with the suggestions made by Kraut et al. (2002).

1.5.4.3 Implicit memory

Implicit memory or non-declarative memory refers to a memory system in which the effect of experience overrides the need for conscious recollection of that learnt information which is mainly used for action (i.e., automatic or unconscious access) (Squire, 2004). Hence, the lack of awareness during the access and use of this information is a distinctive and paramount feature of

implicit memory. Under this form of memory two types of learning processes have been allocated, classical conditioning and operational conditioning. These forms of learning involve the development of associations between stimuli (classical conditioning) or between stimuli and responses (operational conditioning). In a recent review of the literature, Mitchell, Houwer, and Lovibond (2009) suggest that two propositions should be considered in understanding human associative learning. One such proposition is called by the author the "propositional approach" and the other one is called the "dual-system approach". The propositional approach addresses relational binding processes that are consciously accessed, effortful, and affected by verbal instructions. This proposition enables the understanding of the meaning between bound elements. Therefore, this approach resembles more what we know about explicit episodic relational memory. The dual-system approach however incorporates some elements of the propositional approach but it mainly rests on a form of relation called "link formation mechanism" which is not accessible consciously, not susceptible to verbal tagging, and effortless. Through this type of association no information about the nature of the bound elements is accessible nor can it be recollected through conscious access. This form of associative learning fits well with those functions of the implicit memory.

In experimental psychology implicit memory is assessed by measuring the effect of unattended information on performance (e.g., Repetition Priming) and is sometimes called incidental learning paradigm. Nyberg (2006) presented the results of an experiment in which the incidental learning of words- or non-words-sound pairs were assessed. In this study, participants were presented with lists of words or word-sound associations and were then tested for word recognition. They were told nothing about the sound which was indeed the relevant dimension. In the fMRI scanner it was found that words that had been initially paired with sounds elicited activation of

auditory areas whereas those words that were individually presented did not elicit such activations. Hence, this is neat evidence suggesting that implicit learning between sound-word pairs occurred.

Other evidence for the effect of implicit learning on behaviour comes from a study assessing the effect of classical conditioning on the emotional stroop (Richards & Blanchette, 2004). In this study control and anxious participants were presented with words or non-words during a classical stroop test. Words and non-words were initially paired using a classical conditioning paradigm with negative or neutral pictures. This manipulation rendered those words or non-words paired with negative picture as more emotionally loaded stimuli. It was predicted that the presentation of stimuli conditioned by negative emotion would result in higher interference during the classical stroop test, and this effect would be more salient in anxious people. This hypothesis was supported and it confirms that implicit associative learning can also underpin performance during conflicts introduced by emotional stimuli.

The results of this research project are more relevant to the area of explicit memory. However, the evidence presented above does help to understand the role that binding functions play across memory systems, memory domains, and memory operations. I will not deal with the issue of implicit memory binding in any more detail along this thesis but I will rather focus on explicit short- and long-term memory.

1.5.5 Memory binding and interactions between short- and long-term memory

As has been thoroughly discussed in previous sections of this chapter, binding information in visual short-term memory seems to occur automatically, while forming bound representations in long-term memory appears to be a resource demanding an effortful process.

According to the model proposed by Cer and O'Reilly (2006), keeping and updating bound information in visual short-term memory is a function carried out by the prefrontal cortex. This suggestion fits well with the model of working memory proposed by Baddeley and Hitch (1974), in particular to the functions ascribed to the Episodic Buffer (Baddeley, 2000; Allen et al., 2006). Neuroimaging studies have also demonstrated that the prefrontal cortex is actively engaged in the process of binding information in visual short-term memory (see the work by Prabhakaran et al., 2000 discussed in Section 1.5.2.1).

The hippocampus is considered a critical structure for forming episodic memories (Baddeley, 2000; Burgess, Maguire, & O'Keefe, 2002; Gabrieli, Poldrack, & Desmond, 1998; Hannula & Ranganath, 2008; Hodges & Graham, 2001; Kopelman et al., 2007; Milner, 1972). Since forming new episodes in memory and binding information seem to be two functions closely related, the hippocampus has been linked to memory binding (Cer & O'Reilly, 2006; Ruchkin, Grafman, Cameron, & Berndt, 2003). Intracellular recordings in monkeys have shown that the medial temporal lobes structures are populated by neurons which exhibit specific activation during Match-to-Sample and Paired Associate Learning Tasks (Miyashita, 1993). Accordingly, lesions to these regions in humans result in profound memory deficits for associated information (Hannula & Ranganath, 2008; Hannula et al., 2006;

Kan, Giovanello, Schnyer, Makris, & Verfaellie, 2007). Cer and O'Reilly (2006) suggested that since the prefrontal cortex can transiently maintain bound information whereas the hippocampus cannot, these regions are complementary memory systems working together.

Is there any functional relation between binding processes in short-term and long-term memory? Does the information that is bound in short-term memory affect long-term representations and vice versa? Current evidence suggests that long-term and short-term memory involving complex events operate in parallel. Clear-cut evidence supporting this claim comes from the study carried out by Colzato et al. (2006). Using a series of experiments they demonstrated that repeating bindings made of oriented lines (vertical and horizontal) and colours (red and green) resulted in some learning of the highly repeated associations but this learning effect was not transferred to online decisions (i.e., short-term memory performance). Earlier studies carried out by Kahneman, Treisman, and Gibbs (1992) published in Treisman (2006) showed that one new trial was enough to overwrite previous bindings. This would indicate that there is no accumulative effect on performance during visual working memory tasks when bound objects are repeated. Treisman (2006) observed that: (1) repeating bindings within the same task results in learning; (2) this learning did not improve recognition performance in visual working memory; (3) binding in visual working memory seems to be an automatic process. Treisman concluded that binding occurs both in visual working memory and in long-term memory but that there is no interaction between these operations. More recent evidence from the work of Logie et al. (2009) further supports this lack of interaction between short-term and long-term memory for bound information. Binding information in short-term and long-term memory would therefore involve processes occurring at different time scales, forming files of different natures, or using different underlying mechanisms (Colzato et al., 2006).

Are processes responsible for binding information in short-term and long-term memory "completely" independent? Are medial temporal lobe structures not related at all with operations responsible for binding information in visual short-term memory? There seems to be a discrepancy in this area. While one set of evidence coming from amnesia literature suggests that medial temporal lobe structures are important for binding information in short-term memory, other evidence coming from the same background suggests that binding in short-term memory is not affected in these types of patients. It would be worth identifying what are the reasons behind this discrepancy as they may help to improve our understanding of how binding processes operate and what brain regions may subserve these operations. I shall review this issue in the Section addressing memory binding in amnesic patients which is presented in the second part of this chapter.

Before, addressing the literature on amnesia, it would be worth a brief discussion of the review carried out by Moses and Ryan (2006) which addressed the relational and conjunctive hypotheses of the hippocampal functions and which was briefly mentioned in Section 1.5.4.1. In this review the authors accrued evidence from human and animal literature looking for insights about the role of the hippocampus in the formation of relations or conjunctions of features in memory. According to Moses and Ryan (2006), the relational hypothesis of the hippocampal functions accounts for the representation of associations between items in long-term memory (e.g., objects and locations, faces and names). Once this associated information is represented in long-term memory, either the whole association or its constituent parts can be easily accessed. This type of representation is additionally flexible in that it can link to other associations either via its elements or via the unified representation itself (Mayes et al., 2007; Moses & Ryan, 2006). These binding processes are thought to mediate the formation of

long-term associations in memory, representing by this means the basis for associative learning (see also Cer & O'Reilly, 2006 and Brown & Warburton, 2006). The conjunctive hypothesis of the hippocampal functions accounts for the formation of integrated or "unified" units (e.g., shapes and colours into coloured shapes). These representations appear to be less flexible than those formed via relational binding in that once individual features are bound into these units, they cannot be accessed individually (Moses & Ryan, 2006). Changing a feature would result in the formation of a new representation. In the recent literature on short-term memory binding, a form of conjunctive representation that resembles this description has been proposed (Allen et al., 2006; Gajewski & Brockmole, 2006; Treisman, 2006). According to this evidence, these conjunctive units can be effectively held in memory for the duration of the task in which features are bound (Colzato, et al. 2006; Logie, et al., 2009; Treisman, 2006) and they are over-written in memory as soon as a new trial is presented, leaving no long-term traces of this bound information.

One crucial conclusion to which this review arrived (Moses & Ryan, 2006) is that the relational hypothesis is better accounted for by what we know about the hippocampal functions than the conjunctive hypothesis. One reason behind this conclusion may be that the conjunctive hypothesis could be accounted for by functions carried out by structures outwith the medial temporal lobe structures. Despite the fact that this review addressed the hippocampus as a structure responsible for forming long lasting memory representations of relational information, the authors acknowledge that there are gaps left by the conjunctive hypothesis which still require further research. One such gap is related to short-term memory binding. Moses and Ryan (2006) argued: "…*If "rapidly forming conjunctive representations'' includes conjunctive information processing in short-term memory, then Ryan and Cohen's findings contradict conjunctive theory, as this process can be carried out without an intact hippocampus*" (p.56, paragraph 2).

Therefore, the hypothesis of a complete separation of short- and long-term memory systems for processing bound information does not seem to be supported by the studies discussed above. Furthermore, Hollingworth (2005; 2007) have reported that when processing natural scenes, those elements previously learnt about these scenes do impact on online decisions during the ensuing short-term memory task. This suggests that the nature of the to-be-bound information is an essential aspect to determine whether short- and long-term memory would interact.

The literature reviewed above mainly concerns to young healthy adults. As the aim of this research project also extends to healthy older people, in the next Section I shall review the available literature on memory binding in normal ageing. I will try to find insights on what could be the mechanisms supporting memory functions in healthy old age and how they may differ from those driving abnormal ageing.

1.6 Memory binding in the normal ageing

There is accrued evidence suggesting that the efficiency of processes responsible for binding information in memory changes across the lifespan. Cowan et al. (2006) described some working memory processes related to binding as undergoing an inverted-U shape, suggesting that the efficiency of these processes is poorer at both edges of life and is maximal in the middle years. As people get older, it is an everyday experience to forget the location of common objects, the name of relatives or friends, and other complex events. These memory problems have been also replicated in experimental settings, where it has been shown that deficits in associating objects to locations (Chalfonte & Johnson, 1996; Mitchell et al., 2000), names with faces

(Naveh-Benjamin, Guez, Kilb, & Reedy, 2004; Sperling et al., 2003) , or objects with colours (Chalfonte & Johnson, 1996), are underlying these episodic memory problems observed in older people.

These memory limitations however, have not been accounted for by deficits in perceptual binding. It has been demonstrated that older adults have problems in processing visual information when stimuli are difficult to discriminate or when the time allowed to perceive these stimuli is short (Cerella, 1985; Cerella, Poon, & Fozard, 1982; Schefrin, Tregear, Harvey Jr., & Werner, 1999; Scialfa, Guzy, Leibowitz, Garvey, & Tyrrell, 1991; Scialfa, Kline, & Lyman, 1987). This evidence has led to the suggestion that limitations of top-down mechanisms (i.e., binding via attention) may not be responsible for the deficits in feature integration observed in older adults during perceptual tasks (Gottlob & Madden, 1998; Madden, Gottlob, & Allen, 1999; Madden, Spaniol, Bucur, & Whiting, 2007; Madden, Whiting, Cabeza, & Huettel, 2004; Whiting, Madden, & Babcock, 2007). For instance, older adults have shown equivalent performance to that of younger adults when additional cues are provided to guide the visual search for targets defined by conjunctions of features. Examples of these cues are colours (Madden et al., 2002; Madden et al., 1999), or highly informative guidance, such as anticipating the type of changing display or increasing the proportion of the changing modality within the searched array (e.g., the target is one of three items with the same colour and the distracters are items of different colours) (Bucur et al., 2007; Madden et al., 2002; Madden et al., 2007; Madden et al., 2004).

Therefore, the difficulties observed in older adults during visual search tasks seem to respond to bottom-up limitations (i.e., resulting from sensory processing) rather than impairments of top-down processes (i.e., attention) (Madden et al., 2002; Madden et al., 1999; Madden et al., 2004). Furthermore,

the general slowing affecting cognitive processing in older adults has also been considered a mechanism limiting performance in tasks assessing search for conjunctions of features (Bucur et al., 2007). Both factors are tightly related to high task demands as has been demonstrated in previous studies (Madden, 2007; Madden et al., 2007). These findings support the view that the ability to associate or "bind" information at a perceptual level is preserved in ageing once factors affecting older people such as sensory limitations or slow processing speed are controlled for age (e.g., by improving the discriminability of visual objects, reducing perceptual load, or presenting visual materials for longer periods of time).

In long-term memory however, age does seem to impair the mechanisms responsible for binding information, and this impairment seems not to be associated to memory load, presentation time, or types of information. Naveh-Benjamin (2000) proposed an Age-Related Associative Memory Deficit Hypothesis which suggests that memories encompassing complex events are more deteriorated in older adults than memories of single or unrelated events. For example, older adults' difficulties in remembering word-word or face-name associations are far greater than memory difficulties for individual words or individual faces (Naveh-Benjamin, 2000; Naveh-Benjamin et al., 2004). Chalfonte and Johnson (1996) devised a task to investigate long-term memory deficits for bound information in older adults. In this task, young and older participants were presented with arrays of common objects in different colours or in different locations for 90 seconds. After the memory phase, participants were provided with recognition sheets and they where asked to selected, in an additional 90 seconds, the colours, the objects, the locations, or the combinations of these items. The authors found a paramount memory deficit for the combination of features in older adults as compared to memory for the individual features. Additional evidence has been provided by experiments investigating source memory

which has confirmed that these problems in associating information in long-term memory in older adults are not material specific (Hashtroudi, Johnson, & Chrosniak, 1989; Henkel, Johnson, & De Leonardis, 1998; Johnson, De Leonardis, Hashtroudi, & Ferguson, 1995).

The effects of age on processes responsible for binding information in short-term memory have been less thoroughly investigated. Recent experimental evidence suggests that age may also affect the mechanisms responsible for holding bound information in visual short-term memory. Particularly, this memory binding problems seem to be related to a limitation in associating or "binding" in visual short-term memory items (i.e., objects or colours) to locations. Two studies have been published supporting this view (Cowan et al., 2006; Mitchell, Raye, Johnson, & Greene, 2006). However, Olson, Zhang, Mitchell, Johnson, Bloise, and Higgins (2004), asked older adults to remember arrays of spatial locations (Experiment 1) and they found that when the number of locations was small enough as to enable the binding of these locations into configural patterns, older adults could retain these arrays in working memory without difficulties.

Olson et al. (2004) also found that older people could retain incidentally the location of 2 items (Experiment 2). These results led the authors to suggest that short-term memory for spatial information is preserved in older adults. However, this generalization should be treated cautiously as in the Experiment 1 of Olson et al.'s study, spatial locations may not have been remembered as separate spatial entities (i.e., dots) but as patterns made of the association of these entities. In this case, were not individual locations but configurations what older people were actually holding in working memory (see Cowan et al., 2006 for a similar criticism to these results). In fact, when the number or locations were increased from three to six (in Olson et al.'s Experiment 1), the likelihood of using configural representation was reduced

and performance of older adults dropped considerably. In the case of the incidental learning (Experiment 2), it is known that this form of memory is less demanding that the explicit learning hence, any effect of age is less likely to show under this condition (Kester, Benjamin, Castel, & Craik, 2002).

This evidence suggests that short-term memory for bindings involving locations seems to be the function impaired by age. However, it remains unexplored whether these age-related binding deficits in visual short-term memory extend to the representation of the multiple surface features that define objects such as colour and shape. It is unknown whether such cognitive changes with age are specific to long-term memory, or if they also affect visual short-term memory. As was discussed in Section 1.5.5, the functional relation of binding processes operating in short- and long-term memory is not well understood. We do not know whether binding in these memory systems reflects the operation of the same processes, some kind of shared mechanism, or whether binding operates separately in both types of memories. Is it also unknown whether these functions are differentially vulnerable to the effects of age.

1.7 Summary

There are some theoretical implications resulting from this part of the literature review which are relevant to my research project:

1. Binding in short-term memory is a relatively novel research subject. We have a clearer understanding of processes responsible for binding within long-term memory thanks to the numerous investigations on the role of the medial temporal lobes structures both in human and animal models. Binding operations carried out in verbal short-term memory are better

understood than those occurring in visual short-term memory. This is thanks to the intensive research in language processing and on the phonological loop. Concerning visual short-term memory, recent evidence has begun to suggest that the Episodic Buffer may help in accounting for these operations. However, to what extent binding in short-term memory is an automatic or resource demanding process, how long-term associations interact with short-term bindings, which factors affect the representation format of bound information in short-term memory, are issues still open to questions. In this thesis I will address some of these questions by investigating binding in short-term memory both in normal individuals and in patients with brain damage.

2. Binding occurs in short- and long-term memory. How these processes operate in these memory systems, whether or not they interact, and what is the final representation of complex events in short- and long-term storages, seem to be issues still to be clarified. Evidence accrued and discussed here suggests that short- and long-term memory for bound information may be more functionally linked than what has been thought to date. The medial temporal lobe structures may be seen as the functional bridge that connects binding processes carried out in short- and long-term memory. However how these links operate seems to depend on the nature of the information that these complex experiences encompass.

3. Normal ageing impairs those processes responsible for binding information in long-term memory in a non-material specific way. Processes responsible for binding information in short-term memory however, seem to be impacted by age when items (e.g., colours or objects) have to be bound to locations forming different relational representations (as discussed in Section 1.5.5). It remains unexplored whether these age-

related short-term memory binding deficits extend to other forms of bindings such as those comprising features that define objects' identities (e.g., shapes and surface colours) (i.e., conjunctive bindings).

The next part of this review will present evidence on how operations responsible for binding information in memory break down following brain damage, with special emphasis on Alzheimer's Disease.

Part II - Memory binding in brain damage: with emphasis to Alzheimer's Disease

The main aim of this second part of the literature review is to present evidence suggesting that the cognitive processes responsible for binding information can be impaired after brain injuries. The study of brain damage individuals has opened an immense window of opportunity to increase our understanding not only of the mechanisms underlying brain diseases, but also of those operating under normal conditions. In this part, I will present examples of diseases that affect binding processes from perception to memory. I will devote special attention to Alzheimer's Disease as this is the condition that was more thoroughly investigated in this project. As Alzheimer's Disease is primarily an amnesic syndrome, I shall review the literature on amnesia first in order to widening the scope of the interpretation of the associative memory deficits observed in these brain disorders. I will then address other functional and structural brain disorders in which binding operations have been found to be impaired. This may shed light into the extension of the functional networks required to perform binding operations in the human brain.

1.8 Binding deficits in amnesia

Damage to the temporal lobes results in memory impairment (Tulving, Habib, Nyberg, Lepage, & McIntosh, 1999). Evidence has been accrued from neuroimaging and neuropsychological studies supporting the relation between medial temporal lobes structures and memory functions (Cipolotti et al., 2001; Corkin, Amaral, Gonzalez, Johnson, & Hyman, 1997; Kopelman

et al., 2007; Kopelman et al., 2003; Mayes, 1995; Milner, 1972; Milner, 2005; Shimamura, 1990). The role of temporal lobes in memory binding however is a more recent subject. Structures of the temporal lobe such as the hippocampus, parahipocampal regions (e.g., perirhinal cortex), are important for associative memory (Brown & Warburton, 2006). Patients who have undergone temporal lobe surgery in which their amygdala and hippocampus have been removed (Kessels, Hendriks, Schouten, Van, & Postma, 2004), or patients with vascular lesions in the temporal lobes (Kessels, Jaap, de Haan, & Postma, 2002), are less able to bind together location information with object–identity information within memory. Kessels et al. (2004) suggested that this evidence supports the hypothesis of the left hippocampus acting as a "binding device", a suggestion that arose both from animal experiments (Eichenbaum, 1995; Eichenbaum & Bunsey, 1995; Eichenbaum, Yonelinas, & Ranganath, 2007) and studies with amnesic patients (Chalfonte, Verfaellie, Johnson, & Reiss, 1996).

The role of the hippocampal formation in the binding of information in long-term memory has been studied in amnesic patients. The role of the medial temporal lobe regions in binding information in short-term memory is less well understood. In Section 1.5.5 was suggested that one controversial area within memory binding is how short- and long-term memory interact during the integration process. The neuropsychology literature may help to find insights about this interaction as some recent studies suggest that medial temporal lobe structures, areas thought to be involved in associative learning, can support the representation of bound information in short-term memory. However, there are discrepancies across these studies. While some of them have proposed that the pattern of impairment observed in amnesic patients suggests that medial temporal lobes structures seem to subserve short-term memory binding operations, others have arrived to different conclusions. It might be worth looking at the type of stimuli used in these

studies and the precise experimental conditions adopted as to find out insights about this discrepancy.

To accomplish this aim I shall group some of these studies into two categories, those that found relations between short-term memory binding functions and medial temporal lobe structures and those that did not find such a relation. In doing so, I will try to determine to which of the two hypotheses proposed by Moses and Ryan (2006) (i.e., relational or conjunctive binding) the methodology used in these studies can be better adjusted. Differences between studies across and within these two categories may shed light onto the functional roles of short-term memory binding and their relations with structures located in the medial temporal lobes. These studies are summarized in Table 1.2.

Table 1.2. Relations between short-term memory binding and medial temporal lobe structures, evidence form the literature.

Authors	Stimuli	Hypothesis	Results	Interpretation
Hannula et al., 2006	Exp 1. Spatial relations among scene elements. Exp 2. Face-scene pairs	Relational ¥	Amnesics (6 = Anoxia) performed poorly in both forms of relations, more pronounced in Exp. 1.	The hippocampus is critical for relational memory even at short lags.
Hannula, Ryan, Tranel, and Cohen, 2007	Face-scene pairs	Relational ¥	Amnesics (4 = Anoxia, 2 = Seizures) performed poorly.	The hippocampus is critical for relational memory.

Table 1.2. Contd.

Authors	Stimuli	Hypothesis	Results	Interpretation
Hannula and Ranganath, 2008	Object-location	Relational	fMRI study: activation in anterior and posterior left hippocampus, and perirhinal cortex bilaterally.	The hippocampus and related MTL structures contribute to successful encoding and retrieval of relational information in visual short-term memory.
Olson, Moore, Stark, and Chatterjee, 2006	Exp 1. Arrays of spatial locations. Exp 2. Face recognition. Exp 3. Colour-Location associations	Conjunctive Configural Relational	Amnesics (pt. MS = Encephalitis, pt. HT = Meningitis, pt. CT = Encephalitis) performed poorly on the three tasks.	The MTL, possibly the hippocampus, are critical for accurate visual WM, refuting the hypothesis that the MTL is only involved in LTM.
Olson, Page, Moore, Chatterjee, and Verfaellie, 2006	Object-location conjunctions	Relational	Amnesics (6 = Anoxic, 3 = Encephalitis) performed poorly.	MTL is important for holding in WM conjunctions of features.
Piekema, Kessels, Mars, Petersson, and Fernandez, 2006	Object–location associations Object–colour associations	Relational Conjunctive	fMRI study: Right fMRI hippocampal activation. No hippocampal activation	The hippocampus is involved in memory for feature combinations that include spatial information which have to be used online.

Table 1.2. Contd.

Authors	Stimuli	Hypothesis	Results	Interpretation
Turriziani, Fadda, Caltagirone, and Carlesimo, 2004	Face-Face Face-Occupation	Relational	Amnesics (3 = Anoxia, 1 = Diabetic coma, 1 = Chemotherapy, 1 = Resection of the Fornix, 4 = Haemorrhage , 1 = Head Trauma) performed poorly on both associations	Amnesics are deficient in the learning of all kinds of between-item associations.
Ryan and Cohen, 2004	Addition, deletion, or left-right switch of objects in natural scenes	Relational ¥	Amnesics (pt. AK = Head Injury, pt CA = Anoxia in Status Epilepticus, pt. SD = Aneurysm, pt. DR = tumour removal) showed spared short-term and affected long-term retention for these types of information.	Amnesia associated with hippocampal damage results in a relational memory deficit, specifically of long-term memory.
Mayes et al., 2004; Mayes et al., 2002	A large battery of tasks assessing associative recognition of intra-item and inter-item information of the same and different types.	Relational and Conjunctive	Amnesic (YR = ischemic infarct). YR performed more poorly tasks assessing recognition of associations of different types of information. Her recognition of intra-item associations was not impaired.	The hippocampus is crucial for representing in memory associations between different types of information.

¥ In these studies, eye movements variables were used to investigate long-term memory effects during online decisions (i.e., short-term memory tasks). In round brackets: patients assessed (pt.) and the cause of their amnesia; MTL: medial temporal lobes; WM: working memory; LTM: long-term memory.

Evidence presented in Table 1.2 provides a clear picture of why the hippocampal functions can account for the relational hypothesis predictions better than for the conjunctive hypothesis predictions discussed in Section 1.5.5. Most of this work assessed the retention of independent and arbitrarily combined information in short- and long-term memory such as item-location, face-scene, and others that have been linked to hippocampal functions. It is worth noticing that in the work by Piekema et al. (2006) when object–colour associations were assessed the hippocampus was found no active. Similarly, YR, a patient with a selective damage to the hippocampus, exhibited paramount difficulties in the recognition of associations between different types of information (e.g., pictures and location, z = -5.5.) while her recognition of intra-item associations (e.g., features within faces, z = -0.7) was not impaired. This suggests that the hippocampus may be relevant to bind different types of information in inter-item combinations (e.g., the spatial representation of objects as suggested by Piekema et al., 2006) and it seems to be less involved in the intra-item binding.

The fact that Ryan and Cohen (2004) found preserved short-term memory when natural scenes were visually scanned may be explained under the argument that the actual spatial component of these tasks was very low. In their study and for all tasks they used, they did not present arrays of spatially distributed locations within these natural scenes. For example in their Experiment 3 changes consisted of left-right switches of object's locations and in Experiments 1 and 2 locations were less relevant as the task consisted of identifying new or old elements in that scenes. However, when the spatial component is more relevant (Hannula et al., 2007; Hannula et al., 2006; Olson et al., 2006), short-term memory performance for relational information which involves location is found to be dramatically impaired in amnesic patients.

In summary, this literature reviewed above suggests that binding processes are dramatically impaired after damage to medial temporal lobes structures, particularly, the hippocampus. As Alzheimer's Disease is an amnesic disorder which targets the hippocampus in its very early stages, it may be worth reviewing the literature on associative memory and Alzheimer's Disease in order to boost the evidence suggesting functional relations between binding operations and medial temporal lobe structures. This literature will be reviewed in the next Section.

1.9 Alzheimer's Disease

The processes responsible for associating information in memory are impaired in the early stages of Alzheimer's Disease (Blackwell, Sahakian, Vesey, Semple, Robbins, & Hodges, 2004; Fowler, Saling, Conway, Semple, & Louis, 2002; O'Connell, Coen, Kidd, Warsi, Chin, & Lawlor, 2004; Swainson et al., 2001). Patients with mild Alzheimer's Disease perform better in tasks assessing memory for unrelated information (e.g., list of words, list of faces or names, series of object drawings, etc.), than in tasks challenging memory for related information (e.g., pairs of related or unrelated words, faces with names, faces with locations, or objects with locations) (Alberoni, Baddeley, Della Sala, Logie, & Spinnler, 1992; Dudas, Clague, Thompson, Graham, & Hodges, 2005; Granholma & Butters, 1988; Hodges & Greene, 1998; Lindeboom, Schmand, Tulner, Walstra, & Jonker, 2002). This suggests that early in the course of the disease, there is an impairment in the ability to bind different kinds of information in memory. However, no study has explicitly explored whether deficits in building these associative memories in patients with Alzheimer's Disease could be accounted for by difficulties in binding different pieces of information into unified representations.

Notwithstanding the growing literature on binding in memory in healthy young (Luck & Vogel, 1997; Wheeler & Treisman, 2002) and elderly volunteers (Chalfonte & Johnson, 1996; Cowan et al., 2006; Johnson et al., 1995; Mitchell et al., 2000; Naveh-Benjamin, 2000), the issue of memory binding *per se* has yet to be investigated directly in Alzheimer's Disease. I will first discuss the usefulness of associative learning tasks in the early detection of Alzheimer's Disease. I will then address the question of whether Alzheimer's Disease patients' difficulties in associating information could arise from problems in forming conjunctions of features in perception, or in holding these conjunctions in memory. Finally, I will address the issue of whether there is a relationship between anatomical changes in Alzheimer's Disease and binding problems or learning deficits.

1.9.1 Associative memory problems in the early stages of Alzheimer's Disease

Swainson et al. (2001) used a set of neuropsychological tasks to investigate which were the most effective in differentiating between patients with Alzheimer's Disease from healthy elderly and those affected by Depression or Mild Cognitive Impairment. They found that the performance on the Paired Associates Learning Task discriminated Alzheimer's Disease from Depression, Mild Cognitive Impairment and normal ageing far better than a range of others memory tasks which did not require associative memory.

Swainson et al. (2001) also reported that Mild Cognitive Impairment patients' performance on the Paired Associates Learning Task split into two clusters. One cluster whose performance was close to that of Alzheimer's Disease patients, and a second cluster performing closer to healthy controls. The authors labelled patients within the first cluster "converter Mild Cognitive

Impairment" and those within the second cluster "non-converter Mild Cognitive Impairment". They posited that the performance on the Paired Associates Learning Task may predict conversion from Mild Cognitive Impairment to Alzheimer's Disease. A follow up study carried out by Blackwell et al. (2004) confirmed that the same Paired Associates Learning Task used by Swainson and collaborators (2001) is useful indeed not only in differentiating Alzheimer's Disease from other age-related conditions such as Depression and Mild Cognitive Impairment, but also for predicting Mild Cognitive Impairment to Alzheimer's Disease conversion. These studies highlighted the possibility that tasks assessing associative learning could aid the differential diagnosis of Alzheimer's Disease and be used for its early detection (Blackwell et al., 2004; de Jager, Milwain, & Budge, 2002; Fowler et al., 2002; O'Connell et al., 2004; Swainson et al., 2001);

The Paired Associates Learning Task used by Swainson et al. (2001), Blackwell et al. (2004), and Fowler et al. (2002) was taken from the Cambridge Automatic Neuropsychological Battery (CANTAB) (Cambridge Cognition, 2007). In the Paired Associates Learning Task of the CANTAB, participants are consecutively presented with an increasing number of patterns in different positions on a computer screen. Participants are requested to recall in which position each pattern was presented. To succeed in this task, participants must remember both the patterns and their locations. It is therefore possible that combining objects and locations is the process that is affected by Alzheimer's Disease.

Indeed, further studies assessing the delayed recall of object/location associations (Brandt, Shpritz, Munro, Marsh, & Rosenblatt, 2005), and the recognition of face/location associations (Dudas et al., 2005) confirmed the observation that Alzheimer's Disease patients present with a severe impairment in such association tasks.

It may be argued that a deficit in the above association tasks may be explained by the processing of locations alone which is also affected in Alzheimer's Disease (Brandt et al., 2005; Kalov, Vlcek, Jarolýmov, & Bures, 2005; Nguyen, Chubb, & Huff, 2003; Rosenbaum, Gao, Richards, Black, & Moscovitch, 2005). The contribution of this difficulty to the impairment in the Paired Associates Learning Task of the CANTAB cannot be ruled out. However, in support of a specific associative learning deficit there is a large number of publications reporting impairments in patients with Alzheimer's Disease in associative memory tasks involving information other than location.

For example, Lindeboom et al. (2002) devised a Paired Associates Learning Task they labelled "Visual Association Test". In this task participants are presented with cards displaying two interactive pictures (e.g., a monkey holding an umbrella). After the initial presentation a memory card displaying one of two items (e.g., the monkey) is presented and participants are requested to recall the other item. Lindeboom et al. (2002) applied the Visual Association Test to groups of patients with Alzheimer's Disease, Vascular Dementia, Frontotemporal Dementia, Subcortical Dementia, and patients with Lewy Body Dementia. They reported that the Visual Association Test discriminated Alzheimer's Disease from other non-Alzheimer's Disease dementias with high specificity. Table 1.3 summarises some of these studies detailing the type of association required and the results found.

Table 1.3 Deficits in associative learning tasks in Alzheimer's Disease

Study	Type of Association/Task	Participants (n=)	Results
Granholma and Butters, 1988	Pairs of words (Recall of words with and without associated cues)	AD (10), HD (10), HE (10), HY (10)	Without associated cues AD < HE << HY With associated cues AD << HE << HY
Alberoni et al., 1992	Faces, voices, and locations during conversations	AD (19), HE (19)	AD <<< HE
Hodges and Greene, 1998	Faces with names (Recognition, identification and naming of famous faces)	AD (24), HE (30)	Recognition, AD < HE Identification, AD <<< HE Naming, AD <<< HE
Della Sala et al., 2000	Objects with colours (Matching Colours to Objects)	AD (33)	7 out of 33 AD patients showed clear deficits associating colours to objects
Lindeboom et al., 2002	Objects with objects (Immediate recall of paired associates objects)	AD (48), VaD (37), FTD (9), DLB (7), SD (15), HE (204)	AD <<< VaD/FTD/SD AD <<< HE
Tippett et al., 2003	Objects Parts (Recognition of objects made-up of different body parts e.g. chicken body with a monkey head)	AD (16), HE (16)	AD <<< HE
Gallo, Sullivan, Daffner, Schacter and Budson, 2004	Pairs of words (Recognition of new and rearranged pairs of words)	AD (12), HE (12)	AD <<< HE
Pariente et al., 2005	Faces with names (Forced Recognition Task)	AD (12), HE (17)	Accuracy, AD <<< HE Reaction Time, AD > HE
Swainson et al., 2001	PAL-CANTAB Visual patterns in different spatial locations	Mild AD (26), MCI (46), HE (39), Depression (37)	¥ (6-Patterns errors) AD >> MCI > HE = Depression
Lee et al., 2003	PAL-CANTAB	Mild AD (10), SmD (11), fvFTD (12)	AD >>> SmD> fvFTD
O'Connell et al., 2004	PAL-CANTAB	Mild AD (34), HE (16)	AD >>> HE
Fowler et al., 2002	PAL-CANTAB	MCI-S (12), MCI-D(9), AD (16), HE (19)	AD >> MCI-D > MCI-S >> HE
Blackwell et al., 2004	PAL-CANTAB	Non-converter MCI (11), Converter MCI (29)	Follow up for 32 Months Converter MCI >>> Non-Converter MCI

AD: Alzheimer's Disease; DLB: Dementia with Lewis Bodies; FTD: Fronto-Temporal Dementia; fvFTD: Frontal variant of Fronto-Temporal Dementia; HD: Huntington Disease; HE: Healthy Elderly; HY: Healthy Young; MCI-D: Mild Cognitive Impairment deteriorating; MCI-S: Mild Cognitive Impairment stable (patients were classified based on the initial performance on the Paired Associate Learning Task (PAL) - CANTAB. This also applies to converter and non-Converter MCI); SmD: Semantic Dementia; SD: Subcortical Dementia; VaD: Vascular Dementia; < ($p < 0.05$); << ($p < 0.01$); <<< ($p < 0.001$); ¥ The variable "6-Patterns errors" represents the number of errors committed when 6 patterns were presented on the screen. This has proved to be the most sensitive variable of the PAL Task of the CANTAB.

The results summarized in Table 1.3 support the view that the mechanisms underlying memory for combined information are affected by Alzheimer's Disease. In none of these published studies however, was the observed associative learning problem interpreted as a possible deficit in binding information in memory. Moreover, the tasks described in these papers were not explicitly designed to explore this hypothesis. However, from their outcomes it could be inferred that a breakdown of mechanisms responsible for the binding of information in memory may underlie the observed memory difficulty in the course of Alzheimer's Disease. Binding deficits could also account for a wide range of difficulties experienced by patients with Alzheimer's Disease in daily life activities. Keeping track of conversations carried out by several people is a task in which patients with Alzheimer's Disease show particular problems (Alberoni et al., 1992; Muller & Guendouzi, 2005). During conversations several types of information must be bound together (e.g., faces, voices, spatial location of the speakers, temporal order, and so forth) and these bindings should also be updated online in order to accurately keep track of who said what.

Patients with Alzheimer's Disease also present with problems in remembering meaningful associations between item properties such as colours and objects (e.g., traffic signs as it was shown by Uc, Rizzo, Anderson, Shi, & Dawson, 2005, or figures with colours as demonstrated by Della Sala et al., 2000 and by Lloyd-Jones, 2005). Della Sala et al. (2000) demonstrated impairments in a subgroup of patients with Alzheimer's Disease in a task requiring matching colours to figures. Patients with Alzheimer's Disease also experience difficulties when they have to remember the names of people (Greene, Baddeley, & Hodges, 1996; Hodges & Greene, 1998; Sperling et al., 2003). Lloyd-Jones (2005) assessed the recognition of bound information in patients with Alzheimer's Disease. The author found a priming effect on memory in patients with Alzheimer's Disease when they

had to use colour clues to identify common objects. This priming effect was found either when objects were presented with congruent colours (e.g., yellow banana) or with incongruent colours (e.g., purple banana), suggesting that patients with Alzheimer's Disease could access long-term storages at least to retrieve shape-based information (as objects appeared in natural or unnatural colours). However, in the explicit memory test, when the recognition of these shapes bound with colours was required, patients with Alzheimer's Disease showed significant impairment. Lloyd-Jones (2005) suggested that the semantic processes that provide the 'glue' that integrates perceptual features into single units are impaired in Alzheimer's Disease.

According to this evidence, problems associating or "binding" information in memory in Alzheimer's Disease may involve different types of information as well as different retrieval processes. Most of these impairments reflect a difficulty in holding in memory different pieces of information together what may result from the functional breakdown of widely distributed networks responsible for integrating or "binding" multimodal information across different brain regions.

The studies summarized above however, do not allow one to interpret these findings as specific deficits in binding information in memory. In fact, none of these studies assessed the extent to which the memory defect for combined information was accounted for by deficits in memory for the individual pieces of information composing these complex events. For example the Paired Associates Learning Task of the CANTAB does not reflect in its final scores how much of the poor associative memory performance could be accounted for by deficits in recalling locations only. Similarly, Lindeboom et al. (2002) asked patients to recall the missing items after they had studied pairs of interactive stimuli however, they did not assess whether patients' memory for each of these items was impaired. To

offer a precise account of the associative memory problems in Alzheimer's Disease from a binding perspective it is essential to assess the extent to which the memory impairment for complex figures is greater than the memory impairment for the independent items composing these figures.

Furthermore, whether the binding difficulties in Alzheimer's Disease are due to failures in forming conjunctions of features in perception or in holding these conjunctions in memory is a matter open to debate. In the next Section I will review the available literature on this issue.

1.9.2 Perceptual binding in Alzheimer's Disease

According to the Feature Integration Theory of Attention proposed by Treisman and Gelade (1980) and discussed in Section 1.3.1 of the first part of this review, for features to become objects in perception a certain amount of attention should be allocated to the spatial region where these features are located. When the individual features are attended they can then be bound together forming integrated objects. Hence, attention acts as the cognitive glue which keeps different parts of the perceived objects together (Treisman & Zhang, 2006; Treisman & Gelade, 1980; Wheeler & Treisman, 2002). Without attention not only is the binding of these features not encoded but information may not be actively maintained in memory. Therefore, attention seems to be required for both combining information in perception and holding this in memory (Treisman, 2006).

Considerable evidence has accrued that attention is affected by Alzheimer's Disease (e.g., Amieva, Phillips, Della Sala, & Henry, 2004; Balota & Faust, 2001; Della Sala, Laiacona, Spinnler, & Ubezio, 1992; Perry & Hodges, 1999; Perry, Watson, & Hodges, 2000), and that attention deficits may account for the difficulties that Alzheimer' Disease patients experience in tasks involving

the visual search of targets defined by conjunctions of features (Foster, Behrmann, & Stuss, 1999; Hao et al., 2005). Tales, Butler, Fossey, Gilchrist, Jones, and Troscianko (2002) investigated the effect of Alzheimer's Disease on visual search and the visual processing of conjunctions of features. In this study, patients and controls were presented with two conditions exploring the visual search of targets defined by single features and one condition exploring the search of targets defined by the combination of features. Targets in the first two conditions were vertical bars among horizontal bars (pop-out condition) or a larger vertical bar among smaller vertical bars (size condition). In the conjunction search, targets were vertical dark bars among vertical light bars and horizontal dark bars. Participants were required to detect the presence of the target as quickly and as accurately as possible by pressing a response key. It was found that compared to single features, processing conjunctions of features was affected by Alzheimer's Disease. The authors suggested that patients with Alzheimer's Disease could have problems with the binding of features in the visual system resulting from a drop in the efficiency of segmentation (which allows extracting relevant features from complex scenes), grouping (ability to jointly represent similar members of a set distributed across space, process that requires continuous changes of attention), or deficits in general attention mechanisms.

Hao et al. (2005) evaluated patients with Alzheimer's Disease using a methodology similar to the one used by Tales et al. (2002). They collected behavioural and fMRI data simultaneously. Behavioural responses showed that Alzheimer's Disease patients made more errors and were slower during the conjunction tasks (objects defined by colour and orientation) than during the single features tasks. fMRI data revealed less activation in parietal, temporal and frontal lobes in patients with Alzheimer's Disease during the conjunction test compared to controls. The authors concluded that Alzheimer's Disease may impair general attention mechanisms required for

the binding of features and that this could explain the deficit in visual search tasks.

Behaviourally, Alzheimer's Disease patients experience a range of perceptual problems and one of the most typical problems is a difficulty in recognizing faces (Estévez-Gonzalez et al., 2004; Giannakopoulos, Gold, Duc, Michel, Hof, & Bouras, 2000; Hodges & Greene, 1998; Hodges, Salmon, & Butters, 1993). The processing of faces requires the integration of features and therefore it may be possible that this impairment arises from a difficulty in binding information within perception.

In an attempt to explore the extent to which deficits in feature integration may contribute to the perceptual deficits in Alzheimer's Disease, Kurylo, Allan, Collins, and Baron (2003) explored the relation of a set of perceptual tasks with deficits in the integration of visual information during face recognition. The set of perceptual tasks included a Test of Proximity, a Test of Alignment, the Glass Patterns Test, and a Test of Perception of Large Shapes and Small Shapes. In the first two tests participants discriminated between horizontally or vertically grouped dots. The Glass Patterns Test was constructed by superimposing matrices of original and transposed points. These stimuli elicited the perception of concentric, fragmented circles that contained a central area. Participants indicated the position of the central area as either left or right. In the last two tests participants indicated whether the dots formed a square or a diamond. The perceptual attributes of these arrays were varied making them progressively more difficult (e.g., for glass patterns, the displacement between element pairs was made progressively more random, which obscured the position of the central area). The authors found poor performance by Alzheimer's Disease patients in all perceptual tests as compared to healthy older controls. Moreover, only the glass patterns Test correlated with facial recognition deficits in patients with Alzheimer's

Disease. The authors argued that perceptual organization in the glass patterns task, probably more than in any of the other tasks used in this study, relies on the global analysis of the stimulus, a process that requires the integration of features.

Yonelinas, Kroll, Dobbins, and Soltani (1999) studied memory for faces, the inner or outer features of which were manipulated. Faces resulting from these manipulations had to be recognized in up-right position or upside-down, and they were presented among new faces or among faces made of the recombination of features of faces previously presented. Yonelinas et al. (1999) found that whenever features of faces could be treated as a whole (up-right faces), the mechanisms responsible for binding features within items are triggered and familiarity-based processes responsible for face recognition are activated. It is possible that these binding mechanisms are not working efficiently in patients with Alzheimer's Disease.

In summary, problems in forming associations in perception probably resulting from attention deficits (Kurylo et al., 2003; Levinoff, Li, Murtha, & Chertkow, 2004), as well as difficulties in holding these associations in memory (Blackwell et al., 2004; Dudas et al., 2005; Fowler et al., 2002; O'Connell et al., 2004; Swainson et al., 2001) have been found in patients with Alzheimer's Disease. This leads to the question of whether it is a difficulty in forming conjunctions of features or in holding these conjunctions in memory that gives rise to the associative learning problems in Alzheimer's Disease. If Alzheimer's Disease affects the binding of information at a perceptual level, it might be expected that deficits in the associative memory tasks result from problems that precede memory formation.

Since grouping in perception and holding associations in memory are functions carried out by different regions of the brain, and both seem to be

affected by Alzheimer's Disease, it may be useful to analyze the anatomical changes of early Alzheimer's Disease in order to gather further insights about which processes are impaired in these patients. In the next Section I will address this issue.

1.9.3 An anatomical approach to memory binding and associative memory deficits in Alzheimer's Disease

The hippocampus is important for memory (Hoesen & Hyman, 1990; Kohler et al., 1998; Kohler, McIntosh, Moscovitch, & Winocur, 1998) and damage to this structure has been considered responsible for memory problems in the early course of Alzheimer's Disease (Dubois, 1995; Kohler et al., 1998). There is a large corpus of publications showing that the hippocampal regions are targeted early by the neurodegenerative processes of Alzheimer's Disease (Braak, Griffing, Arai, Bohl, Bratzke, & Braak, 1999; Braak & Braak, 1991; 1996; Braak, Braak, & Bohl, 1993). Moreover, as was discussed in Sections 1.5.4 and 1.5.5, the hippocampus is also important both for memory binding (Mayes et al., 2007; Mayes et al., 2004; O'Reilly et al., 2003) and associative learning (Luo & Niki, 2005; Mayes et al., 2007; Mitchell et al., 2000).

The fact that since very early Alzheimer's Disease affects the hippocampus and it also impairs associative learning offers strong evidence in support of the relation between this brain region and this memory function. This evidence is further supported by the observation that the associative learning tasks can discriminate patients with Alzheimer's Disease from patients with other forms of dementia which spare the hippocampus (Brandt et al., 2005; Lee et al., 2003; Lindeboom et al., 2002).

To explore the possible relation of hippocampal damage with associative learning deficits in Alzheimer's Disease, Sperling et al. (2003) studied fMRI activation during a task involving the association of faces with names. They compared behavioural and neuroimaging data of patients with Alzheimer's Disease, healthy older and younger controls during the recognition of new and old pairs of faces and names. They found that compared with older controls, Alzheimer's Disease patients showed significant reduction of the activation of hippocampal formation for both novel and old pairs. They did not find significant differences between older and younger healthy controls, leading to the suggestion that possibly, different mechanisms underlie the explicit memory deficits in Alzheimer's Disease and healthy elderly people. However, Mitchell et al. (2000) had previously reported that older healthy adults are less accurate and show less activation in the left anterior hippocampus than younger control during recognition of items defined by combined information (i.e., objects and locations). Similar findings have also been reported by Johnson et al. (1995) and Chalfonte and Johnson (1996). Therefore, deficits in binding information in long-term memory, rather than being specific to Alzheimer's Disease, could be a process which is accelerated by this condition with respect to normal ageing.

Hoesen and Hyman (1990) reported that at some stage of the disease, Alzheimer's Disease becomes functionally a hippocampectomy. From this perspective, the lack of connectivity between the hippocampus and other cortical regions such as the posterior association cortex and the prefrontal cortex, as well as within these cortical regions, could mediate those deficits observed in Alzheimer's Disease patients in both forming conjunctions of features and holding these conjunctions in memory.

The suggestion of Hoesen and Hyman (1990) fits well with the model of binding proposed by O'Reilly et al. (2003). According to this model, the

posterior cortex is involved in a slow learning process termed cortical coarse-code conjunctive binding. This slow learning process solves, to some extent, the explosion of combinations that could result when several sensory inputs are coming through sensory pathways. The hippocampus accomplishes the episodic conjunctive binding, which contrary to coarse-code binding, is a faster learning mechanism encoding higher order conjunctions of many features. Prefrontal binding is a transient form of binding more related to operative mechanisms of working memory which manipulates bound information until it is required. The prefrontal cortex also allows a rapidly updatable maintenance of information in an active state. Prefrontal cortex also seems to play some role in regulating the transfer of information between coarse-code units (which contain few lower order conjunctions) into larger higher order conjunctions held by the hippocampus (Cutting et al., 2006; O'Reilly et al., 2003).

Mayes et al. (2004) acknowledge that the model proposed by O'Reilly et al. (2003) accounts for the memory deficits shown by YR patient (see Section 1.8). Her failure during the recognition of associated information can be explained using O'Reilly's model, whereas the model fails to explain some results from tasks in which YR performed well above chance (e.g., recognition of intra-item associations and recognition of association of items of the same type).

Contrary to the pattern of performance presented by YR, deficits in associating information in Alzheimer's Disease are not material-specific and involve intra as well as inter items associations (Dudas et al., 2005; Kurylo et al., 2003; Lindeboom et al., 2002; Tippett et al., 2003). Analysing the evidence from associative learning tasks performance in patients with mild Alzheimer's Disease together with YR's deficits, whose damage was restricted to the hippocampus, it would be possible to argue that different

types of binding could subserve the associative learning mechanisms, and that regions and pathways activated during this integration depend on the type of information to-be-bound. This assumption on the one hand may help us understanding why YR failed to remember some types of binding while she performed well with other types, and on the other hand posits that binding deficits in Alzheimer's Disease are reflecting a widespread damage which might result from the disconnection among several functional regions.

1.9.4 Can memory binding deficits account for the associative memory problems in Alzheimer's Disease?

There is compelling evidence suggesting that patients with Alzheimer's Disease have paramount difficulties associating information in memory, but it has not been explored whether these associative memory impairments are accounted for by deficits in binding information in memory. There is a tendency in the literature on memory to refer to memory binding and associative learning interchangeably. In a recent paper published by Lowndes and Savage (2007) the authors offer a thorough review of the current perspectives of associative learning tasks for the early assessment of Alzheimer's Disease. They emphasize that the difficulties observed in these patients while performing these tasks reflect memory binding problems. There are some important issues to be considered when trying to establish causal links between memory binding problems and associative learning deficits. One such issue is functional and is related to the current knowledge on what is associative learning and what is memory binding. Another issue is methodological and has to do with how memory tasks are devised to assess the process of binding information in memory.

In regard to the first issue, there is evidence that associative learning is a function carried out by hippocampal regions, mainly the hippocampus. There are now computational models (Cutting et al., 2006; O'Reilly et al., 2003), fMRI (Mitchell et al., 2000), and neuropsychological data (Hannula & Ranganath, 2008), supporting this evidence. Binding however, is a process that seems to place less demand on medial temporal lobes structures and more demand on neocortical regions (Cutting et al., 2006; Prabhakaran et al., 2000). Binding contrary to learning, should be considered an automatic process which occurs effortlessly relying mainly on the coordinated activity of frontal and posterior cortical regions (Allen et al., 2006; Treisman, 2006). Learning however, is a rather slow and resource demanding process which guarantees that this bound information is coherently transferred to long-term storages (Brown & Warburton, 2006; Cutting et al., 2006). Experimental evidence supports this functional segregation as it has been found that repetition of bound information results in the learning of these bindings but has no impact on performance when these bindings have to be held in working memory (Colzato et al., 2006; Logie et al., 2009; Treisman, 2006). This suggests that processes responsible for forming and holding bindings in short-term memory and for storing these bindings in a more durable representation may not be the same. Therefore, the associative memory deficits observed in Alzheimer's Disease patients would not predict short-term memory binding deficits in these patients.

In regard to the methodological issue, it is worth noticing that none of the tasks in the series of studies reviewed were "explicitly" devised to assess memory binding. Binding is a new research subject in memory (Zimmer et al., 2006). We are learning that methodological problems are plaguing the literature within this area and are leading to different interpretations of perhaps common issues (Gray, 1999; Wheeler & Treisman, 2002). In order to offer an accurate account for the associative memory problems from a

binding perspective the contribution of item memory must be separated from the contribution of binding these items in memory to form integrated events. Examples of these methodological caveats were mentioned in Section 1.9.1 (Swainson et al., 2001 and Lindeboom et al., 2002). Therefore, a clear-cut design aimed at detecting binding problems in Alzheimer's Disease should take this methodological constraint into consideration.

Finally, it is worth noting that for the purpose of detecting deviations from normal ageing (e.g., Alzheimer's Disease), it becomes necessary to use tasks that separate normal from abnormal old age reliably. Unfortunately, this is not the case for the Paired Associate Learning Task of the CANTAB as well as for other associative learning tasks in which older adults have also shown poor performance when they have been compared to younger participants (see de Jager et al., 2002).

1.9.5 Summary on Alzheimer's Disease and experimental hypotheses

The evidence reviewed here suggests that the associative learning problems seen in Alzheimer's Disease could result from impairments in the neural mechanisms responsible for either forming integrated representations of objects in perception or for storing these representations in memory.

Episodic memory deficits are considered the hallmark of Alzheimer's Disease. One conclusion that may be reached based on evidence presented here is that the neurodegenerative processes accompanying Alzheimer' Disease in its early course impact on the episodic memory system responsible for associating information. This suggestion could also explain why early in the disease, patients have significantly more problems at remembering episodes defined by complex memories (e.g., objects and

locations, faces and names) than those involving single aspects (e.g., words, faces). This dissociation suggests that what is usually defined as episodic memory might be a system characterized by different processes, some of which are aimed at holding associations of information while others are responsible for holding unbound pieces of information. Recent reports on the unit of capacity of visual working memory stress the possibility that features and bindings are stored by separate systems (Wheeler & Treisman, 2002). If the Parallel Storage Hypothesis accounts for both short-term and long-term memory, there could be two independent subsystems serving episodic memories, one dedicated to the management of object properties (as single features) and another dedicated to operate the relationship among these properties (colour with objects, objects with location, items and temporal order, etc.).

This research project is built on the hypothesis that Alzheimer's Disease affects the processes involved in the association of objects properties early in the course of the disease and more severely and selectively than episodic memory for other information. The fact that the Paired Associate Learning Tasks discriminated Alzheimer's Disease from other dementia and also converter from non-converter Mild Cognitive Impairment patients better than non-associative memory tasks, suggests that deficits in associative memory may result more directly from the early neuropathological changes in Alzheimer's Disease than form a more general deficit in episodic memory.

However, it is still unclear which of these binding mechanisms may be affected in Alzheimer's Disease. As has been shown here, deficits in associating information can be observed in patients with Alzheimer's Disease at cognitive stages as early as perception. If the information cannot accurately be combined at this early step, what we are observing in episodic memory tasks could reflect a deficit occurring well before processes

responsible for the consolidation of this bound information in memory or maybe a more complex problem where perceptual and memory binding deficits coexist. Most of the studies presented in this review on Alzheimer's Disease involved binding in long-term memory. No evidence has been provided to date suggesting whether binding information in short-term memory is also impaired in patients with Alzheimer's Disease.

If it is true that Alzheimer's Disease primarily affects medial temporal lobe structures, these are not the only regions affected by the neurodegenerative course of the disease. There is evidence suggesting that posterior parietal regions and frontal regions are also affected in different stages of Alzheimer's Disease (Kaida, Takeda, Nagata, & Kamakura, 1998; Pariente et al., 2005; Wang et al., 2007). As these regions have found to be important for short-term memory binding (see Section 1.5.2.1), I will review the neuropsychology literature involving patients with damage to these regions. This would increase the evidence available to account for memory binding problems in patients with Alzheimer's Disease, should the hypotheses presented in Section 1.9.5 prove valid.

1.10 Binding deficits in posterior parietal damage

Balint's syndrome is a brain disorder resulting from damage to the posterior parietal regions. Patients with this disorder exhibit a great deal of visual and attention deficits (Valenza, Murray, Ptak, & Vuilleumier, 2004). Particularly, these patients have been found to be impaired at encoding local relations between parts of visual stimuli. This impairment renders them poorer at using local elements to group in perception and makes them more prone to rely on holistic visual representations for object recognition (Shalev, Humphreys, & Mevorach, 2004). The mechanism responsible for this impairment in perceptual grouping has been associated with problems in

binding information. Particularly, it has been suggested that the attentional processes required for binding information across the master map of locations (as proposed by the Feature Integration Theory of Attention; Treisman & Gelade, 1980) are impaired in these patients (Friedman-Hill, Robertson, & Treisman, 1995). Patients with Balint's syndrome show difficulties searching for conjunctions of features in visual arrays as well as a remarkable increased number of illusory conjunctions (Friedman-Hill et al., 1995). Therefore, Balint's syndrome offers a model of brain damage in which visual-perceptual deficits are accounted for by deficits in binding information in the early stages of visual processing. This model also provides support to the functional implications of the Feature Integration Theory of Attention (Treisman & Gelade, 1980) in brain damaged individuals.

1.11 Binding deficits in frontal damage

As was discussed in Section 1.5.2.1, the frontal lobes are important for binding information in memory (Johnson, Mitchell, Raye, & Greene, 2004; Mitchell et al., 2000; Prabhakaran et al., 2000; Sala & Courtney, 2007). Studies carried out in patients with frontal lobe lesions have shown that these patients present with deficits in source memory. Patients with frontal damage are less able to store contextual information associated to events. Janowsky, Shimamura, and squire (1989) asked patients with frontal lobe lesions to recall facts associated to context and time. They found a profound impairment in these patients for retrieving the source while they showed normal memory for the facts. Memory deficits for the temporal sequence of events have been also reported in frontal damaged individuals (Shimamura, Janowsky, & Squire, 1990). These difficulties in accessing contextual information have been linked with the high rate of false recognition observed in patients with lesions in their frontal lobes (Budson, Dodson, Vatner,

Daffner, Black, & Schacter, 2005; Budson, Sitarski, Daffner, & Schacter, 2002; Davidson, Cook, Glisky, Verfaellie, & Rapcsak, 2005; Davidson, Troyer, & Moscovitch, 2006; Thaiss & Petrides, 2003). Such difficulties reflect a loss of the ability to hold bound information in memory or to retrieve bindings from long-term memory.

Most of these studies however, investigated associations made in long-term memory. The involvement of frontal lobes in visual short-term memory for bound information has been less well investigated in brain damaged individuals. The introduction of the Episodic Buffer into the working memory model (Baddeley, 2000; 2007b) has stimulated research on the relationship between binding in working memory and frontal lobes. This seems to offer a promising model to improve our understanding of how this brain region supports this memory function. However, based on neuroimaging and behavioural data collected from healthy volunteers we can argue that the frontal lobes may be seen as important regions forming part of that networks wherein processes responsible for holding transient bindings are carried out. Previous findings in long-term memory studies suggest that perhaps the frontal lobes form part of more extensive networks which support both short-term maintenance of bound information as well as storage and retrieval of long-term associations (Prince, Daselaar, & Cabeza, 2005; Sala & Courtney, 2007).

Memory binding problems have also been reported in patients with Schizophrenia. In these patients the frontal lobes are not structurally but functionally impaired (Highley, Walker, Esiri, McDonald, Harrison, & Crow, 2001). One of the physiopathological mechanisms responsible for the florid symptomatology of schizophrenic patients is the hypofunctionality of frontal lobes (Barch & Csernansky, 2007; Vance, Hall, Bellgrove, Casey, Karsz, &

Maruff, 2006; Wolf, Vasic, Hose, Spitzer, & Walter, 2007; Wolf, Vasic, & Walter, 2006). Lepage, Montoya, Pelletier, Achim, Menear, and Lal (2006) used behavioural and neuroimaging measures to investigate long-term memory for related and unrelated information in healthy controls and schizophrenic patients. They observed that patients with schizophrenia were less able to recognize pairs of objects as compared with individual items. Neuroimaging data (fMRI) showed greater activation in the left dorsolateral and right inferior prefrontal cortices in controls as compared to schizophrenics. The authors concluded that hypofunctionality of the prefrontal cortex is the basis for the selective associative memory encoding and recognition deficit seen in schizophrenia. Working memory for objects bound to locations has been found to be impaired in schizophrenic patients (Burglen et al., 2004).

However, Gold, Wilk, McMahon, Buchanan, and Luck (2003) used a paradigm similar to that of Luck and Vogel (1997) and found that limitations in binding colours to locations in schizophrenics were not greater than their impairments for remembering locations only (see Burglen et al., 2004 for a critical appraisal of this finding). More recently Luck, Foucher, Offerlin-Meyer, Lepage, and Danion (2008) found that using letters and locations presented as individual or bound items, schizophrenic patients were far poorer when they had to hold in working memory the combination (i.e., letter + locations) than when they had to remember letters or locations only. Therefore, evidence from schizophrenic patients may add to the role of frontal lobes in subserving working memory functions in general and the action of the Episodic Buffer for storing larger chunks of multimodal information (Baddeley, 2000).

1.12 Summary

The evidence discussed in this literature review suggests that binding functions are affected by several brain diseases. These functions represent the operation of fragile mechanisms which may be affected by several factors including experimental ones (e.g., number of stimuli, types of information, format of this information, and others). As was posited above, this research project investigated short-term memory binding in normal and brain damaged individuals. Therefore, it becomes necessary to assess which experimental factors should be taken into consideration when short-term memory binding functions are under investigation.

The series of experiments devised for this project were aimed at investigating the passive storage of information over short time scales in verbal or visual formats (see Section 1.5 for attempts to establish the boundaries between memory systems). Therefore, the term "short-term memory" will be used throughout this thesis. It was predicted that by adopting this theoretical position it would be possible to focus on the assessment of the different short-term memory subcomponents (i.e., verbal and visual) and to draw interpretations that may add new evidence to the available memory models (Baddeley, 1992; 2000; Baddeley & Hitch, 1974; Cowan, 1988; 2008; Logie, 2003).

Chapter 2 addresses the effects of methodological factors which may underpin the variability of outcomes reported in the literature (e.g., object-based vs. feature-based visual working memory, or interference between to-be-bound features). In accomplishing this goal, the results of Chapter 2 allow the selection of tasks to investigate the hypotheses of this project and delineate the most suitable task parameters to be used with the target populations.

CHAPTER 2

Binding information in visual short-term memory: assessment across feature dimensions and under different memory and perceptual loads

2.1 Introduction

In Sections 1.5.1 and 1.5.2 of Chapter 1 the available literature on visual short-term memory and binding was reviewed. Three main areas were identified wherein controversies concerning these issues are still seen. One such area concerns the relationship between the type of to-be-bound features and the representational format in which objects composed of these features would be stored in short-term memory. One way of assessing this relationship would be for example by using a set of change detection tasks which present different types of stimuli. This would enable us to investigate the extent to which the type of information affects the efficiency of visual short-term memory to store integrated objects. A second area concerns the interference effect that arises when the to-be-bound features are processed within or across feature dimensions. As was discussed in Section 1.5.2 of Chapter 1, the amount of interference resulting from this integrative process affects the outcomes of the integration (e.g., the efficiency of binding processes). A third area concerns the relation between the capacity of visual short-term memory and methodological factors such as memory and perceptual load.

Therefore, the efficiency with which visual-short memory stores integrated objects seems to be affected by first, the type of the information to be

integrated, second, the level of competition for resources within and between feature dimensions, and third, by memory and perceptual load. The effect of these factors will be addressed in this chapter in line with two main aims.

The first aim is to provide new evidence about the functional properties of visual short-term memory for storing multi-feature objects a) when these objects comprise features that are processed across different dimensions and b) when the representation of these objects occurs under different memory and perceptual loads. The second aim is to set the ground for future experiments involving brain damaged individuals and older people. For this purpose, it is necessary to have available a pool of features and tasks which would suit particular research questions and target populations.

2.2 Experiment 1

2.2.1 Aims

Experiment 1 was aimed at investigating whether there is a relationship between the efficiency with which bound information is represented as integrated objects in visual short-term memory and the type of features to-be-bound into these objects.

2.2.2 Methods

2.2.2.1 Participants

Twelve undergraduate students from the Psychology Department of the University of Edinburgh with mean age of 20.5 years (SD = 2.3), average

education of 15.6 (SD = 1.73) years, and average verbal IQ as assessed by the Wechsler Test of Adult Reading (Wechsler, 2002) of 110.36 (SD = 4.5) entered Experiment 1. All gave their written consent prior to participation.

2.2.2.2 Stimuli and Apparatus

Visual arrays of stimuli were presented on a 15″ personal computer (PC) screen over a gray background [RGB = 192, 192, 192]. Stimuli consisted of single features such as shapes, colours, orientations, or combination of features such as oriented shapes, oriented coloured shapes, coloured shapes, or bicoloured objects (see Figure 2.1 for examples of these stimuli). Visual arrays consisted of 4 items[6]. Each stimulus sustained 1 cm horizontally and vertically. Viewing distance was not constrained. The discriminability of shapes and colours was initially piloted[7]. Two sets of 18 colours and 18 abstract shapes were first given to a group of 20 participants with a mean age of 28.25 years (SD = 7.17). In order to make these colours more difficult to name, their RGB values were changed to different values of that of primary colours. Participants were then presented with pairs of shapes or colours on a PC screen and they were asked to make speeded decisions as to whether the pairs consisted of the same or different shapes or colours. Shapes and colours from combinations resulting in response times below the lower bound of the confidence interval at 95% (cut-off score) were selected. Eight shapes and colours matched this criterion. The corresponding RGB values of colours matching this criterion are [0, 232, 232], [128, 128, 0], [128, 0, 128], [38,

[6]As one aim of this experiment was the investigation of the efficiency of visual short-term memory for holding complex objects, the use of the number of items that matches the average capacity proposed for this memory system may offer a sensitive approach to fulfil this aim.

[7] Stimuli piloted in this study were used in all experiments presented in this thesis which assessed visual short-term memory for shape only, colour only, or shape-colour binding.

157, 38], [70, 130, 180], [255, 0, 213], [255, 215, 0], [250, 128, 114]. Shapes are shown in Figure 2.1A. This piloting of materials was required to ensure that the colours and shapes were easy to discriminate visually, but could not readily be remembered in terms of their names (also see Appendix 1 for the whole set of shapes and colours used in this pilot study). For constructing stimuli arrays, features were selected from a set of 8 shapes (Figure 2.1A), a set of 8 colours, a set of 8 orientations (Figure 2.1B), and a set of 6 object shapes (Figure 2.1C). Pilot studies showed no differences in performance across the different object shapes used for presenting combinations of colours. Similarly, Wheeler and Treisman (2002) reported no effect on memory of the distribution of colours within bicoloured objects.

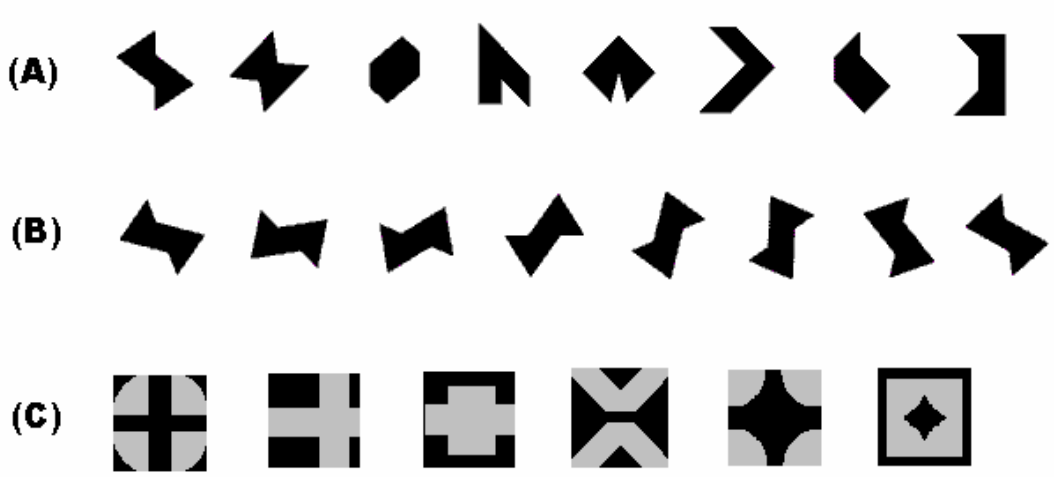

Figure 2.1. Examples of shapes (A), orientations (B), and object shapes (C) used in Experiment 1.

2.2.2.3 Design

Trials began with a fixation cross in the centre of the screen for 500 msec. After this fixation a study display showed four items for 1000 msec. This study screen was followed by 900 msec blank retention interval after which the test display was presented. The test display consisted of the same items

presented in the study display (50% of the trials) or different items. Participants were requested to remember as many items as possible from the study display and to decide whether the items in the test display were the same or different. For the "same" and "different" trials, items randomly changed their locations in the test display as compared to the study display. This manipulation rendered location an irrelevant feature to the task. Participants were requested to respond "different" or "same" depending on whether or not they detected changes between displays. They were told to take time to make their decision as their responses would not be timed. They entered these responses using a button box. There was then a gap of 1000 msec until the next trial.

Three conditions were used to assess memory for single features and four conditions to assess memory for the binding of these features. For conditions assessing memory for single features, no feature was repeated within displays. For conditions assessing the binding of features, features could be repeated within display, but not within objects, no more than twice. Features were evenly used across conditions (Figure 2.2).

Memory for shape only: In this condition participants were presented with arrays consisting of four black shapes in the study display (Figure 2.1A). In the different trials two shapes were replaced by two new shapes in the test display.

Memory for colour only: In this condition arrays consisted of four colours. For this condition, one shape was evenly and randomly selected from the set of eight to construct stimuli for each trial (no shape information was available). Each shape displayed a different colour. In the different trials two new colours replaced two colours previously presented in the study display.

Memory for orientation only: In this condition participants were presented with four oriented shapes all in black colour. Orientation values were selected from a set of eight possible degrees of rotation (22^{o}, 45^{o}, 67^{o}, 90^{o}, 112^{o}, 124^{o}, 166^{o}, and 188^{o}) (Figure 2.1B). For this condition one shape was evenly and randomly selected from the set of eight to construct stimuli for each trial. As the same shape was used to construct stimuli for each array, the information about shape was irrelevant to the task. Within each display oriented shapes differ from each other in at least 2 steps of rotation (e.g., 22^{o}, 67^{o}, 112^{o}, and 166^{o}). Similarly, in the different trials, the new orientations differed from the replaced orientations in 2 rotation steps (e.g., from 90^{o} to 124^{o}). This manipulation was aimed at maximizing perceptual differences between items within each display as well as between changing items. In the different trials two new orientations were presented in the test display.

Memory for shape-colour binding: In this condition four shape-colour combinations were presented. In the different trials two shapes swapped their colours in the test display. Participants were told that memory for the combination of shapes and colours was required for detecting changes between displays.

Memory for shape-orientation binding: In this condition combinations of black shapes and orientations were presented in the study display. The same procedure for selecting orientations described in orientation only condition was applied to this condition for oriented shapes. In the different trials two shapes swapped their orientations. Participants were told that memory for the combination of shapes and orientations was required for detecting changes between displays.

Memory for colour-orientation binding: In this condition participants were presented with different colours in different orientations. The shape showed

in Figure 2.1B was selected to construct stimuli for this condition. Colours and orientations were randomly combined using this shape. In the different trials two colours swapped their orientations. Participants were told that memory for the combination of colours and orientations was required for detecting changes between displays.

Memory for colour-colour binding: In this condition participants were presented with four bicoloured objects. Six different object layouts were used for constructing these bicoloured objects (Figure 2.1C). Layouts consisted of a figure and a ground area each representing 50% of the total surface of the objects. These areas were filled with colours randomly selected from the set of eight. For each trial one layout was randomly selected from the set of six. Layouts were evenly used within this condition. Participants were requested to remember the association of colours within objects during the study display. In the different trials two objects swapped one of their colours either from the figure or from the ground area. Participants were told that memory for the combination of colours within objects was required for detecting changes between displays.

2.2.2.4 Procedures

Before the experiment, participants were asked general questions about their age, education, or health problems. Then, their vision for colours was assessed using the Colour Blindness Test (Dvorine, 1963). Participants with score above 2 in this test were excluded from the experiment. After this general assessment, 15 practice trials were provided for each condition which were followed by 32 test trials per experimental condition. All conditions were blocked and delivered in a counterbalanced order. Participants were provided with breaks along the experiment.

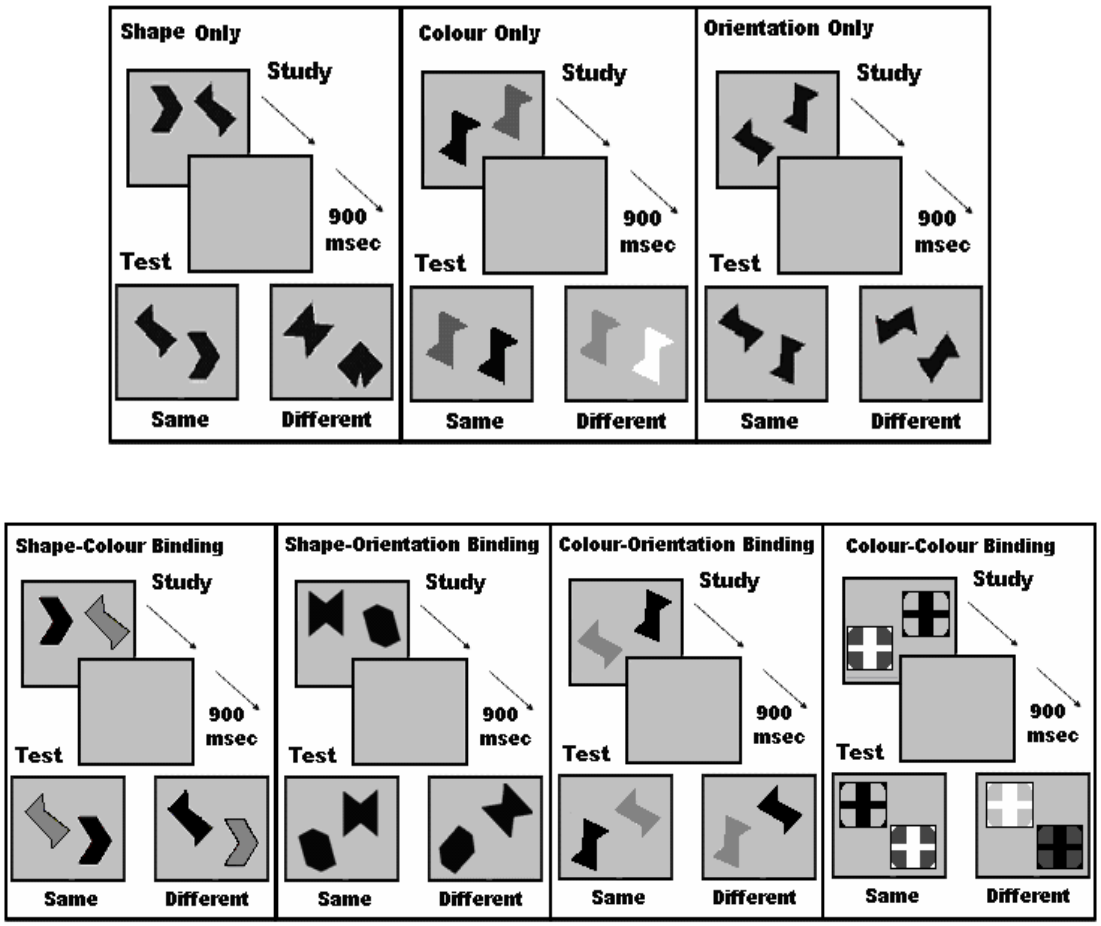

Figure 2.2. Example of the trial sequence for the each condition of Experiment 1. The actual arrays presented 4 items in each experimental condition.

2.2.2.5 Analysis

The change detection paradigm has been considered a useful tool to investigate visual short-term memory for conjunctions of features in normal individuals (Cowan et al., 2006; Luck & Vogel, 1997; Wheeler & Treisman, 2002; Xu, 2002). However, two issues have been raised from change detection tasks that I will briefly discuss in this Section from the perspectives of the Signal Detection Theory.

Signal Detection Theory

One such issue is the degree with which people can extract information about the presence or absence of a target in the middle of the noise (i.e., separating signal from noise) which has been called "detection threshold" or "sensitivity". This problem has been considered relevant in "yes/no" or "same/different" tasks. For example, if targets are two shapes swapping colours and these changes have to be detected among other non-changing coloured shapes, the noise would comprise the number of distracters (no changing items), how similar the distracters and targets are, what are the changing magnitudes, and for how long these visual arrays are presented. The second issue affecting the change detection is the response bias that is, the likelihood (i.e., by preference) of choosing one of the available responses (e.g., "same" vs. "different"). The major contribution of the Signal Detection Theory to psychology is the separation of response bias and sensitivity from the response (Stanislaw & Todorov, 1999).

One measure proposed by the Signal Detection Theory is d'. It has been suggested that d' is unaffected by response bias if: (1) The signal and noise distributions are both normal, and (2) the signal and noise distributions have the same standard deviation (Stanislaw & Todorov, 1999). Therefore d' is a parametric measure of sensitivity. Stanislaw and Todorov (1999) pointed out that these assumptions cannot actually be tested in "yes/no" or "same/different" tasks as the distribution of the noise may be far from normal and the assumption regarding the equality of the signal and the noise standard deviations is unlikely to be sustained (Swets, 1986a; Swets, 1986b). For this reason several nonparametric measures of sensitivity have been proposed (Nelson, 1984; Nelson, 1986), A′ being the most popular. A' was devised by Pollack & Norman (1964) and it typically ranges from 0.5 (which indicates that signals cannot be distinguished from noise) to 1 (which

corresponds to perfect performance). Values less than 0.5 may arise from sampling error or response confusion; the minimum possible value is 0. Therefore, for change detection tasks where chance occurs in 50% of the trials, and only two items change in these different trials the Signal Detection Theory would provide a reliable measure of the ability to extract that signal from the surrounding noise. Some authors consider that A' would assess memory performance in this type of paradigm better as this measure does not have the indeterminacy of d' when a participant makes no false "yes" responses (i.e., no false alarms) (Donaldson, 1993; Xu, 2002). For example for correcting this limitation of d', Cowan et al. (2006) lowered to 0.99 individual mean hit rates of 1.0 and raised to 0.01 individual mean false-alarm rates of 0.

Response bias in a "yes/no" or "same/different" tasks is often quantified with β. β is based on a ratio of the probability of hits and the probability of false alarms (Stanislaw & Todorov, 1999). Using the natural logarithm of this ratio, negative values of ln(β) indicates bias toward "no/same" responses (rejecting the change), whereas positive values of ln(β) indicates bias toward "yes/different" responses (accepting the change). A value of 0 indicates no response bias (McNicol, 1972).

In the current experiment the Signal Detection Theory was implemented using A' and β. The logic was assessing how sensitivity and response bias would affect change detection of objects composed of features processes by separate feature dimensions. Therefore, the independent variables used in this experiment were, accuracy as measured by the percentage of correct recognition, A', and β.

For the sake of the comparison across feature dimensions and for establishing baseline performance using single feature conditions, collected data was processed using four separate analyses: shape-colour (i.e., shape

only, colour only, and shape-colour binding conditions), shape-orientation (i.e., shape only, orientation only, and shape-orientation binding conditions), colour-orientation (i.e., colour only, orientation only, and colour-orientation binding conditions), and colour-colour (i.e., colour only and colour-colour binding conditions). One-way repeated measures-ANOVAs were carried out for each analysis using Condition as the within-subjects factor. The results of these analyses are shown in Figure 2.3.

2.2.3 Results

2.2.3.1 Shape-colour analysis

A one-way repeated-measures ANOVA with Condition (shape only vs. colour only vs. shape-colour binding) as the within-subjects factor and percentage of correct recognition as the dependent variable showed a significant main effect of Condition [$F(2,26) = 45.17$, $p < 0.001$].

Post-hoc tests using Bonferroni corrections showed that performance in the condition assessing memory for colour only was better than performance in conditions assessing memory for shapes only [MD = 18.93, SE = 2.58, $p < 0.001$] (MD = Mean differences between conditions; SE = Standard error) and memory for shape-colour binding [MD = 27.07, SE = 2.69, $p < 0.001$]. Performance in conditions assessing memory for shape only and shape-colour binding did not differ [MD = 8.14, SE = 3.42, p = n.s.] and both were significantly different from chance [shape: $t = 9.65$, $p < 0.001$; shape-colour binding: $t = 11.92$, $p < 0.001$].

Therefore, the main effect of Condition was driven by colour only as the easiest feature to remember.

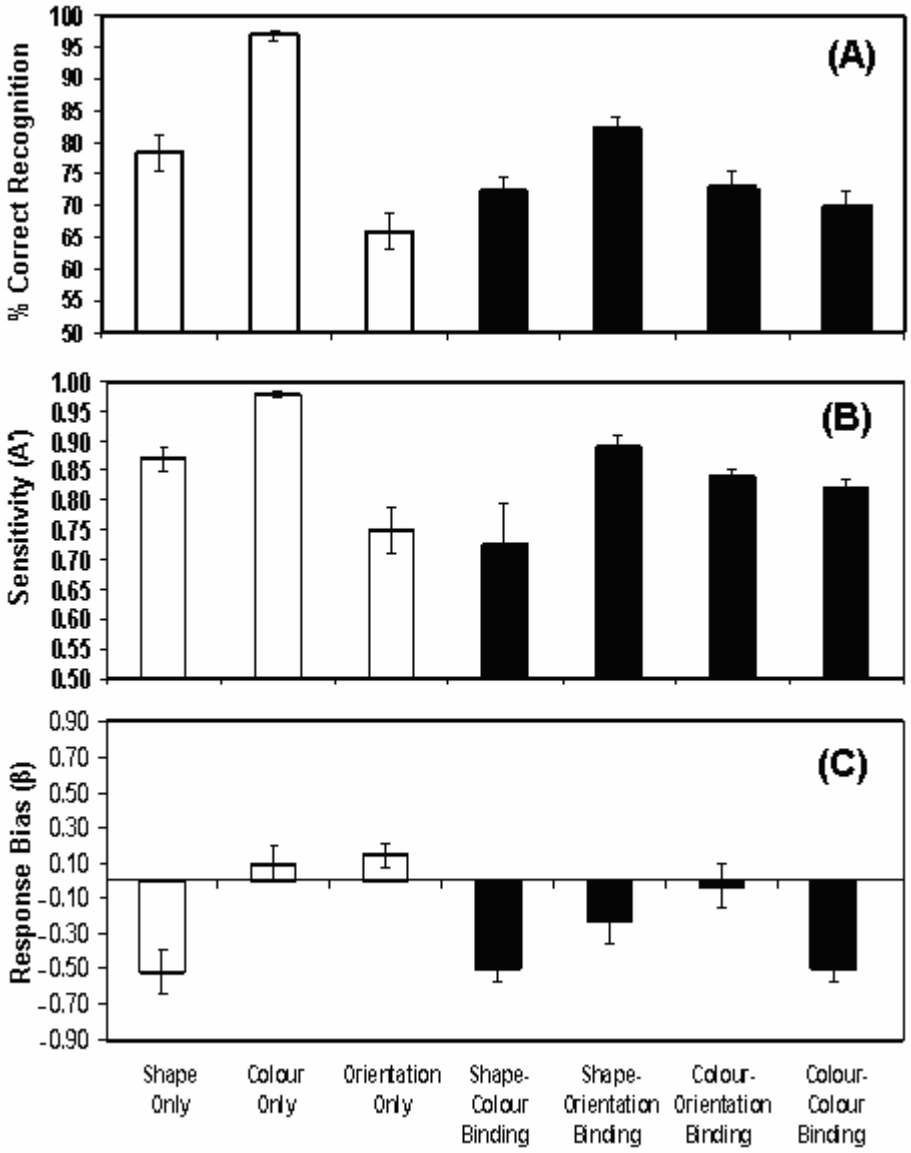

Figure 2.3 (A) Percentage of correct recognition above chance (50%), (B) Sensitivity (A'), and (C) β for conditions assessing memory for single features (□) and the binding of these features (■) (Error bars represent the standard errors of the mean).

When A' was entered in the analysis the assumption of sphericity was violated hence the Greenhouse-Geisser correction was used. A significant effect of Condition was found [$F(1.07,14.0) = 12.61$, $p < 0.01$]. Post-hoc tests using Bonferroni corrections showed that sensitivity in the condition assessing memory for shape only was poorer than sensitivity in the condition

assessing memory for colour only [MD = -0.11, SE = 0.018, $p < 0.001$] but it was no different from sensitivity in the condition assessing memory for shape-colour binding [MD = 0.19, SE = 0.078, p = n.s.]. Sensitivity in conditions assessing memory for colour only was higher than sensitivity for detecting changes in the condition assessing memory for shape-colour binding [MD = 0.31, SE = 0.071, $p < 0.01$].

For β a significant effect of Condition was found [$F(2,26) = 20.63$, $p < 0.001$]. Post-hoc tests showed that response bias in the condition assessing memory for colour only was close to 0 and it was significantly different from conditions assessing memory for shape only [MD = -0.60, SE = 0.10, $p < 0.001$] and memory for shape-colour binding [MD = 0.66, SE = 0.12, $p < 0.001$]. Response bias in conditions assessing memory for shape only and shape-colour binding were remarkably negative (suggesting bias toward "same" response) and they did not differ from each other [MD = 0.06, SE = 0.12, p = n.s.].

2.2.3.2 Shape-orientation analysis

A one-way repeated-measures ANOVA with percentage of correct recognition as dependent variable showed a significant effect of Condition [$F(2,26) = 16.55$, $p < 0.001$]. Post-hoc tests showed that performance in the condition assessing memory for orientation only was poorer than performance in the condition assessing memory for shape only [MD = -12.14, SE = 2.85, $p < 0.01$] and than performance in the condition assessing memory for shape-orientation binding [MD = -16.00, SE = 2.73, $p < 0.001$]. Performance in conditions assessing memory for shape only and shape-orientation binding did not differ [MD = -3.86, SE = 3.12, p = n.s.] and both were significantly different from chance [Shape-orientation binding: t =

14.69, $p < 0.001$]. Therefore the main effect of condition was driven by the poor performance in the condition assessing memory for orientation only which also was different from chance [Orientation: $t = 5.32$, $p < 0.001$].

For A' a significant effect of Condition was found [$F(2,26) = 20.10$, $p < 0.001$]. Post-hoc tests showed that sensitivity in the condition assessing memory for shape only did not differ from the condition assessing memory for shape-orientation binding [MD = -0.02, SE = 0.022, p = n.s.]. The sensitivity for change detection in the condition assessing memory for orientation only was poorer than sensitivity in conditions assessing memory for shape only [MD = -0.13, SE = 0.03, $p < 0.01$] and shape-orientation binding [MD = -0.16, SE = 0.03, $p < 0.01$].

For β a significant effect of condition was found [$F(2,26) = 11.71$, $p < 0.001$]. Post-hoc tests showed that the condition assessing memory for shape only resulted in more bias toward "same" response than the condition assessing memory for orientation only [MD = -0.64, SE = 0.13, $p < 0.01$] but not than the condition assessing memory for shape-orientation binding [MD = -0.24, SE = 0.16, p = n.s.]. Response bias in the condition assessing memory for shape-orientation binding did not differ from bias in orientation only [MD = 0.39, SE = 0.09, p = n.s.]. This suggests that the main effect of condition was driven by the remarkable tendency to response "same" in the condition assessing memory for shape only.

2.2.3.3 Colour-orientation analysis

A significant effect of Condition was found [$F(2,26) = 68.02$, $p < 0.001$]. Post-hoc tests showed that performance in the condition assessing memory for colour only was significantly better than performance in conditions assessing

memory for orientation only [MD = 31.07, SE = 3.0, $p < 0.001$] and than performance in the condition assessing memory for colour-orientation binding [MD = 24.00, SE = 2.23, $p < 0.001$]. Performance in the condition assessing memory for orientation only did not differ from that in the condition assessing memory for colour-orientation binding [MD = -7.07, SE = 2.01, p = n.s.]. Performance in the condition assessing memory for colour-orientation binding was significantly different from chance [$t = 18.61$, $p < 0.001$]. Therefore the main effect of Condition was driven by memory performance for colour only being better than both memory performance for orientation only and colour-orientation binding which did not differ from each other.

For A' a significant effect of Condition was found [$F(2,26) = 29.58$, $p < 0.01$]. Post-hoc tests showed that sensitivity for change detection in the condition assessing memory for colour only was better than for orientation only [MD = 0.24, SE = 0.03, $p < 0.001$] and than for colour-orientation binding [MD = 0.16, SE = 0.03, $p < 0.001$]. Sensitivity for changes in orientation only and colour-orientation binding did not differ [MD = 0.08, SE = 0.04, p = n.s.]. The analysis of response bias showed little bias for the three experimental conditions and no significant difference in any of the post-hoc comparisons.

2.2.3.4 Colour-colour analysis

A paired-sample t-test showed that memory for colours only was significantly better than memory for colours bound into bicoloured objects [$t(22) = 11.65$, $p < 0.001$]. For A' and response bias, it was found that the condition assessing memory for colours bound resulted in less sensitivity for change detection [$t(22) = 9.11$, $p < 0.001$] and in a significantly greater bias toward the "same" response [$t(22) = 4.59$, $p < 0.001$].

2.2.4 Discussion

Colour was found to be the easiest feature to remember. Colours are considered pop-out stimuli which are quickly processed along low-order visual streams (Allen et al., 2006; Wheeler & Treisman, 2002). It has been suggested that the visual system possesses chromatic channels which allow for fast processing colour information (colours guide the attentional processes) (Hannus et al., 2006). Orientation was found to be the most difficult feature to remember although memory for this type of feature was far from chance. Shape information was more difficult to remember than colour but was easier than orientation.

More information seems to be lost on shape and orientation than on colour. This resulted in shape and orientation driving memory for complex objects comprising these types of features. Similar findings were reported by Wheeler and Treisman (2002) and Allen et al. (2006). These authors suggested that the most difficult feature drives memory for bindings involving this feature. In the current experiment this was the case for coloured shapes and oriented colours. However, it was observed that despite orientation being more difficult to remember than shape, when these two features were combined, memory for shapes drove memory for the binding. That is, memory for shape drove memory for the binding when it was combined with colour and with orientation. As Figure 2.3A shows, when participants retrieved coloured shapes or oriented shapes, memory for colour or orientation accounted less for memory for bindings than memory for shape. However, when people retrieved oriented colours, orientation drove the binding. According to these findings it might be argued that the visual system relies more on shape information to identify complex objects than on their colour or orientation. It is worth noticing that other response components such as sensitivity for change detection and response bias

further support these arguments as sensitivity and bias for shape only did not significantly differ from sensitivity and bias for oriented shapes or coloured shapes. These findings strongly suggest that the nature of the information bound into integrated objects is an important factor affecting the efficiency of visual short-term memory for complex objects. This observation had been also made by Olson and Jiang (2002). Finally, memory for bicoloured objects was significantly poorer than memory for unicoloured objects.

The results of Experiment 1 suggest that information of shape, colour, and orientation can be represented in an object-based format in visual short-term memory (e.g., memory for shape-colour binding or shape-orientation binding was not poorer than memory for shape only, or memory for colour-orientation binding was not different than memory for orientation only with performance in all conditions being far from chance). When these objects consist of the same type of feature however (e.g., bicoloured objects), this object-based format is lost. There is evidence in the literature suggesting that binding features processed within a single feature dimension results in greater interference, hence in a poorer integration than binding across different feature dimensions (Allen et al., 2006; Olsson & Poom, 2005; Wheeler & Treisman, 2002).

The analysis of the Signal Detection Theory showed that changes in sensitivity (A') accurately reflected upon recognition. As Figure 2.3B shows, graphs of A' almost mirror in shape graphs of percentage of correct responses. A bivariate Pearson correlation analysis showed a strong positive correlation between A' and percentage of correct recognition ($r = 0.85$, $p < 0.001$) suggesting that changes in sensitivity strongly account for changes in correct recognition. In the case for response bias (Figure 2.3C), a remarkable tendency to respond "same" was observed for conditions assessing memory

for bound features. This agrees with previous works on visual short-term memory in which the change detection paradigm has been used (Cowan et al., 2006). As was mentioned in Section 1.4.3, the mechanism underlying these biased responses may be that features on both displays (study and test) are the same but rearranged in different combinations in the test display. This may convey a high sense of familiarity what would make the option "same" more likely to be chosen.

Summarizing, the results of Experiment 1 suggest that the nature of the information to be integrated into objects does affect the efficiency with which these complex objects can be held in visual short-term memory. Features of different types can be represented as integrated objects in visual short-term memory, observation that fits well the hypothesis proposed by Luck and Vogel (1997) and with the conclusions by Xu (2002). Features of the same type however (i.e., colours) seem not to be integrated into unified representation, mismatching Luck and Vogel (1997) object-based hypothesis and supporting the feature-based hypothesis proposed by Wheeler and Treisman (2002). This divergence between different/same bindings is in line with the idea that competition for resources within feature dimensions can limit the efficiency of processes responsible for integrating features into objects (Olson & Jiang, 2002; Wheeler & Treisman, 2002). This interference effect will be addressed in Experiment 2.

2.3 Experiment 2

Wheeler and Treisman (2002) investigated visual working memory for combinations of colours and shapes or colours and locations. In their experiments the authors introduced a condition they called "either" in which both features were presented together but only one of them could change in

the different trials. This change could be either new colours or new shapes replacing colours or shapes previously presented in the study display. Therefore, memory for the binding between features was not required. Wheeler and Treisman (2002) observed that when colours were combined with shapes, the either condition resulted in poorer performance for both types of feature than when features were assessed separately. The authors observed that this was not the case for colours bound to locations where performance on both single feature conditions and on either condition was equivalent for both feature types. Wheeler and Treisman (2002) suggested that this difference reflects a process of competition for resources. As colour and location are features processed by separate visual streams (i.e., ventral and dorsal respectively) while shape and colour are processed within the same visual stream (i.e., ventral stream), combining shape with colour would result in more competition. Allen et al. (2006) adopted this methodology in order to replicate Wheeler and Treisman's (2002) findings. The authors found similar results and also suggested that some shared processing capacity between feature dimensions may underlie this pattern performance.

In the current experiment the either condition was incorporated to investigate whether shapes and colours selected for these experiments share resources and consequently interfere with each other when the have to be kept together in visual short-term memory. This methodology was adopted because shapes used in this experiment were visually more abstract (see Figure 2.1A) than shapes used by Allen et al. (2006) and by Wheeler and Treisman (2002). These authors used concurrent verbal load tasks to suppress verbal rehearsal of the studied materials. In this experiment, and for the series of experiments presented in this thesis, this methodology was not used as one aim of this study was devising tasks that may keep the performance of brain damage individuals well far from chance. Therefore, our aim was to design a task which imposes high demands on visual short-term memory

(i.e., abstract shapes and colours difficult to name) without the additional requirements of a concurrent task to suppress verbal rehearsal (see Cowan, 2008 for a discussion of the interfering effects introduced by concurrent verbal load tasks).

2.3.1 Aims

Experiment 2 addressed the question of whether the process of integrating the shapes and colours selected for this study in visual short-term memory would face interference due to competition for central resources and whether this interference would be reflected upon performance.

2.3.2 Methods

2.3.2.1 Participants

Sixteen new undergraduate volunteers with mean age of 21.44 years (SD = 1.66), average years of formal education of 16.75 (SD = 2.65), and VIQ of 109.50 (SD =4.50) entered this experiment. All gave their informed consent prior participation.

2.3.2.2 Design

For this experiment we used the same shapes and colours described in Experiment 1. In addition to the conditions assessing memory for shape only, colour only, and shape-colour binding, a new condition was added which explores visual short-term memory for shapes and colours when both features are presented as parts of the same objects but they do not have to be

kept bound in memory. In this condition either the colour or the shape of two items could be replaced by new colours or new shapes. As changes consisted of new features, the binding of features into objects was not required. Additionally, participants were explicitly told about the nature of the change as to ensure that they would not attempt to bind features together. The other task parameters were exactly the same as described for Experiment 1.

2.3.2.3 Procedures

The same procedures described in Experiment 1 were used in Experiment 2.

2.3.3 Results

Figure 2.4 shows mean data. A one-way repeated-measures ANOVA with Condition as within-subjects factor (shape only vs. colour only vs. either colour vs. either shape vs. shape-colour binding) and percentage of correct recognition as the dependent variable was performed. After using the Greenhouse-Geisser epsilon to correct the violation of the assumption of sphericity, a significant main effect of Condition was found [$F(2.40,36.04) = 15.26$, $p < 0.001$]. Post-hoc Tests using Bonferroni corrections showed that performance in the condition assessing memory for colours only was better than performance in the condition assessing memory for shape only [MD = -12.54, SE = 2.5, $p < 0.01$] and for shape-colour binding [MD = 19.92, SE = 2.20, $p < 0.001$]. Memory performance in shape only and shape-colour binding conditions did not differ [MD = 7.38, SE = 2.47, p = n.s.]. Remembering shapes presented as single features was easier than remembering shapes presented as part of coloured shapes (i.e., either condition) [MD = 18.01, SE = 5.45, $p = 0.047$], and it was no different than remembering colours also presented as part of coloured shapes [MD = -3.89, SE = 5.06 p = n.s.].

Remembering colours presented as single features was no different than remembering colours presented as part of coloured shapes [MD = 8.64, SE = 4.06 p = n.s.]. Memory performance for shape-colour binding was no different than memory performance for shapes presented as part of coloured shapes (i.e., either condition) [MD = -10.70, SE = 4.67, p = n.s.] or than colours presented as part of coloured shapes [MD = 11.27, SE = 4.74, p = n.s.].

When A' was analyzed using the same ANOVA model, a significant effect of Condition was found [$F(4,60) = 8.50$, $p < 0.001$]. Post-hoc tests showed that sensitivity for detecting changes in colour only was higher than for shape only [MD = 0.087, SE = 0.019, $p < 0.01$] and than for shape-colour binding [MD = 0.133, SE = 0.02, $p < 0.001$]. Sensitivity did not differ in conditions assessing memory for shape only or shape-colour binding [MD = 0.046, SE = 0.022, p = n.s.]. Detecting changes in shapes presented as single features was no different than detecting changes in shapes presented as part of coloured shapes (i.e., either condition) [MD = 0.07, SE = 0.04, p = n.s.] or in colours also presented as part of coloured shapes [MD = -0.011, SE = 0.03 p = n.s.]. Detecting changes in colours presented as single features was easier than detecting changes in colours presented as part of coloured shapes [MD = 0.076, SE = 0.022 p = 0.032]. Sensitivity for change detection in the condition assessing memory for shape-colour binding was no different from sensitivity for shapes presented as part of coloured shapes (i.e., either condition) [MD = 0.019, SE = 0.034, p = n.s.] or for colours presented as part of coloured shapes [MD = -0.058, SE = 0.029, p = n.s.].

For β a significant main effect of Condition was found [$F(4,60) = 14.55$, $p < 0.001$]. Post-hoc tests showed that bias during change detection in colour only was 0 and no different than bias in shape only [MD = -0.252, SE = 0.112, p = n.s.]. Bias toward "same" response in shape-colour binding was more pronounced than in colour only [MD = 0.546, SE = 0.107, $p < 0.01$] but not

than in shape only [MD = 0.294, SE = 0.104, p = n.s.]. Less bias was observed for shapes only than for shapes presented as part of coloured shapes [MD = 0.416, SE = 0.103, p = 0.011]. Bias did not differ in conditions assessing memory for colours only or colours presented as part of coloured shapes [MD = -0.184, SE = 0.181, p = n.s.]. Bias in the condition assessing memory for shape-colour binding was no different from bias in the condition assessing memory for shapes presented as part of coloured shapes (i.e., either condition) [MD = 0.123, SE = 0.126, p = n.s.] but it was greater than in the condition assessing memory for colours presented as part of coloured shapes [MD = -0.729, SE = 0.179, p = 0.010].

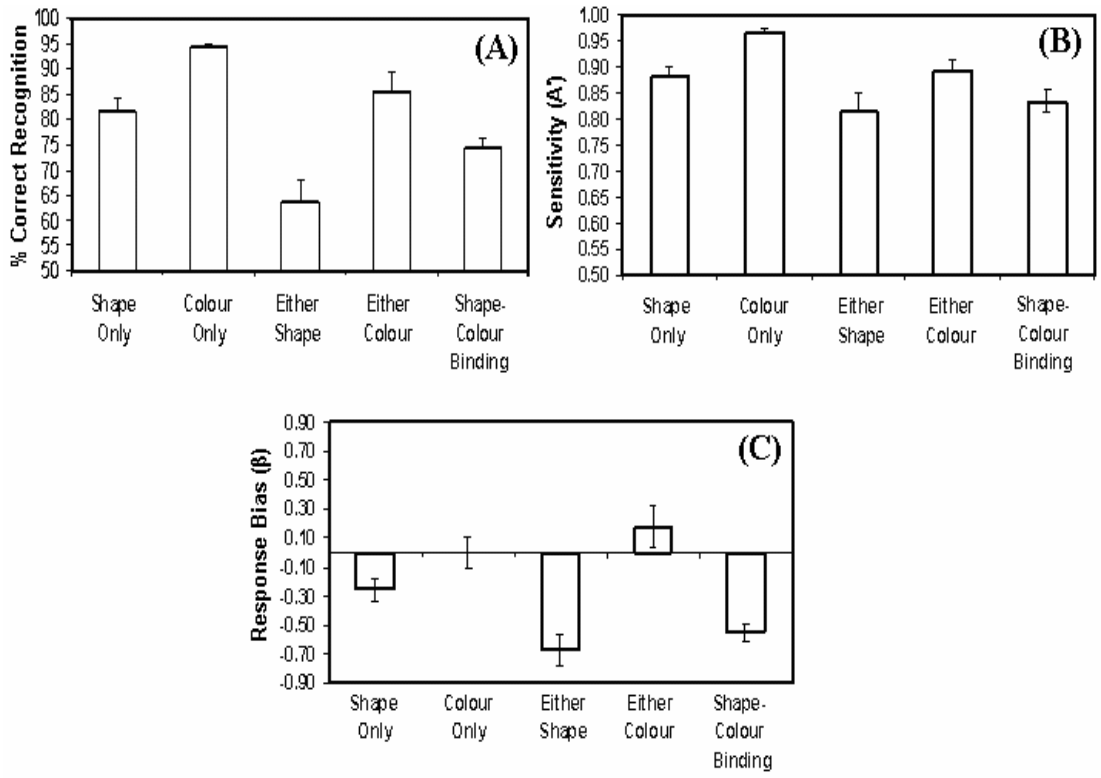

Figure 2.4. (A) Percentage of correct recognition above chance level (50%), (B) Sensitivity (A'), and (C) Response Bias (β) for the four conditions used in Experiment 2 (Error bars represent the standard errors of the mean).

2.3.4 Discussion

The results of Experiment 2 confirmed the findings of Experiment 1 suggesting that shapes and colours can be bound in visual short-term memory in an object-based format. The fact that remembering coloured shapes was no different than remembering shapes only suggests so. These findings are in agreements with those by Luck and Vogel (1997). In line with findings in Experiment 1, shape was a feature more difficult to remember than colour and it drove memory for the shape-colour binding. The results of Experiment 2 gave support to the statement that when shapes and colours have to be kept together in visual short-term memory, as was the case for both the either and binding conditions, interference arises and shape seems to be the feature most affected by this interference (see also Allen et al., 2006 and Wheeler & Treisman, 2002). This in line with the hypothesis for Experiment 2 that the shapes and colours selected for this study would interfere when they were bound together. These results also extend previous findings to shapes and colours that are difficult to name and which were held in visual short-term memory without the use of articulatory suppression.

Memory performance in both either-shape and either-colour conditions dropped as compared to conditions assessing memory for each feature individually. However, for either-shape condition this drop was more pronounced than for either-colour. This poor performance in the either-shape condition was not accounted for by poor sensitivity in change detection as A' for either-shape and shape only conditions did not differ. A' for either-colour and colour only conditions significantly differed. This suggests that interference impacts on change detection even when this change occurs in the easiest feature to remember (i.e., colour). On the other hand, the high

tendency to respond "same" during shape only condition was more pronounced than during colour only condition but less remarkable than during either-shape and shape-colour binding conditions, and it did not differ between these last two conditions. This finding fits well with the suggestion that the most difficult feature to remember drives memory performance for bindings involving that feature (Allen et al., 2006; Wheeler & Treisman, 2002). The fact that memory performance in the condition assessing memory for shape-colour binding did not differ from performance in conditions assessing memory for either-shape or either-colour suggests that visual short-term memory retains that information about the to-be-bound features that survives interference. Information about these features is then represented in an object-based format.

Following this evidence it can be concluded that colour and shape compete for central resources when they have to be kept together in visual short-term memory. Olson and Jiang (2002) suggested that the Multiple Resources Theory would predict that accuracy should be equivalent in the heterogeneous single feature condition (i.e., either-shape or either-colour) and in the conjunction condition (i.e., shape-colour binding) and that both should retain twice as many features as the homogeneous single feature conditions (i.e., shape only and colour only). In this experiment we observed that memory for either-shape or either-colour was no different than memory for shape-colour binding and that both retained twice as may features as conditions assessing memory for single features.

These findings therefore provide further support to the Multiple Resources Theory. They also suggest that the abstract shapes and colours used in these experiments may interfere with each other when they have to be held in visual short-term memory simultaneously as part of multifeature objects.

In sum, the results of Experiment 2 confirm previous findings suggesting that the efficiency of visual short-term memory for multi-features objects depends to some extent on shared capacities across features dimensions. It is possible that features that are more difficult to remember (e.g., shapes) would be more vulnerable to interference effects resulting from the integration processes. Because interference implies information loss, the most difficult feature will more likely drive memory performance for multi-feature objects.

The results of Experiments 1 and 2 suggest that the type of information to-be-bound seems to impact on the unit of capacity of visual short-term memory to represent multi-feature objects (i.e., object-based or feature-based) as well as on the efficiency of processes responsible for feature integration. There are however other factors that have been claimed to impact on the capacity of visual short-term memory for multi-features objects. One such factor is the amount of information to-be-remembered which is determined by both the number of features and the number of objects in which these features are integrated (Alvarez & Cavanagh, 2004).

The results of Experiments 1 and 2 further suggest that shapes selected for this study are difficult to remember. It might be possible that four abstract shapes presented for one second have imposed a high perceptual load which resulted in poor memory. As one aim of this chapter was to assess which task parameters and stimuli may be suitable for further experiments of this thesis, such as investigating age-effects on memory binding or memory binding deficits in neuropsychological patients, it would be worth investigating the impact that memory and perceptual load may have on the capacity of visual short-term memory for integrated objects in healthy individuals. Experiment 3 addressed these issues. In this new experiment participants were healthy older adults. Experiments 1 and 2 addressed the issue of binding in short-

term memory in younger participants. Experiment 3 investigates visual short-term memory performance for multifeature objects in older people.

2.4 Experiment 3

For this new experiment a measure of memory capacity was computed. According to Luck and Vogel (1997), the quantitative approach devised by Pashler (1988) would suit this aim as it considers the capacity of visual short-term memory as the number of items effectively retained as a function of the total number of items to-be-remembered (array size). This approach also controls for the effect of guessing by considering the rate of false alarms.

Following this approach, visual short-term memory capacity was computed using the expression: K = [S * (H - F)] / (1 - F), where K is capacity, S the array size, H is the observed hit rate (H = hits / [hits + misses]), and F is the observed false alarm rate (F = false alarms / [false alarms + correct rejections]).

2.4.1 Aims

Experiment 3 investigated: First, whether memory load as determined by the number of features and objects would impact on visual short-term memory capacity.

Second, whether perceptual load, as determined by the time allotted to studying visual arrays, would affect this capacity. Finally, this experiment investigated possible patterns of interaction between these factors.

2.4.2 Methods

2.4.2.1 Participants

Two groups of healthy older participants (n = 14 and n = 12) entered Experiment 3. The demographic variables and task parameters used in this experiment are shown in Table 2.1. As these were older people, it was important to rule out sensory or perceptual problems. Therefore, participants underwent a colour vision assessment using the Colour Blindness Test (Dvorine, 1963). Participants had to score less than 3 errors in this test to enter the study.

Table 2.1. Demographic, psychometric, and task variables for the two groups entering Experiment 3.

	Demographic variables			Task design	
	Age	Education	VIQ	Set Size	PT
Group 1 (n = 14)	71.86 (6.73)	15.43 (4.32)	110.07 (4.79)	2,4,6	2000
Group 2 (n = 12)	67.33 (5.93)	15.83 (4.53)	110.25 (4.90)	2,4,6	1000
t	1.80	0.23	0.09		
p	n.s.	n.s.	n.s.		

PT: presentation time; VIQ: verbal IQ as assessed by Wechsler (2002).

In addition to colour vision, perception for shape-colour bindings was assessed. The perceptual task presented participants with two arrays of four coloured shapes each, one in the upper and another one in the lower half of the screen. In 50% of the trials both arrays consisted of the same coloured shapes and in the other 50% two shapes either from the upper or the lower half swapped colours. Participants were requested to make speeded decisions as to whether both arrays consisted of the "same" or "different" shape-colour combinations and to press two keys correspondingly. Participants who scored less than 90% in accuracy (18 out of 20 trials correct)

were excluded from this study (see Appendix 2 – IA for an example of this perceptual task).

2.4.2.2 Design

For this experiment the same task described in Experiment 2 was used. From this task, conditions assessing memory for shape only, colour only, and shape colour binding were selected. Additionally, the number of items presented (set sizes) and the presentation time for the study display were changed as shown in Table 2.1. All other tasks parameters and procedures remained the same as in Experiment 2 (See Appendix 2 –II for the instructions given to participants during the experiment).

2.4.2.3 Statistical analysis

As the task design was homogenous across groups and only the presentation time was varied across them, a three-way mixed-ANOVA analysis was carried. In this analysis, Group (Group 1 vs. Group 2), which determined the perceptual load, was the between-subjects factor and the within-subjects factors were Condition (shape only vs. colour only vs. shape-colour binding) and Set Size (2 vs. 4 vs. 6), this last one determining memory load. It was predicted that if the process of holding integrated versus single features in visual short-term memory is cost-free whenever these features are parts of individual objects as suggested by Luck and Vogel (1997), the capacity of this memory system would not be differentially affected when the amount of unifeature or multifeature objects increases.

Alternatively, if storing bound features in visual short-term memory is not a cost-free process, holding shapes bound with colours would result in a

memory capacity drop which would be larger than the capacity drop resulting from storing objects defined by shape only or colour only. One second prediction concerns perceptual load as imposed by the presentation time. If the time allowed to encode visual information has an effect on the capacity of visual short-term memory, then shorter presentation times would result in a visual short-term memory capacity drop.

2.4.3 Results

A significant main effect was found for Group (i.e., presentation time) [$F(1,24) = 4.76$, $p = 0.039$], whereby capacity drop was found to be larger with presentation time of 1000 than 2000 msec. When within-subjects factors and the interaction were analyzed, the assumption of sphericity was violated for Set Size and for the interaction of Condition by Set Size hence Greenhouse-Geisser corrections were applied to the analysis of these effects. Condition also resulted in a significant main effect [$F(2,48) = 23.83$, $p < 0.001$] being capacity for bound features smaller than capacity for single features. A significant main effect was also found for Set Size [$F(1.49,35.97) = 15.50$, $p < 0.001$] suggesting that as the array sizes increased more items were held in short-term memory. When the interactions were analyzed, it was observed that the presentation time did not interact with Condition [$F(2,48) = 2.19$, p = n.s.] or Set Size [$F(2,48) = 1.74$, p = n.s.]. A significant interaction was found between Condition and Set Size [$F(2.41,57.80) = 4.86$, $p < 0.01$]. The three-way interaction was non significant [$F(4,96) = 1.76$, p = n.s.] (Figure 2.5 A and B).

To further explore the Condition by Set Size interaction, post-hoc tests were carried out using Bonferroni corrections. Six pairwise contrasts were carried with an adjusted alfa level of 0.008. This analysis showed that the drop in memory capacity for shape-colour binding was not significantly larger than

for shape only [MD = 0.68, SE = 0.20, p = n.s.] but it was significantly larger than for colour only [MD = 1.29, SE = 0.20, p < 0.001]. Capacity drop for shape and colour only did not significantly differ [MD = 0.61, SE = 0.16, p = n.s.]. When post-hoc test were carried out across Set Size, it was found that visual short-term memory capacity for 4 items was greater than for 2 items [MD = 0.75, SE = 0.09, p < 0.001]. No other pairwise contrast resulted in significant effect. This suggests that once visual short-term memory capacity is reached (probably 4 items) the amount of information above that limit is lost.

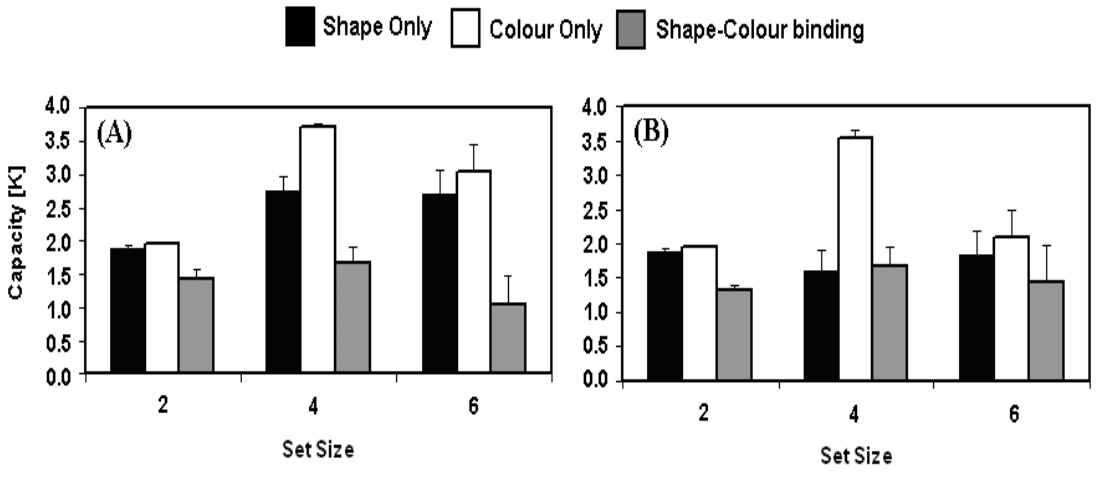

Figure 2.5. Mean visual short-term memory capacity across experimental conditions and set sizes for presentation times of 2000 msec (A) and 1000 msec (B) (Errors bars represent the standard errors of the mean).

However, as Figure 2.5 shows, the Condition by Set Size interaction seems to be driven mostly by an impact of Set Size on short-term memory capacity for single features than for integrated objects, an effect that was less evident when the presentation time was reduced. To assess this possibility further post-hoc tests were separately carried out for each condition across set sizes (9 pairwise contrasts). This analysis was repeated across presentation times (18 pairwise contrasts with alfa set at 0.0027). For a presentation time of 2000 msec (Figure 2.5A), capacity for shape only differed when it was compared

across set sizes 2 and 4 [MD = 0.89, SE = 0.17, $p < 0.001$] being larger in the last one. For colour only capacity was larger at set size 4 than at set size 2 [MD = 1.74, SE = 0.067, $p < 0.001$] and it was no different between set sizes 4 and 6. For shape-colour binding none of the contrasts were found to be significant. For the presentation time of 1000 msec (Figure 2.5B), the only post-hoc comparisons that resulted in a significant differences were in the colour only condition and it was between set sizes 4 and 2 [MD = 1.58, SE = 0.14, $p < 0.001$]. So, as it was predicted, only the conditions assessing memory for single features were significantly affected by memory load.

2.4.4 Discussion

The results of Experiment 3 further support the claim that the capacity of visual short-term memory is set by both the amount and nature of the information (Alvarez & Cavanagh, 2004; Olson & Jiang, 2002). Remembering features bound into unified objects resulted in a greater capacity drop than remembering individual features. As Figure 2.5 shows, whereas short-term memory capacity for single features increased as the number of the to-be-remembered items increased, capacity for integrated objects was stable across set sizes and it never surpassed 2 items. It is worth noticing that integrated objects presented twice as many features as the unifeature objects but the number of objects was always the same across conditions. This suggests that to keep the object-based representational format of visual short-term memory suggested by Luck and Vogel (1997), extra capacity is required to hold in this memory system integrated objects as compared to objects composed of only one feature. Therefore, the integration of features in visual short-term memory does not seem to be a cost-free process as suggested by other authors (Luck & Vogel, 1997). One important difference between the current experiment and the previous study by Luck and Vogel (1997) is that

in the current study the binding between features was explicitly assessed whereas in this earlier study it was not as in the changing trials new features replaced features previously presented (e.g., as in the either condition assessed in Experiment 2). The fact that the intentional binding between features was required in the current experiment suggests that storing the relatedness between features into multifeature objects may require an extra capacity in short-term memory. Furthermore, these results suggest that visual short-term memory may asymptotically approach its capacity limit as the number of items increases. This limit seems to differ between features and objects. As Figure 2.5 shows this limit seems to be around 3 items for single features and around 2 for integrated objects. Taken together, these results suggest that the capacity of visual short-term memory for the abstract shapes and non-nameable colours used in this series of experiments would be 2 or 3 integrated objects or 3 or 4 individual features. These values approximate those described in previous literature (Cowan, 2001; Vogel et al., 2001) involving younger volunteers.

One other finding of this experiment which may offer an account for findings of Experiments 1 and 2 is that of the smaller short-term memory capacity for shape only than for colour only. Despite both conditions presented the same number of objects and features, storing in visual short-term memory abstract shapes required more capacity than storing colours. One possible explanation for this finding may be that despite colours being non-primary, hence difficult to name, participants were still able to use some verbal labels to encode them, aiding by this mean visual short-term memory. This verbal tagging was less likely for shapes, as these six-side random polygons were very difficult to name as demonstrated by previous pilot studies. This suggests that in situations in which no verbal aids are available, the capacity of visual short-term may be found to be smaller than otherwise. This does not entirely fit with Vogel et al.'s (2001) views, who suggested that the use of

a concurrent verbal load task during a visual short-term memory task had no effect on the capacity of this memory system for features or objects. It might be possible that suppressing articulation may not be an entirely safe procedure to prevent the bypass of colour information, as used by Vogel et al. (2001), from visual to verbal memory (see Cowan, 2008 for a similar view). In sum, this finding may provide an account to explain why memory for coloured shapes is driven more by memory for shapes than by memory for colours.

Finally, it was observed that the presentation time had no differential effects on short-term memory capacity for features or objects; nor did it interact with the number of objects to-be-remembered. However, the presentation time reduced memory capacity overall. By reducing the presentation time the possibility of encoding visual information was reduced. If the perceptual demands for multifeature objects were greater than for unifeature objects, one might expect to find a reduced short-term memory capacity when these complex objects are presented as the amount of information encoded would be limited. The results of Experiment 3 suggest that this does not seem to be the case, as the encoding of the unifeature or multifeature objects presented in this experiment was not differently affected by the presentation time. This suggests that once objects are attended and encoded into memory, it does not matter how many features they comprise as these features will be represented as parts of integrated objects. So, the short-term memory cost found for storing multifeature objects as compared to unifeature objects in visual short-term memory does not seem to arise from perception, suggesting that perception and memory for multifeature objects seem to operate under different functional principles. This finding fits well with the predictions of the Feature Integration Theory of Attention which suggests that once objects are attended their constituent parts will be bound together

and treated as a whole in successive stages of cognitive processing (Duncan, 1984; Treisman, 2006; Treisman & Gelade, 1980).

In previous literature on feature integration and perception it has been suggested that searching for conjunctions of features on visual arrays takes more time than searching for single features, as features are encoded preattentively while complex objects require attention and are serially processed (Treisman, 1982; Treisman & Sato, 1990). One characteristic of these earlier studies is that they used large matrices of visual stimuli (see Huang & Pashler, 2005 for recent insights about the relation of attention capacity and the difficulty of visual search tasks) what rendered these arrays more difficult to search. According to the results of the current experiment, when the number of objects does not overload the attentional capacity to a great extent, i.e., four objects or chunks (Cowan, 2001), these objects can be searched with equivalent efficiency when they are presented either for 1 sec or 2 sec. As Huang and Pashler (2005) suggested, "…*the visual search might have no attention capacity limit when the set size is smaller than a certain number, but still show attention capacity limits when the set size exceeds that number*" (see also Pashler, 1987 for a similar suggestion).

2.5 General discussion

There are three main issues concerning the capacity and the representational format of visual short-term memory that I would like to highlight from the results of the series of experiments presented in this chapter.

First, visual short-term memory can retain combinations of features used in these experiments in an object-based representational format. This format however, may vary depending on the nature of the information to-be-

remembered. As the results of Experiment 1 showed, different types of binding (i.e., coloured shapes, oriented colours, or oriented shapes) can be represented within integrated objects in visual short-term memory whereas the same type of information (i.e., colours bound into bicoloured objects) cannot. Similar results have been found by other authors who have suggested that the capacity of visual short-term memory for bicoloured objects is set by the number of colours rather than by the number of objects (Wheeler & Treisman, 2002; Xu, 2002). It was also observed that the efficiency of visual short-term memory for holding bindings of different types also varies across feature dimensions, suggesting that binding operations across dimensions may undergo different levels of difficulties depending on the types of features to be integrated. In line with this finding, it has been suggested that the complexity of visual information comprised within complex objects significantly impacts on visual short-term memory capacity (Alvarez & Cavanagh, 2004).

Second, the results of this series of experiments suggest that the integrative process (i.e., binding) may be fed by separate feature dimensions, each with its own capacity. The capacity within each dimension seems to determine the capacity of visual short-term memory. This may explain why binding the same type of feature into multifeature objects (e.g., bicoloured objects) may require more capacity than binding coloured shapes, as resources within the single colour dimension would be depleted faster. In the case of shape-colour binding however, each dimension would provide independent resources that would be additive during the integration process.

Third, the competition for resources seems to happen even for different types of features that are processed within the same visual stream. Shapes and colours (both processed within the ventral stream) interfere with which other when they have to be held in visual short-term memory together or

simultaneously. This process of integration, results in a drop in short-term memory capacity as compared to retaining individual features. In line with other studies (Cowan, 2001; Luck & Vogel, 1997; Vogel et al., 2001), it was found that visual short-term memory can effectively retain information from about 3 to 4 objects with one feature each and about 2 objects composed of two features.

2.6 Leading Ideas

There are two results from the series of experiments presented here that provide background to assess the hypotheses set in other chapters of this thesis.

Features selected for this study can be represented in visual short-term memory as integrated objects and these objects can be held in this memory system in a number that resembles that reported in the literature. This finding shows that these tasks could be used to assess whether binding processes are impaired in patients with brain disorders. It is predicted that this impairment may be presented as either a loss of the ability to bind features into integrated objects in visual short-term memory or as a reduction in the capacity of this memory system for multifeature objects.

Moreover, the finding that visual short-term memory can hold 3 to 4 objects, which replicates the results of previous studies involving young volunteers, was observed in older participants. It has been suggested that age affects those processes responsible for binding in memory different sources of information (Chalfonte & Johnson, 1996). It seems possible that the form of short-term memory binding assessed in the current experiments is not affected by age.

Following on from the results of Experiment 3, in Chapter 3 the issue of age effects on memory binding will be addressed aiming at investigating in more details whether this memory function is preserved in older people. To accomplish this aim, the tasks devised for the series of experiments presented in this chapter will be used and performance of older and younger adults in these tasks will be compared.

CHAPTER 3

Age effects on short-term memory binding

3.1 Introduction

The investigation of the effect of age on short-term memory binding undertaken in this chapter was driven by four related reasons. (1): As was pointed out in Section 1.9, Alzheimer's Disease was the main brain disorder investigated in this research project. Hence, it was important to assess how short-term memory binding functions operate in the normal older brain. This was particularly important due to the fact that (2): vast literature has been delivered suggesting that age impairs in a non-material specific way those brain mechanisms responsible for representing in long-term memory the relatedness or "binding" between items (Bastin & Van der Linden, 2005; Castel & Craik, 2003; Chalfonte & Johnson, 1996; Chee et al., 2006; de Jager et al., 2002; Naveh-Benjamin, Hussain, Guez, & Bar-On, 2003; Puglisi, Park, Smith, & Hill, 1985) (see Section 1.6). (3): Less research has been carried out investigating short-term memory binding in normal ageing. However, the little literature published on this subject also points to a failure of those short-term memory binding processes responsible for processing object-location associations (Cowan et al., 2006; Mitchell et al., 2000; Mitchell et al., 2006). (4): It remains unknown whether age also impairs those brain mechanisms that subserve short-term memory binding functions which process the relation between features that are part of the same objects (e.g., shapes and colours).

This chapter presents the results of three experiments aimed at investigating memory binding in visual short-term memory in healthy older adults. The

main aim of this series of experiments was to provide empirical evidence on the efficiency of processes responsible for binding information into single objects in visual short-term memory in a sample of healthy older people. This issue was investigated when these objects were composed of multiple surface features of different types (e.g., shapes with colours) or the same type of features (e.g., colours bound into bicoloured objects). It was predicted that if age impacts on short-term memory binding processes responsible for integrating surface features into single objects in a similar manner as it does on processes responsible for binding items to their spatial locations (Cowan et al., 2006; Mitchell et al., 2000; Mitchell et al., 2006), then older people would perform worse in tasks requiring the binding in memory of shapes with colours than in tasks requiring memory for shapes or colours only.

3.2 Experiment 4

3.2.1 Aims

The aim of Experiment 4 was to investigate whether the ability to form integrated representations of shapes with colours in visual short-term memory was worse in older adults than in younger adults.

3.2.2 Methods

3.2.2.1 Participants

Twelve healthy younger adults (age: M = 21.5, SD = 1.88) and 12 older adults (age: M = 67.3, SD = 5.93) entered Experiment 4. Younger participants were undergraduate psychology students who took part for payment and older

participant were members of the Edinburgh Psychology Department panel of volunteers from the general public. The two groups did not significantly differ on estimated Verbal IQ (young adults: M = 110.7, SD = 4.81; older adults: M = 110.2, SD = 4.90; p = 0.83; t = 0.21, p = 0.835) as measured by the Wechsler Test of Adult Reading (Wechsler, 2002) and years of formal education (young adults: M = 16.8, SD = 2.40; older adults: M = 16.6, SD = 3.40; t = 0.67, p = 0.505). All participants gave their written consent to take part in the study.

3.2.2.2 Task design

The task for Experiment 4 consisted of three conditions. Two assessed visual short-term memory for single features and one assessed visual short-term memory for the binding between these features. These conditions were: memory for shape only, memory for colour only, and memory for shape-colour binding.

A full description of these experimental conditions was given in Sections 2.2.2.2 to 2.2.2.4 (Experiment 1). The only difference between the current and previous conditions is that in the colour only condition of the current experiment, colours were presented as coloured squares rather than as coloured shapes. All the other task parameters remained the same as in Experiment 1.

3.2.2.3 Procedures

All participants underwent the colour vision assessment and the perceptual test described in Section 2.4.2.1 (Appendix 2 – IA) prior to the experiment. Conditions were blocked and counterbalanced across participants. Also see

Appendix 2 – II for the instructions given to participants during the experiment.

3.2.3 Results

A two-way mixed-design ANOVA with Group (younger vs. older) as the between-subjects factor and Condition (shape only vs. colour only vs. shape-colour binding) as the within-subjects factor was carried out entering percentage of correct recognition as the dependent variable. Figure 3.1A shows mean data. A significant main effect was found for Group [$F(1,22) = 15.81$, $p < 0.001$] whereby older adults performed poorer overall. The Mauchly's Test of sphericity was found to be non significant. A significant effect of Condition was observed [$F(2,44) = 43.43$, $p < 0.001$] as well as a significant Group by Condition interaction [$F(2,44) = 3.83$, $p = 0.029$].

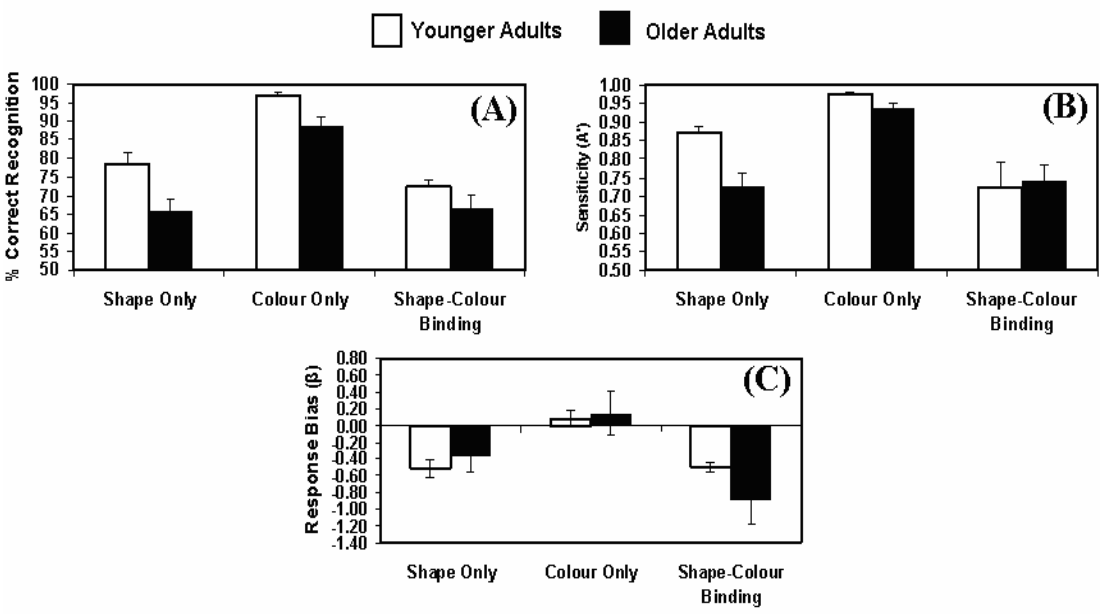

Figure 3.1. (A) Percentage of correct recognition above chance (50%), (B) Sensitivity (A') and (C) Response bias (β) for the three conditions in younger and older adults in Experiment 4. (Error bars represent the standard errors of the mean).

Post-hoc tests were carried out across Group and Condition (2 x 3 = 6 contrasts) using Bonferroni corrections with alfa set at 0.0055. The analysis across groups showed that older people performed poorer than younger adults only in the condition assessing memory for shape only [MD = 17.72, SE = 4.15, $p < 0.001$]. The analysis performed across conditions showed better performance in the condition assessing memory for colour only than in shape only [MD = 17.31, SE = 2.79, $p < 0.001$] and than in shape-colour binding [MD = 22.52, SE = 2.54, $p < 0.001$]. Performance in conditions assessing memory for shape only and shape-colour binding however, did not significantly differ [MD = 5.21, SE = 2.72 p = n.s.].

The Signal Detection Theory (see Section 2.2.2.5 for a description of this theory) was also incorporated into this analysis to investigate whether other response components mediating performance in change detection tasks such as sensitivity for the change detection (A') and response bias (beta) (Stanislaw & Todorov, 1999; Wilken & Ma, 2004) were affected by age (Figure 3.1 B and C). A' was entered into the same ANOVA model described above. Mean sensitivity data are shown in the Figure 3.1B. This analysis yielded a significant main effect of Group [$F(1,22) = 11.07$, $p < 0.01$]. Condition also resulted in a significant main effect [$F(2,44) = 24.88$, $p < 0.001$], as well as the interaction between factors [$F(2,44) = 3.50$, $p = 0.039$]. Post-hoc tests carried out across groups using the same alfa threshold showed that only shape was the contrast in which younger and older adults showed significant differences in sensitivity for change detection [MD = 0.17, SE = 0.043, $p < 0.001$]. Post-hoc tests across conditions showed better sensitivity for change detection in the condition assessing memory for colour only than in shape only [MD = 0.14, SE = 0.025, $p < 0.001$] and than in shape-colour binding [MD = 0.18, SE = 0.029, $p < 0.001$]. Sensitivity in conditions assessing memory for shape only and shape-colour binding however, did not differ [MD = 0.036, SE = 0.028, p = n.s.].

Beta was also entered in the two-way mixed-ANOVA analysis. Mean bias data are shown in the in the Figure 3.1C. This analysis showed no effect of Group [$F(1,22) = 0.20$, p = n.s]. Using the Greenhouse-Geisser correction a significant main effect was found for Condition [$F(1.6,35.20) = 16.38$, $p < 0.001$], but not for the interaction [$F(1.6,35.20) = 0.06$, p = n.s.]. Post-hoc tests across Condition showed a significantly increased tendency to respond "same" in the condition assessing memory for shape-colour binding as compared to memory for shape only [MD = 0.51, SE = 0.135, p = 0.003] and for colour only [MD = 1.07, SE = 0.199, $p < 0.001$]. Response bias in conditions assessing memory for shape or colour only did not differ.

3.2.4 Discussion

The results of Experiment 4 suggest that the effect of age on visual short-term memory for colours and shapes bound into unified objects is no greater than the overall effect of age on visual short-term memory for individual shapes or individual colours. When the two-way interaction observed in the analysis of the percentage of correct recognition was further assessed using post-hoc tests, it was observed that both groups only differed in their visual short-term memory performance for shapes. This suggests that the ability to hold bound features in visual short-term memory may be preserved in older people. The results of Experiment 4 may have implications for two main areas. One is related to the effects age on the representation format of visual short-term memory. A second one is related to the structure of visual short-term memory for single and bound information.

According to the first issue, older adults' memory for shapes bound with colours was not poorer than their memory for shapes only, although they had overall poorer memory as compared to younger adults. Therefore, from these findings it is possible to conclude that older adults' memory for bound

features is not affected to a greater extent than is their memory for the individual features. This suggests that the overall age-related drop in visual short-term memory performance is not specific to a particular representational format (i.e., features or objects).

The analysis of the Signal Detection Theory suggests that older adults were less sensitive in detecting changes occurring in shapes only than in colours only or in coloured shapes. As was discussed in Section 1.6, there are a number of factors that may affect older adults' performance during cognitive tasks such as visual complexity of stimuli or processing speed. It may be possible that the shapes and colours used in this experiment were difficult to process for older adults in 1000 msec. Shapes were abstracts and colours were difficult to name as their RGB values were changed from that of primary colours. Interestingly, when shapes and colours were bound together, older adults' sensitivity for detecting changes did not differ from that of younger adults. Hannus et al. (2006) suggested that the visual system is equipped with chromatic channels which enable processing colour information faster and additionally, they speed up the processing of non-colour information (e.g., shapes) whenever this information is bound with colours. Furthermore, Madden et al. (2004) suggested that adding colour clues may enhance perceptual discriminability in older adults when they search for conjunctions of features. This evidence may support the current findings of better sensitivity in older adults for detecting changes occurring in coloured shapes than in black shapes.

The analysis of response bias suggests that both groups were more likely to choose "same" responses when coloured shapes were presented than when shape only or colour only were shown. A similar pattern of response bias had been reported by Cowan et al. (2006) in a change detection task investigating memory for colour-location bindings. The explanation for these

findings was discussed in Sections 1.4.3 and 2.2.2.5. The fact that in the shape-colour binding condition both displays (i.e., study and test) presented the same features but in the different trials, features were rearranged in new combinations in the second display, induces a high sense of familiarity which has been described as the responsible mechanisms for this response preference observed in short-term change detection tasks (Cowan et al., 2006).

It might be argued that the lack of age effect reported here could be due to a lack of power of the method as both groups were integrated by only 12 participants. However, a power analysis performed showed that even with 50 participants per group enough power would not be encountered as to provide a reliable Group by Condition interaction (n = 50, power = 0.475). It was also found that by using the same model (2 by 3 mixed-ANOVA), if an effect size of 0.8 (a large effect size according to Cohen, 1988) would have been found for the interaction, with only 10 participants per group a Power of 86% would have been reached, suggesting that the sample size by itself does not explain the lack of interaction found in these experiments. Therefore, this analysis suggests that the results of this experiment reflect a genuine lack of age by condition interaction which would be very unlikely to appear even with a larger sample size.

According to the second issue, the results of Experiments 1-3 of Chapter 2 suggested that visual short-term memory seems to be able to retain information about multi-feature objects in an object-based format as suggested by Gajewski and Brockmole (2006) and by Luck and Vogel (1997). In the current experiment this finding was replicated and it was observed that memory for bindings of shapes with colours was not poorer than memory for shape only, suggesting that even when the number of features was doubled (i.e., the binding condition), both young and older participants

remembered as many objects as they did when they were presented with unifeature objects (e.g., shape only condition). Colour, consistently with findings of the Experiment 1-3 of Chapter 2, was the easiest feature to remember (similar to Cowan et al., 2006 and Wheeler & Treisman, 2002). Following the results of the current experiment and Experiments 1-3 of Chapter 2, it seems to be possible that less colour information is lost in this short-term memory paradigm than shape information. This explains why the success of retrieving the correct bindings seems to be more linked to successful memory for shape information than for colour information. This further supports previous suggestions which stressed that when shapes are bound with colours, memory for the shapes drive memory for the bindings (Allen et al., 2006; Wheeler & Treisman, 2002). However, as in the binding condition both the colours and the shapes are relevant to the task, participants seem to be able to retain pairs of these features integrated into single objects as well as they retain shape information, suggesting that visual short-term memory for this type of associations seems to be object-based.

In summary, the hypothesis that the ability to form integrated representations of shapes with colours in visual short-term memory would be worse in older adults than in younger adults was rejected. The results of Experiment 4 support the claim that age spares processes responsible for binding surfaces features into integrated object representations. However, Experiment 4 investigated memory for bindings of different types of information (i.e., shapes with colours). In order to investigate further this preserved ability to integrate surface features into unified objects in older adults, it would be worth assessing whether this generalizes to visual short-term memory for objects that are composed of the same type of feature. In Experiment 5 this hypothesis was addressed using a task that assesses memory for objects defined by two colours. In the visual short-term memory literature involving young adults it has been reported that immediate

memory performance for objects composed of two colours is poorer than immediate memory for objects composed of only one colour (Olson & Jiang, 2002; Wheeler & Treisman, 2002; but see Vogel et al., 2001 for a different view). However, memory for within-dimension features has never been used to assess aging and binding in visual short-term memory.

3.3 Experiment 5

3.3.1 Aims

Experiment 5 addressed two main questions. Firstly, it investigated whether age may dissociate the superior memory for unicoloured versus bicoloured objects reported in the literature in younger adults (Olson & Jiang, 2002; Wheeler & Treisman, 2002) and discussed in Sections 1.4.2 and 1.5.2 of Chapter 1. Memory for bicoloured objects has never been assessed in older people. Comparing memory performance for unicoloured objects with memory performance for bicoloured objects across participant groups allows an investigation of whether there is a specific age-related effect on memory for colour-colour bindings or whether age has a more general impact on visual short-term memory which results in a similar effect on memory for single colours and memory for bound colours.

Secondly, it was assessed whether age had an effect on the cost of remembering the precise combination of colours presented as parts of bicoloured objects. Comparing memory performance for bicoloured objects with colours bound (i.e., memory for colour association required) and unbound (i.e., memory for each colour within the objects is required but not for the association) across participant groups allows an investigation of whether there is a specific age-related effect on the cost of remembering the

precise combination of colours, that is, the binding. It was predicted that if colours are treated as surface features of bicoloured objects, the cost of holding in visual short-term memory these integrated features would be equivalent in younger and older adults.

3.3.2 Methods

3.3.2.1 Participants

Participants for Experiment 5 were 14 new young (age: M=20.7, SD=1.3) and 14 new older adults (age: M=65.9, SD=5.9). The two groups did not significantly differ in Verbal IQ (Wechsler, 2002) (young adults: M=114.2, SD=4.3; older adults: M=113.0, SD=2.0; $t = 0.99$, $p = 0.348$).

Although younger adults were slightly more educated than older adults (young adults: M = 16.3, SD = 1.38; older adults: M = 13.86, SD = 2.8; $t = 2.91$, $p = 0.007$), pilot analyses revealed that when the number of years of education was entered as a covariable, this factor did not interact with the other experimental factors. Hence, it was no longer entered in the ANOVA model. All participants gave their written consent to take part in the study.

3.3.2.2 Stimuli and Apparatus

Stimuli for this task were constructed using the object shapes shown in Figure 2.1C. Arrays of three stimuli were presented to participants using the design described below. The other stimuli parameters were the same as presented in Section 2.2.2.2.

3.3.2.3 Task design

Three different experimental conditions were devised for this task which was based on the change detection paradigm (the sequence for each trial was the same as that described in Section 2.2.2.3 with the only exception that the study display for the current task was presented for 2000 msec). One condition assessed memory for colours only and two conditions assessed memory for bicoloured objects. Of these last two, one was the same as that presented in Experiment 1 (Section 2.2.2.3 - Memory for colour-colour binding). This condition required the retention in memory of colours and their association within objects. The other condition required the retention in memory of colours but not the association between them (i.e., Colours unbound) (Figure 3.2). These conditions are explained in more detail below.

Memory for colour only: In this condition the figure area of each object displayed a different colour and the ground area remained black for all. In the different trials two colours in the test display were replaced by two new colours not presented in the study display.

Memory for colours unbound: In this condition the figure and the ground area of each pattern display a different colour. Participants were instructed to remember the colours presented in the study display without making any association between them. In the test display one colour of two objects either from the figure or ground area was replaced by a new colour. To detect this change the binding between colours was not required. Firstly, participants were explicitly instructed not to make any association between colours. Secondly, because in different trials new colours were presented in the test display, this pop-out stimulus did not require memory for the association in order to be detected.

Memory for colour-colour binding: In this condition the figure and the ground area of each pattern displayed a different colour. Participants were requested to remember the association of colours within each object. In the different trials either the figure or the ground colour of two objects swapped in the test display. To detect this change the memory for the binding was required. Participants were explicitly instructed to remember the association between colours within objects. They were also told that colours within both displays would be the same but in some occasions colours would be rearranged in different combinations in the test display. Therefore, participants must remember how colours were initially bound in order to detect the change.

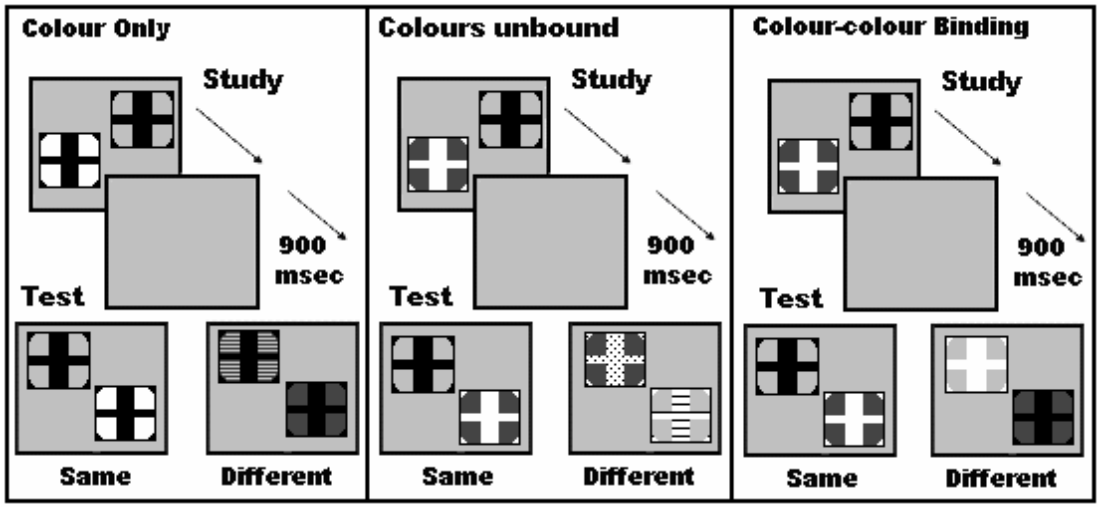

Figure 3.2. Experimental conditions and trial sequence used in Experiment 5. The actual array size was three for each experimental condition.

It is worth noticing that conditions exploring memory for unbound colours and colour-colour binding presented participants with the same type and amount of information. However, in the condition assessing memory for colour-colour binding additional memory was required to retain the relatedness between colours within objects. This methodology allowed the investigation of whether remembering this additional piece of information

about how features combine imposed an additional cost to memory and whether this cost differ between healthy younger and older participants.

3.3.2.4 Procedures

The same procedures described in Experiment 4 were followed in this experiment. The perceptual task used in this new experiment was similar to that described in Experiment 3 (see Appendix 2 – IB). The difference was that in the current task items were the object shapes used in this experiment rather than the coloured shapes used in experiments 3 and 4. In the different trials two objects either from the upper or lower half swapped one colour which could be from the figure area (50%) or from the ground area (50%). The other parameters of the perceptual task remained the same. The experimental conditions were blocked and fully counterbalanced across participants. For each condition 32 trials were presented. The different and same trials were randomly presented within each block. In the Appendix 2 – II the instructions given to participants before the task are presented.

3.3.3 Results

The percentage of correct recognition in the change detection tasks was analysed with a two-way mixed-design ANOVA with Group (young vs. older) as between-subjects factor and Condition (colour only vs. colours unbound vs. colour-colour binding) as the within-subjects factor. The mean data for each condition are shown in the Figure 3.3. The analysis yielded a significant effect of Group whereby older adults showed poorer memory performance overall [$F(1,26) = 7.12$, $p = 0.013$]. A significant main effect was also found for the type of experimental condition [$F(2,52) = 39.40$, $p < 0.001$]. No interaction of Group by Condition was found [$F(2,52) = 0.56$, p = n.s.].

Pairwise comparisons carried out using Bonferroni corrections showed that performance in the colour only condition was significantly better than performance in the unbound colours condition [MD = 10.71, SE = 1.6, p <0.001], and than performance in the colour-colour binding condition [MD = 16.97, SE = 1.78, p < 0.001]. Memory for unbound colours was significantly better than memory for colour-colour binding [MD = 6.25, SE = 2.34, p = 0.039] (Figure 3.3A).

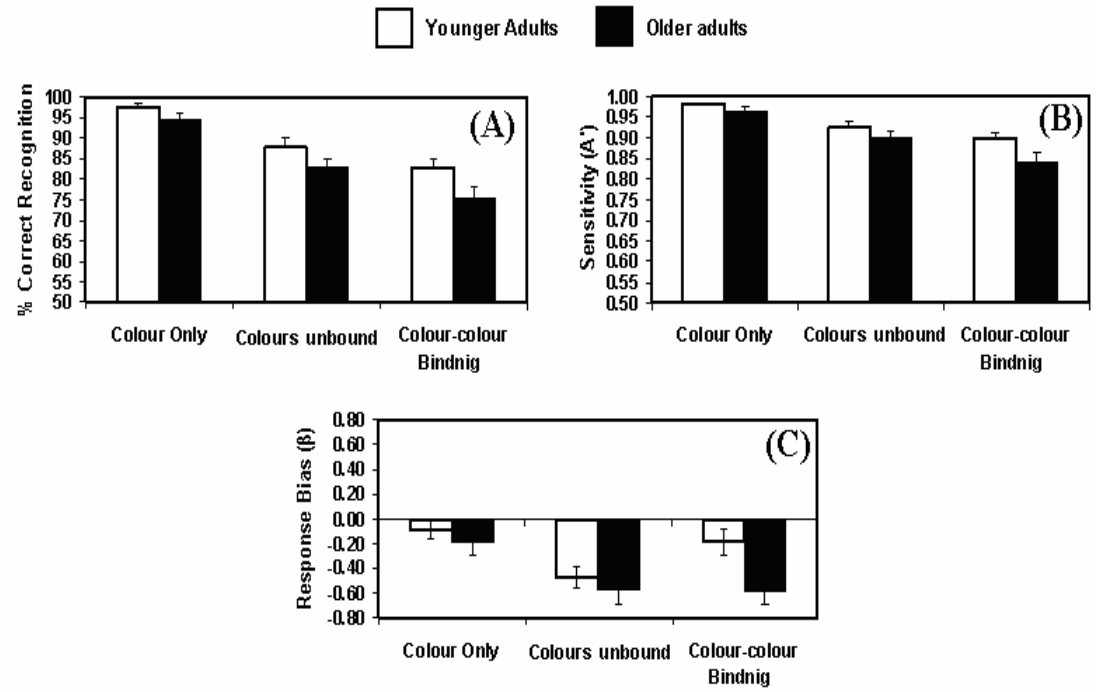

Figure 3.3. (A) Percentage of correct recognition above chance (50%), (B) Sensitivity (A'), and (C) Response bias (β) for the three conditions in young and older adults in Experiment 5. (Error bars represent the standard errors of the mean).

The analysis of A' (Figure 3.3B) yielded a significant effect of Group [$F(1,26) = 5.78$, $p = 0.024$], reflecting an overall poorer sensitivity in older adults. After applying the Greenhouse-Geisser correction, the type of experimental condition also resulted in a significant effect [$F(1.4,36.46) = 20.34$, $p < 0.001$]. No Group by Condition interaction was found in this analysis [$F(1.4,36.46) =$

0.77, p = n.s.]. Pairwise comparisons carried out using Bonferroni corrections showed that sensitivity for detecting changes in the colour only condition was significantly higher than for colours unbound condition [MD = 0.06, SE = 0.01, p <0.001] and than for colour-colour binding condition [MD = 0.11, SE = 0.02, p <0.001]. Sensitivity for colours unbound and colour-colour binding did not differ [MD = 0.04, SE = 0.2, p = n.s.].

For Beta the analysis yielded no effect of Group [$F(1,26) = 2.62$, p = n.s.], a significant main effect of the type of experimental condition [$F(1,52) = 5.99$, p = 0.005]. No Group by Condition interaction was found in this analysis [$F(1,52) = 1.64$, p = n.s.]. Pairwise comparisons across conditions showed that bias toward "same" response in the colours unbound condition was significantly greater than in the colour only condition [MD = 0.52, SE = 0.15, p = 0.007] but not than in the colour-colour binding condition [MD = 0.26, SE = 0.16, p = n.s.]. Biased responses during conditions assessing memory for colour only and colour-colour binding did not differ [MD = 0.26, SE = 0.14, p = n.s.].

3.3.4 Discussion

As in Experiment 4, the results of Experiment 5 have implications for both the current debate on the structure of visual short-term memory for objects and features and the effect of age on memory binding. Concerning the first point, the results of the Experiment 5 suggest that memory for objects composed of two colours seems to be driven by the number of colours rather than by the number of objects. If colours were integrated in visual short-term memory into single units with no additional cost, as was suggested by Luck and Vogel (1997), one would not expect to find a drop in performance associated with an increased number of colours whenever these colours were bound into a number of objects that does not exceed the capacity of this

memory system. For example, Vogel et al. (2001) found that young volunteers could remember equally well four objects defined by one feature each (e.g., colours) or four objects defined by four features each (e.g., colour, orientation, size, and a black gap). As the results presented here suggest, this does not seem to be the case for combinations of colours; increasing the number of colours bound within a fixed number of objects resulted in a drop in memory performance. Additionally, the results of the comparison of the conditions assessing memory for bound and unbound colours (both conditions presented the same number of objects and colours) suggest that the way colours are combined within objects seems to be an additional piece of information to-be-remembered.

Concerning the second point, the additional cost of remembering bicoloured objects as compared to unicoloured objects seems to be independent of age. The analysis of the Signal Detection Theory suggests that older adults' sensitivity to detect changes did not vary differentially across experimental conditions. The response "same" was more frequently chosen in the unbound colours condition than in colour only but this did not differ across groups. In the colour-colour binding condition however, response bias was not more pronounced than in colour only or unbound colours conditions. Despite the Group by Condition interaction not being significant for this variable, Figure 3.3C shows that in the colour-colour binding condition older but not younger adults had more tendency to choose the response "same". Hence, the remarkable tendency to report "no change" in change detection tasks reported in Experiment 4 as well as by other authors (Cowan et al., 2006), seems also to apply when bindings comprise the same type of feature.

The results of Experiment 5 confirmed previous findings suggesting that remembering bicoloured objects is a more demanding task than remembering unicoloured objects. These results also suggest that memory

for multi-coloured objects is determined by the number of colours that visual short-term memory can retain and this is true for both young and older participants. Finally we found that age does not have a differential effect on each of the above manipulations but that there is an overall effect of age on memory performance.

Although performance levels in Experiment 5 were below ceiling, they were still high, particularly in the colour only condition. It might be possible that remembering 3 objects that were presented for 2000 msec resulted in a task that was not sufficiently demanding to be sensitive to the effects of age. In Experiment 6 these task parameters were modified in order to mirror the design used in Experiment 4. The number of objects in each array was increased to 4 and the presentation time reduced by half. As a result, the only difference between Experiment 6 and Experiment 4 is the use of colour-colour binding rather than colour-shape binding. By increasing task demands it is not predicted that there will be any change in the overall pattern found in Experiment 5 that is, that visual short-term memory for colour-colour binding would be poorer than memory for individual or unbound colours.

However, the increased demand on speed of processing should make the tasks more sensitive to any possible effects of ageing on binding colours in short-term memory. This follows on from the idea discussed in Chapter 1 (Section 1.6) about the impact of increased task demands in terms of processing speed or increased cognitive load either in perception or memory on older adults' performance.

3.4 Experiment 6

3.4.1 Aims

To investigate whether under increased cognitive demands as imposed by short presentation time and increased memory load, the lack of age effects on visual short-term memory for bindings comprising the same type of feature observed in the Experiment 5 could be replicated.

3.4.2 Methods

3.4.2.1 Participants

Participants entering Experiment 6 were 12 new young (age: M = 21.5, SD = 1.9) and 12 new older adults (age: M = 67.3, SD = 5.9) none of whom took part in Experiment 5. The groups did not significantly differ in verbal IQ (young adults: M = 110.7, SD = 4.8; older adults: M = 110.3, SD = 4.9; t = 0.21, p = 0.835) and years of education (young adults: M = 16.83, SD = 2.4; older adults: M = 15.83, SD = 4.9; t = 0.67, p = 0.505). All participants gave their informed consent to take part in this study.

3.4.2.2 Task Design

The task for Experiment 6 was the same one used in Experiment 5. The only difference was that in Experiment 6 the arrays consisted of 4 rather than 3 objects and the study display was presented for 1000 msec rather than 2000 msec. The procedures were also as described for Experiment 5.

3.4.3 Results

Performance in the change detection tasks was analysed with the same ANOVA model described in Experiment 5. Mean performance is shown in Figure 3.4. When percentage of correct recognition was analyzed, this yielded no effect of Group [$F(1,22) = 3.78$, p = n.s.]. A significant main effect was found for the type of experimental condition [$F(2,44) = 72.49$, $p < 0.001$]. No Group by Condition interaction was found [$F(2,44) = 0.21$, p = n.s.]. Pairwaise comparisons across conditions showed that performance in the colour only condition was significantly better than performance in the colours unbound condition [MD = 10.29, SE = 1.83, $p < 0.001$], and than performance in the colour-colour binding condition [MD = 24.60, SE = 2.06, $p < 0.001$]. Memory performance for colours unbound was significantly better than memory performance for colour-colour binding [MD = 14.31, SE = 2.25, $p < 0.001$] (Figure 3.4A).

The analysis of A' (Figure 3.4B) yielded no effect of Group [$F(1,22) = 2.66$, p = 0.117.]. After applying the Greenhouse-Geisser correction factor a significant effect of the type of experimental condition was found [$F(1.56,34.44) = 52.60$, $p < 0.001$]. There was no Group by Condition interaction [$F(1.56,34.44) = 0.187$, p = n.s.]. Pairwise comparisons across conditions showed that sensitivity in the colour only condition was significantly higher than in the colours unbound condition [MD = 0.07, SE = 0.01, $p < 0.001$], and than sensitivity in the colour-colour binding condition [MD = 0.21, SE = 0.02, $p < 0.001$]. Sensitivity for colours unbound was significantly higher than for colour-colour binding [MD = 0.13, SE = 0.02, $p < 0.001$].

For Beta (Figure 3.4C) it was observed that bias toward "same" response was more pronounced for the three conditions in both younger and older adults however the analysis yielded no effect of Group [$F(1,22) = 0.005$, p = n.s.], no

effect of the type of experimental condition [$F(2,44) = 1.27$, p = n.s.], and no interaction between these factors [$F(2,44) = 0.658$, p = n.s.].

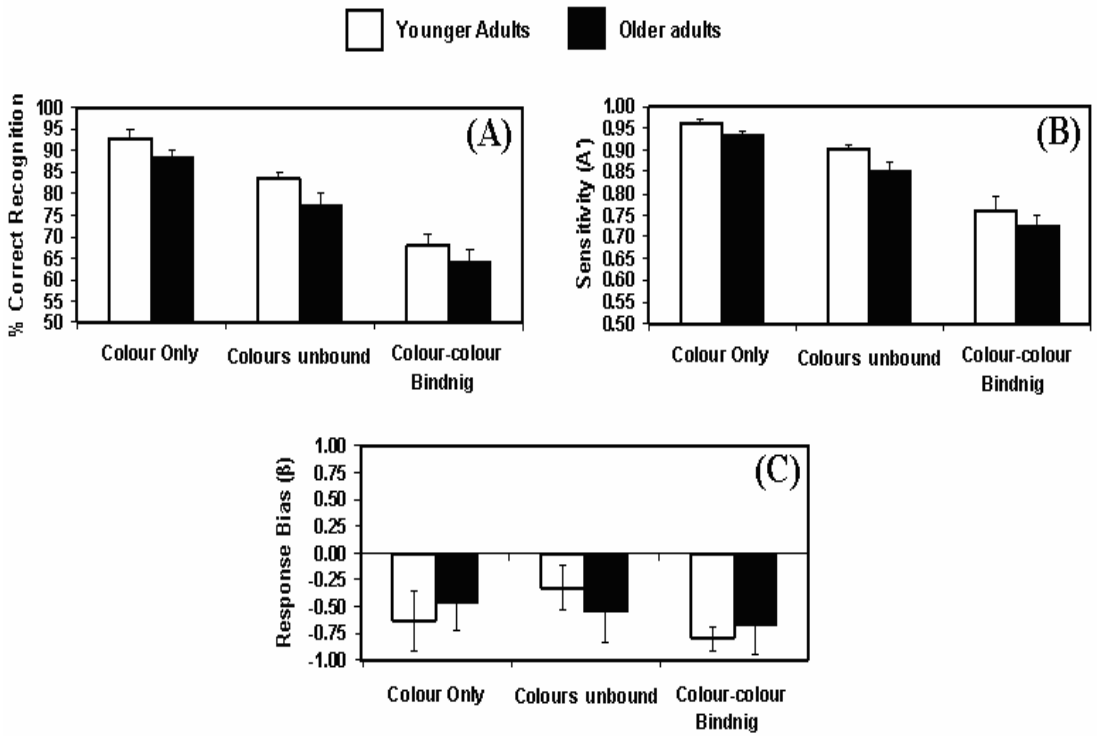

Figure 3.4. (A) Percentage of correct recognition above chance (50%), (B) Sensitivity (A′), and (C) Response bias (β) for the three conditions in young and older adults in Experiment 6. (Error bars represent the standard errors of the mean).

3.4.4 Discussion

Using the task parameters of Experiment 4 the findings of Experiment 5 were replicated in Experiment 6. When the task was made more cognitively demanding, age did not interact with condition indicating that there was no age-related differential effect on visual short-term memory for bound vs. unbound or single colours. However, there was an overall cost of binding for both older and younger groups. The analysis of the Signal Detection Theory suggested that neither the sensitivity for change detection nor the response

bias could add any new evidence above that found when the percentage or correct recognition was analyzed.

3.5 General Discussion

The results of the series of experiments presented here suggest that there is no evidence for an age-related effect on binding over and above the general age-related effect on visual short-term memory. This is in striking contrast to the age-related effect on forming novel associations in long-term memory found in previous studies. Indeed the previous studies have indicated further that age differentially impairs long-term representations of bound features compared with single features regardless of the nature of the information to-be-bound (Chalfonte & Johnson, 1996; Mitchell et al., 2000; Naveh-Benjamin, 2000; Naveh-Benjamin et al., 2004). The results of Experiments 4-6 suggest that the lack of an age-related effect specifically on binding in visual short-term memory applies to binding between (i.e., shape with colour) and within-dimension (i.e., colour with colour) features.

From previous studies reviewed earlier (see Section 1.6), in long-term memory the effect of age on memory binding seems not to be material specific. In contrast, within visual short-term memory ageing seems to affect the processes responsible for binding to location while sparing processes that associate multiple surface features into integrated objects. One exception to this age-related short-term memory binding deficit when location information is involved is that reported by Olson et al. (2004) (see Section 1.6). However, as was discussed in Chapter 1 (Section 1.6), in Olson et al.'s Experiment 1, locations yielded to configural representations what may have rendered this task less reliant on spatial memory and more dependent on object memory. This suggests that whenever the bound information held in

visual short-term memory yields to object identity, this integrative process would be accomplished by older people without difficulties. In sum, the experiments reported here suggest that ageing does not have a differential effect on holding in visual short-term memory combinations of shapes with colours or colours integrated within bicoloured objects as compared to memory for the individual features.

How to reconcile these finding with previous reports in the literature on short-term memory and age?

Two publications have suggested that older adults have difficulties in holding associations between objects and their locations in visual short-term memory (Cowan et al., 2006; Mitchell et al., 2000). In the current experiments it was observed that holding in visual short-term memory shapes bound with colours or bicoloured objects was not impaired in older adults more than holding shapes only or colours only. These results suggest that binding deficits cannot be generalized in older adults, which is a suggestion that limits the scope of the Age-Related Associative Memory Deficit Hypothesis proposed by Naveh-Benjamin (2000). Taking together the current and previous findings, it may be concluded that age affects the processes responsible for binding information in long-term memory regardless of the type of information however, in visual short-term memory, age affects the binding of items to location while it spares the binding of surface features that may help to identify complex objects (i.e., shapes and colours, colours into bicoloured shapes, or locations into configural patterns as shown by Olson et al., 2004). One possible explanation for the dissociation observed in visual short-term memory may be that while combinations of shape and colour are features that define the identity of complex objects, objects and locations do not (Cave & Pashler, 1995; Owen, Milner, Petrides, & Evans, 1996; Treisman & Zhang, 2006). According to this view it may be argued that

ageing does not impair those processes responsible for holding in visual short-term memory bindings of features that are the basis for object identification. For example, while combinations of objects and locations or colours and locations do not define the identity of colours or objects (as a location is an entity independent from the object and both are processed by different visual systems) shapes and colours are features once bound together may identify one object. Stimuli used in this series of experiments possess gestalt principles (e.g., closure, figure and ground) as well as physical properties (e.g., angles and sides) that make each object shape look different from other object shapes in the experiment, a role that location cannot play (Kohler, 1967; Owen et al., 1996; Treisman & Zhang, 2006) (see Sections 1.2.2 to 1.2.4 where the temporal synchronicity elicited by these gestalt principles was discussed).

A functional account for this discrepancy may be that age-related compensatory changes supporting visual short-term memory functions which enable the integration of features that identify objects are more efficient than those changes supporting the representation of bound features that do not identify objects such as location (Grady, McIntosh, & Craik, 2003; Schiavetto, Kohler, Grady, Winocur, & Moscovitch, 2002). Functional reorganization within the ventral stream has been found in older adults while they perform tasks assessing intra-item binding (e.g., face matching) (Grady, 1998; Owen, 1997) whereas they have shown poor frontal activation during short-term memory tasks assessing intentional encoding of item-location binding (Mitchell et al., 2000; Mitchell et al., 2006). This may help to explain why short-term binding of item-location information is impaired in old age while the intra-item binding of features that identify objects is not. This discrepancy does not seem to be due to methodological differences across studies as difficulties in short-term binding of item-location have been observed in older adults using sequential (Mitchell et al., 2000; Mitchell et al.,

2006) or simultaneous presentation (Cowan et al., 2006), common objects, words (Mitchell et al., 2000; Mitchell et al., 2006), or colours (Cowan et al., 2006), retention intervals of 1 sec (Cowan et al., 2006; Mitchell et al., 2006) or 8 seconds (Mitchell et al., 2000), single (Cowan et al., 2006) or whole display probes (Chalfonte & Johnson, 1996), change detection (Cowan et al., 2006) or forced-choice recognition tasks (Chalfonte & Johnson, 1996; Mitchell et al., 2006). On the other hand, the lack of age-effects on visual short-term memory binding reported here have been observed using change detection (Experiment 4) or recall tasks (Brockmole, Parra, Della Sala, & Logie, 2008), delays of 900 msec or 5 sec (Experiment 4 and Brockmole et al., 2008), single or whole display probes (Brockmole et al., 2008). This consistency across task designs supports the claim that intra-item binding in visual short-term memory of features that identify objects seems to be a process unaffected by age.

Therefore, remembering the binding of item with location and remembering the binding of shapes with colours may reflect the operations of different cognitive mechanisms (Cave & Pashler, 1995; Owen et al., 1996; Treisman & Zhang, 2006). Moreover, these mechanisms may operate differently in short-term and long-term memory (Piekema et al., 2006; Treisman & Zhang, 2006), and their vulnerability to the effect of age may also differ (Chalfonte & Johnson, 1996; Cowan et al., 2006).

Although the absence of an age-related impact on binding in visual short-term memory was observed for objects comprising different types of features (Experiment 4) as well as the same feature type (Experiments 5 and 6), one aspect of these experiments was not entirely consistent. Using combinations of colours, it was found that performance was poorer in memory for bound colours than for unbound colours or single colours. Using shapes and colours presented as individual features or as combined features (Experiment 4) it

was found that both young and older adults remembered single features (i.e., shapes) no better than combined features (i.e., coloured shapes).

A possible account for the difference between the results of Experiment 4 (also of Experiments 1 and 2 involving young adults) and the results of Experiments 5 and 6 may stem from the nature of the information presented. Objects constructed for Experiments 5 and 6 were defined by a figure and a ground area. Within each trial, the figure and ground area of each object was the same but differed in colour. It might be argued that the mere fact that the figure occluded the ground area does not necessarily imply that they both would be treated as a single object but they may be rather processed as independent objects sharing the same visual space (e.g., perceiving a red cross over a yellow square rather than a red and yellow flag-like pattern). If this were the case, the cost of holding these bicoloured objects would not be reflecting a different representational format of visual short-term memory but rather an extra capacity required to retain two integrated objects, each of which involves a combination of a colour and a shape (i.e., figure + colour and ground + colour). Participants in the Wheeler and Treisman (2002) studies reported that they had remembered the inside and outside of bicoloured squares not as parts of one unit but as two separate entities.

One reason why this might not offer a full account is that a difference was found between performance in the colours unbound and colour-colour binding conditions, and for both of these conditions, there could be changes to the background or to the foreground colours. Moreover, there was no change of shape between the study and test displays as occurred in Experiment 4. This suggests that differences observed between the results of Experiment 4 and Experiments 5 and 6 may well be because the last ones examined within feature combinations, while the first one used between feature combinations. However, the main focus in the present series of

experiments was on the impact of ageing, so this additional question regarding between or within feature bindings would be an interesting development for future studies.

In conclusion, the evidence here suggests that the age effect on memory for the relationship between features in multi-feature arrays depends on whether the material has to be held over brief periods of time or is the basis for forming longer term associations. The different patterns of results found in these experiments and in previous studies of age in forming associations, also points to the use of separate components of the cognitive system for temporary visual storage (visual short-term memory) and for long-term storage (long-term memory) of individual features and feature bindings. The results of these experiments suggest that older adults have a preserved ability to form temporary bindings between features in visual short-term memory for bound features that define the identity of complex objects.

3.6 Leading Ideas

The evidence that age exerts a differential impact on short-term memory as compared to long-term memory represents a novel finding resulting from the series of experiments presented in this chapter. The literature on age and long-term binding points to an age-related decline of this function in older adults, however as it was demonstrated in the experiments presented here, this cannot be generalized to all memory systems or to all types of information. These findings fit well with the set of evidence discussed in the Chapter 1 about memory for different types of bindings being subserved by different processes (Sections 1.4.2 and 1.5.2). These suggestions were assessed in Chapter 2 involving younger adults and now were thoroughly investigated in older people. Additionally, results of experiments presented

in this chapter support the hypothesis that holding bound information in short- and long-term memory are functions subserved by separate mechanisms. It seems to be possible that visual short-term memory for arbitrary or unfamiliar features (e.g., abstract shapes and colours) operates independently from long-term memory processes responsible for holding other forms of familiar or meaningful associations (see Section 1.5.5). The results of experiments presented in this chapter support this view as the impairment observed in older adults' long-term memory for bound information was not replicated in these short-term memory experiments.

However, this thesis aims at investigating the mechanisms responsible for binding information in short-term memory, particularly in visual short-term memory. The fact that these processes are less vulnerable to the effects of age than other forms of associative memory is relevant to the aims of this project. In the next chapter I will present the results of a series of experiments which investigated how binding in short-term memory can be impaired after brain damage. As was discussed in Chapter 1, it is still unclear how bound information is held in short-term memory (Baddeley, 2000). The fact that young and older people can retain bound features no differently than individual features will serve as the basis for comparing performance of healthy individuals with brain damage patients. It is predicted that this would increase our understanding of this function in both brain pathology and in the intact brain.

CHAPTER 4

Selective impairment in binding in visual short-term memory: evidence from a single case

4.1 Introduction

This chapter presents a series of studies carried out to investigate visual short-term memory binding functions in a brain damaged individual. More specifically, the series of experiments presented here were aimed at providing evidence that short-term memory is equipped with relatively independent mechanisms to processes integrated objects and individual features.

Why should we think that there are separate brain mechanisms to process features and objects?

1. When words are bound into sentences, the capacity of verbal short-term memory is considerably boosted (Baddeley, 2007e; Baddeley et al., 1998; Burtis, 1982; Cowan, 2001; Cowan & Chen, 2009; Gobet et al., 2001; Gobet & Clarkson, 2004; Miller, 1956) (see also Sections 1.5.3 and 1.5.4.2). This suggests that individual words and semantic units formed by these words are either processed by separate mechanisms or that they use different brain resources.

2. There is evidence for an Episodic Buffer responsible for processing complex and perhaps multimodal information (Baddeley, 2000; 2007b; e) which can also be visual in nature (Allen et al., 2006) (see Sections

1.4.2 and 1.5.1.1). The introduction of the Episodic Buffer to the working memory model represents an attempt to account for the retention in working memory of units of information other than single items which could not be accounted for by the initial model proposed in 1974. This suggests that working memory needs separate mechanisms to deal with these single items and complex information.

3. Two propositions have driven the research work within visual short-term memory. These are the object-based (Luck & Vogel, 1997; Vogel et al., 2001) and feature-based (Olson & Jiang, 2002; Wheeler & Treisman, 2002) hypotheses of visual short-term memory. Taken together these hypotheses suggest that features and objects may be represented in memory via different mechanisms (see Sections 1.4.2 and 1.5.2).

4. There are neuroimaging data suggesting a differential brain activation (i.e., in both intensity and brain regions) when integrated objects or individual features are held in working memory (Prabhakaran et al., 2000) (see Section 1.5.2.1 for a review of this research).

According to behavioural and neuroimaging evidence, it would be reasonable to think that binding functions may be selectively impaired after damage to specific brain regions. In fact, in the neuropsychology literature there are reports of patients with impairments in perceptual grouping after focal brain damage. For example, Ward, Danziger, Owen, and Rafal (2002) reported the patient TN, who had selective damage to the right posterior thalamus. TN made significantly more illusory conjunctions (misattribution of colour-shape combinations) when coloured letters (e.g., red Xs and green Os) were presented in the lower quadrant of the contralesional visual field. Friedman-Hill et al. (1995) also reported a high rate of illusory conjunctions

in RM, a patient with symmetrical-bilateral parieto-occipital lesions. Humphreys, Cinel, Wolfe, Olson, and Klempen (2000) reported the patient GK who after a parietal damage showed perceptual deficits for binding shapes with colours in the visual system (see Humphreys, 2003 for a review on different forms of binding deficits in neuropsychological patients).

There has been however no report of patients with selective impairment in binding information in short-term memory. This chapter presents the report of a single case who shows dissociation within binding in short-term memory. The deficits shown by this case reveal some functional properties of short-term memory not described to date which may shed light into still controversial areas such as those dealing with the structure and function of short-term memory when it comes to binding operations. Among these areas, the unit of capacity of short-term memory (i.e., objects or features), the representational format of short-term memory (i.e., object-based or feature-based), and the functional relationships across memory domains (i.e., short-term and long-term memory) are some to which this chapter would make valuable contributions.

4.2 The case ES

ES was examined for the first time in September 2006. She was a member of the Edinburgh Psychology Department panel of volunteers from the general public who had been invited to take part in the Experiment 4 of this thesis as a healthy older volunteer. However, after a few trials of the experiment it was clear that she was having great difficulty holding the bindings of features in visual short-term memory compared to her visual short-term memory for single features. This pattern was quite unlike other participants in that experiment. After arriving for the experiment she mentioned having

had neurosurgery in 2001 which was for a left medial sphenoid ridge meningioma. At the time of this first test session, she reported herself free of symptoms and she had noticed no memory difficulties after the surgery. She was then invited to take part in a single case study to assess her visual short-term memory for binding.

In the initial assessment ES showed paramount difficulties in holding in visual short-term memory bound information as compared to her visual short-term memory for single features. The results of this assessment will be presented here as Experiment 7. After these initial findings ES was invited to take part in a more thorough assessment. A set of 15 new experiments was devised to explore ES's short-term memory across verbal and visual domains, across recall and recognition, across auditory and visual modalities, and across types of information (i.e., features and objects) (see Appendix 3 for a diagrammatic representation of experiments devised to assess ES). Here the results of five of these experiments (Experiments 8 to 12) are presented. ES was also assessed using an extensive neuropsychological battery. Her general and specific assessments will be presented here following the structure of a single case study. This would allow the suggestions about the specific impairment observed in ES to be more cogent. Initially, I will present a brief summary of her clinical history. Then I will show the results of the neuropsychological assessment. Finally, I will present the results of the specific short-term memory assessment through six experiments.

4.2.1 Case history

ES is a right handed lady who completed 9 years of formal education and by the time of the initial assessment (2006) she was 69 years old. In 2001 ES

underwent an elective craniotomy and a complete removal of the left medial sphenoid ridge meningioma was achieved. A follow-up MRI scan 3 months after surgery is shown in Figure 4.1.

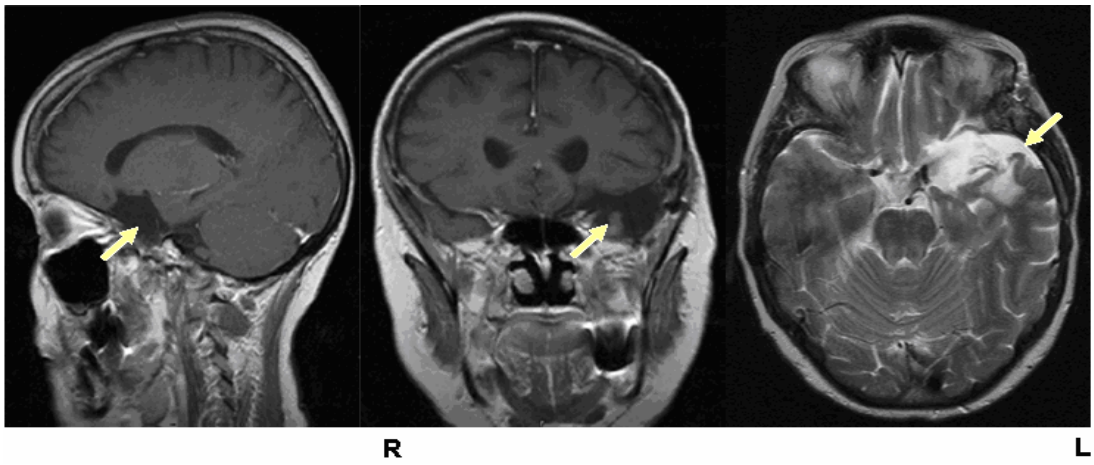

Figure 4.1. ES's 3 month follow-up MRI scan. Arrows indicate the area of resection and oedema.

ES was assessed five years post-surgery. Her colour vision was normal (15/15) using the Colour Blindness Test (Dvorine, 1963).

4.2.2 Neuropsychological assessment

Table 4.1. Results of the neuropsychological assessment of ES.

	ES	**Cut-off scores from norms**
MMSE	28	< 23
ACE	91	< 85
VIQ (WTAR)	98	107.5 (5.06) [a]
Laterality Quotient (Handedness)	80	-100 left / 100 right
Logical Memory		
Immediate Recall	41	37 – 39 [b]

Table 4.1. Contd.

	ES	Cut-off scores from norms
Delayed Recall	30	20 – 22 [b]
Percentage Retention	96.7	78 – 83 [b]
Doors and People Test		
Overall Score	10	9.2(3.4) [a]
Verbal Recall	12	8.9(2.9) [a]
Verbal Recognition	8	9.7(3.4) [a]
Nonverbal Recall	9	10.1(4.5) [a]
Nonverbal Recognition	11	9.1(3.4) [a]
Visual-Verbal Discrepancy	10	10.2(2.2) [a]
Recall-Recognition Discrepancy	10	10.1(2.7) [a]
Rey-Osterrieth Complex Figure		
Copy	33	34.2 (10.8) [a]
Recall	14	18.6 (6) [a]
Ruff 2 & 7 Selective Attention test		
Speed Differences	3	7.08 – 9.30 [b]
Accuracy Difference	4	10.00 - 13.99 [b]
Total Difference	1	5.43 – 7.70 [b]
TMT-A	35	39.14 (11.84) [a]
TMT-B	116	91.32 (28.89) [a]
WCST		
Categories	3	≤ 2 [b]
Perseverations	9	≥ 6.41 [b]
Hayling & Brixton Test		
Spatial Anticipation test	6	Average [b]
Word Fluency Tests		
FAS – Total	40	29.6 (9.4) [a]
Category Fluency – Animals	20	15 (4.3) [a]

Table 4.1. Contd.

	ES	Cut-off scores from norms
Visual Pattern Span	9.8	9.2 (2.25) [a]
VOSP		
Incomplete Letters	19	< 16 [b]
Object Decision	18	< 14 [b]
Dot Counting	10	< 8 [b]
Position Discrimination	20	< 18 [b]

a: mean and SD taken from standardised age matched normative data; b: 50th percentile taken from standardised age matched normative data. MMSE: Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975). The cut-off value presented is internationally accepted as the lowest score indicative of normal cognitive profile; ACE: Addenbrooke's Cognitive Examination. The cut-off score represents the control mean minus 2 SD for an age range of 50-69 and education = 12.9 (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006). VIQ: Verbal Intelligence Quotient as measured by the Wechsler Test of Adult Reading (WTAR) (Wechsler, 2002); Laterality Quotient as measured by the Edinburgh Handedness Inventory (Oldfield, 1971); Logical Memory (The Psychological Corporation, 1998); Doors and People Test (Baddeley, Emslie, & Emslie, 1994); Rey-Osterrieth Complex Figure ((Osterrieth, 1944; Rey, 1941); Ruff 2 & 7 Selective Attention test (Ruff & Allen, 1996). Cut-off scores represent the confidence interval at 95% of the normal population (see also Messinis, Kosmidis, Tsakona, Georgiou, Aretouli, & Papathanasopoulos, 2007); TMT = Trail Making Test (Reitan RM., 1958); WCST: Wisconsin Card Sorting Test, modified version of (Berg, 1948) (48 cards); Hayling & Brixton Test: (see Burgess & Shallice, 1997); Word Fluency Tests form Control Oral Word Association Test - FAS (Sumerall, Timmons, James, Ewing, & Oehlert, 1997); Category Fluency – Animals; Visual Pattern Span (VPT) (Della Sala, Gray, Baddeley, Allamano, & Wilson, 1999); Visual Object and Space Perception (VOSP) Battery (Warrington & James, 1991).

As can be seen from Table 4.1, ES performed within normal ranges in an extensive neuropsychological battery**.** Her memory functions including the recall and recognition of verbal and nonverbal material (Logical Memory Test, Doors and People Tests, Rey Osterreith Figure) was intact. She performed well in attention tasks (2 & 7 Ruff Selective Attention Task and Trail Making Test part A and B). On tests of executive functions she reached a number of categories within the normal limits on the Wisconsin Card

Sorting Test although she scored above the normal cut-off score for the number of perseverations. However she performed within the normal range in the Hayling and Brixton Test and Word Fluency Tests. Visual and perceptual functions as measured by the Visual Object and Space Perception Battery and copy of the Rey Osterreith Figure showed no impairment. Of note her performance on the Visual Patterns Test was unimpaired, indicating intact visuospatial span. It is worth noticing that some of these tasks although not devised to assess memory binding operations, do require integrity of these functions in order to be performed within the expected standard. For example in the Visual Reproduction Test (see Appendix 4 for examples of the designs used in this test) participants are presented with different designs made of combinations of lines in different sizes and orientations. Similarly occurs with the Rey's Figure. In order to make accurate representations of these items in memory, different pieces of information should be bound together. In the case for the Doors and People Test, participants should remember associations of faces and professions, several details of different doors, and other stimuli which also require binding operations in memory. Hence, the results of the neuropsychological assessment also suggest that these long-term memory binding operations are preserved in ES.

4.3 Experiment 7

4.3.1 Aims

Experiment 7 investigated short-term memory binding and more specifically short-term memory for bound information (i.e., objects) as compared with short-term memory for single information (i.e., features) in ES and a group of controls.

4.3.2 Methods

4.3.2.1 Participants

ES and eight controls entered this experiment. They did not significantly differ in age (M = 69.0, SD = 8.3; t = 0, p = n.s.), education (M = 12.1, SD = 2.2; t = -0.90, p = n.s.), or VIQ (M and SD in Table 1; t = -1.77, p = n.s.). All participants gave their signed consent to take part in this study.

4.3.2.2 Task design

The task used in this experiment was the same task described in Experiment 4. For the current experiment, two different set sizes were used. Arrays could display either 2 or 4 items. For each array size 32 trials were presented being 50% "different" trials and 50% "same" trials. Another difference between the current experiment and Experiment 4 is that in the current experiment the study display was presented for 2000 msec. All other task parameters remained unmodified.

4.3.2.3 Statistical Analysis

The statistical analysis was based on that devised by Crawford and Garthwaite (2002) to investigate neuropsychological impairments in single case studies. As the main aim of the present study was to investigate differential impairment in memory for complex objects as compared to memory for single features, this methodology was adjusted to fit with this aim. ES's memory performance for objects and individual features was first compared to that of healthy controls. Then it was investigated whether the discrepancy between memory for objects and individual features differed statistically between ES and controls. To accomplish this goal, the individual

memory score of ES for bound information was compared with her average score across all experimental conditions. A discrepancy was considered statistically significant if the critical one-tailed t-value at the 95% of the confidence interval ($p < 0.05$) as estimated from the same discrepancy in the control group was found.

For all types of analyses the point estimates (PS) of rarity based on ES and controls' performance was computed. This PS, together with the confidence limits, allowed the examination of the percentage of the population that would fall below ES scores, and hence provided a measure of abnormality. The results of this analysis yielded a modified one-tailed t-value, and the probability (p) of abnormality associated to ES's performance (see Crawford & Garthwaite, 2002 for a detailed description).

4.3.3 Results

Mean performances are shown in Figure 4.2 A and B. Compared to controls, ES had no difficulties in remembering abstract shapes [PS = 15.99, t = -1.07, p = n.s.] or colours [PS = 47.88, t = -0.05, p = n.s.] presented as individual features. However, ES showed a significant deficit in memory for bound features [PS = 0.66, t = -3.30, $p < 0.05$] (Figure 4.2A). This binding deficit was observed when she had to remember either 2 objects [PS = 2.38, t = -2.40, $p < 0.05$] or 4 objects [PS = 1.64, t = -2.66, $p < 0.05$] (Figure 4.2B). Only 0.66% of the population would fall below ES's score in memory for shapes bound with colours indicating a profound impairment. Finally, the discrepancy analysis showed that only 3.04% of the population (t = -2.23) would be worse than ES when memory for the binding of shapes with colours is compared to her average performance on the three conditions. In contrast, 68.0% (t = 0.49) and 93.71% (t = 1.74) of the population would perform worse than ES's when her

performance in conditions assessing memory for shape only and colour only respectively are compared to her average performance.

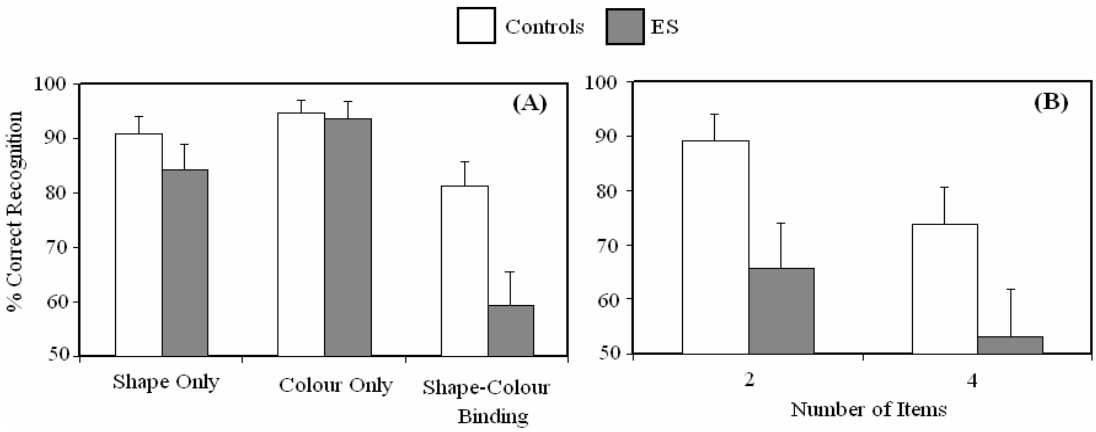

Figure 4.2. (A) Percentage of correct responses above chance (50%) for ES and controls in Experiment 7. **(B)** Performance across array sizes in the condition assessing memory for shape-colour binding. (Error bars represent the standard error of the mean).

4.3.4 Comments

ES displayed a selective deficit for memory of bound information, with spared memory for single information. This is the first report of such a selective deficit in memory for conjunctions of features following brain damage.

However, the task used in Experiment 7 was devised to investigate memory for single and bound features after a short delay. As there was as gap between the study and test displays, this task did not allow assessing whether these features were correctly grouped in perception (i.e., encoded). In order to claim that these deficits observed in ES are specific to binding in

visual short-term memory is important to assess the potential contribution of perceptual binding to this impairment. Experiment 8 addressed this issue.

4.4 Experiment 8

4.4.1 Aims

Experiment 8 was aimed at investigating whether the change detection deficit observed in ES in the condition assessing memory for bound features of Experiment 7 could be accounted for by deficits in binding in perception. If the process of forming conjunctions of features in perception is unaffected in ES, the impairment observed in Experiment 7 would be related to difficulties in retaining feature bindings in visual short-term memory and not to forming these bindings in perception.

4.4.2 Methods

4.4.2.1 Participants

The same participants entering Experiment 7 took part in this new experiment.

4.4.2.2 Task design

The task for Experiment 8 was constructed using the stimuli and apparatus described in Experiment 4. In this new task participants were simultaneously presented with two arrays of four items each in the upper and lower half of a PC screen (see Figure 4.3). Items consisted of the same shapes (shape only

condition – Figure 4.3A), colours (colour only condition – Figure 4.3B), or coloured shapes (shape-colour binding condition – Figure 4.3C) used in Experiment 7. In 50% of the trials both arrays presented identical items whereas in the other 50%, two items changes either in the upper (25%) or in the lower (25%) array. Changes between arrays consisted of two new shapes or two new colours in single feature conditions or two objects swapping colours in the shape-colour binding condition. Participants were requested to search for differences between the two arrays and to respond, by pressing two keys (see Appendix 2 - IA), whether arrays consisted of the same or different items. Participants were instructed to do this with accuracy and in the less possible time hence, the percentage of correct detection was used as the dependent variable. For each condition 20 trials were presented (10 per set size). Conditions were blocked and the "same" and "different" trials were fully randomized within conditions.

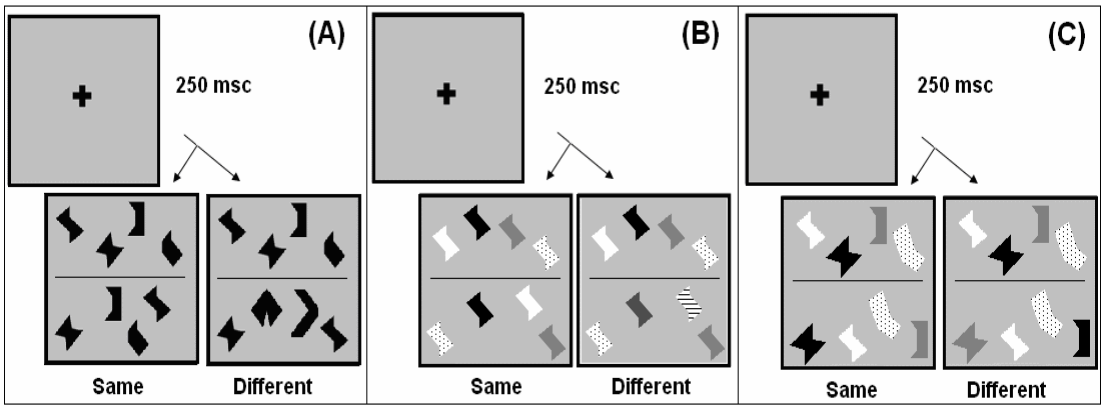

Figure 4.3. Trial sequence used in Experiment 8 for conditions assessing perceptual binding of shapes (A), colours (B), and shape-colour binding (C).

4.4.3 Results

Compared to controls, ES had no difficulties in searching for differences between arrays of shapes [PS = 74.75, t = 0.07, p = n.s.], colours [PS = 72.21, t = 0.619, p = n.s.], or coloured shapes [PS = 56.24, t = 0.163, p = n.s.].

4.4.4 Comments

When the same type of stimuli was used for searching for differences between arrays rather than for holding these arrays in visual short-term memory, ES and controls did not differ. If the difficulty of ES were in forming bindings in perception, a poor performance would have been observed in this perceptual task. These results suggest that ES can accurately integrate features in perception but she cannot hold these bindings in visual short-term memory.

Furthermore, as ES is right handed, we did not expect to find deficits in nonverbal memory associated with her brain lesion which involved the left hemisphere. Experiment 7 was devised to assess memory for nonverbal material (i.e., abstract shapes and colours difficult to name). These findings led to the question as to whether the selective impairment shown by ES in remembering conjunctions would also encompass objects, the features of which are easily nameable, and this was addressed in Experiment 9.

4.5 Experiment 9

4.5.1 Aims

Experiment 9 investigated if the specific deficit for non-verbal bound information observed in ES in Experiment 7 would also encompass her verbal short-term memory for integrated objects. Experiment 9 addressed memory for nameable features and conjunctions of these features using a task that explicitly required holding the information in short-term memory using verbal codes.

4.5.2 Methods

4.5.2.1 Participants

Eight new participants served as controls for ES in this experiment. ES and controls did not significantly differ in age (M = 69.8, SD = 6.22; t = -0.122, p = n.s.), education (M = 12.2, SD = 1.75; t = -1.185, p = n.s.), and VIQ (M= 105.0, SD = 4.34; t = -1.56, p = n.s.). All participants gave their signed consent to take part in this study.

4.5.2.2 Task Design

For Experiment 9 a new task was devised to assess recognition of verbal information. Figure 4.4 shows the experimental conditions and trial designs used in this experiment. Two sets of 11 nameable colours (Red, Blue, Green, Brown, Orange, Yellow, Purple, Gray, Turquoise, Pink, and Black) and 11 nameable objects (Bed, Apple, Banana, Bell, Shoe, Car, Book, Chair, Cup, Guitar, and Button) were used to construct the stimuli arrays. Nameable objects were taken from the International Picture Naming Project (http://crl.ucsd.edu/~aszekely/ipnp/). Colour nameability was piloted in 12 healthy young volunteers, all university students, with age ranging from 20 to 29 years. Red, Blue, Green, Yellow, Purple, Gray, and Black were named using the exact names listed above by 100% of participants, the Brown by 83%, Orange 83%, Turquoise 66% (here Turquoise, Cyan, or Light Blue were valid names whereas Blue was considered an error), and Pink 83%. Although different naming frequencies were found for the selected colours, they were highly distinguishable primary colours. Therefore, to keep an adequate number of colours that matches the number of objects (i.e., as to ensure an even use of stimuli types across the experiment), the colour naming frequency was not restricted to 100%. In Experiment 9 participants

were presented with study arrays consisting of 4 or 6 objects (object only condition), 4 or 6 colours (colour only condition), or 2 or 3 combinations of objects and colours (object-colour binding condition)[8].

The study array was presented for 1.5 sec per feature, that is, when 6 single objects or 3 coloured objects were presented on the screen, the presentation time was 9 sec for each display. This equated the presentation time for the amount of information to-be-remembered as determined by the number of features. Immediately after the study array, participants were given a booklet which contained lists of names of objects, colours, or pairs of objects and colours. The retrieval cues used in this experiment were written words rather than visual objects to ensure that the visual information presented in the initial display would be transposed into verbal codes in order to make the correct selection during the recognition phase. The lists consisted of twice as many items as presented in the study array. For conditions assessing memory for individual items, 50% of the items in the lists were the names of the objects presented in the study display and 50% were distracters. In the condition assessing memory for bound items, 50% of the object-colour pairs in the lists corresponded to the items previously presented, 25% were constructed using the names of the objects previously seen coupled with colour names that were not presented at the study, and the other 25% were

[8] In Experiment 7 the number of objects was kept constant and the number of features was varied. That is, 2 or 4 objects with one feature each in conditions assessing memory for colours or shapes, and 2 or 4 objects with two features each in the condition assessing the binding of shapes with colours. As the total amount of information as determined by the number of features was greater in the binding condition than in conditions assessing memory for individual features, an effect of memory load could not be ruled out. In order to remove this effect from further experiments the task design was varied. In Experiment 9 the number of features across conditions was kept constant and only varied the number of objects holding these features (4 or 6 objects with one feature each in single feature conditions and 2 or 3 objects with two features each in the binding condition). This modification allowed focusing on the specific process of holding bound features once the memory load was controlled.

constructed using the names of the colours previously seen coupled with object names that were not presented at the study. Participants were requested to tick the items that corresponded to the objects previously seen. The task consisted of 18 trials per experimental condition (9 trials per array size).

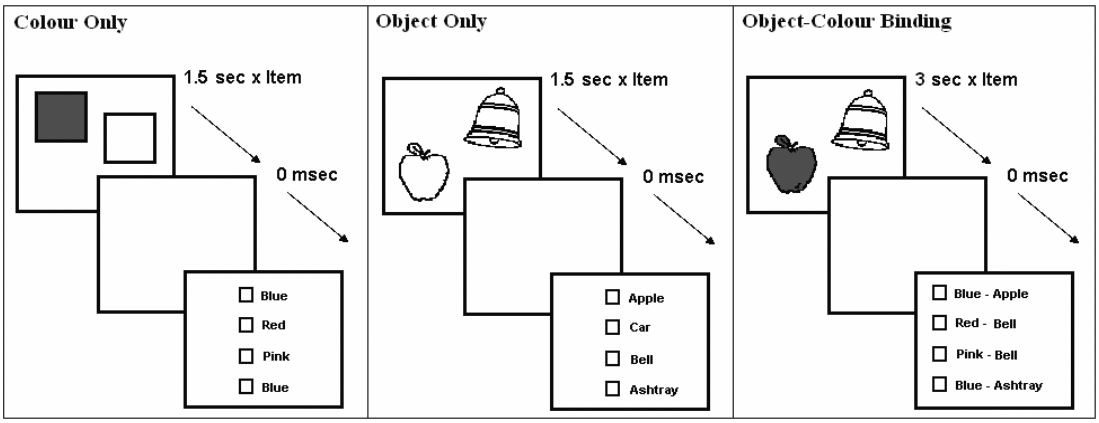

Figure 4.4. Experimental conditions and trial sequence used in Experiment 9 (the actual set sizes used in this experiments were 4 and 6 for colour and object only and 2 and 3 for object-colour binding).

To ensure that participants were able to name the items in the experiment, prior to the first trial they were presented with two arrays one containing 22 objects and another one containing 22 colours. Fifty percent of the objects and colours presented in these arrays corresponded to the actual stimuli used in the experiment while the other 50% were not used in the experiment. Participants were requested to name the objects and the colours aloud (Appendix 5).

4.5.3 Results

Figure 4.5 shows mean performance in Experiment 9. As compared to controls, ES had no difficulties in remembering objects [PS = 5.44, t = -1.83, p

= n.s.], colours [PS = 36.32, t = -0.36, p = n.s.], or objects bound with colours [PS = 55.58, t = 0.14, p = n.s.].

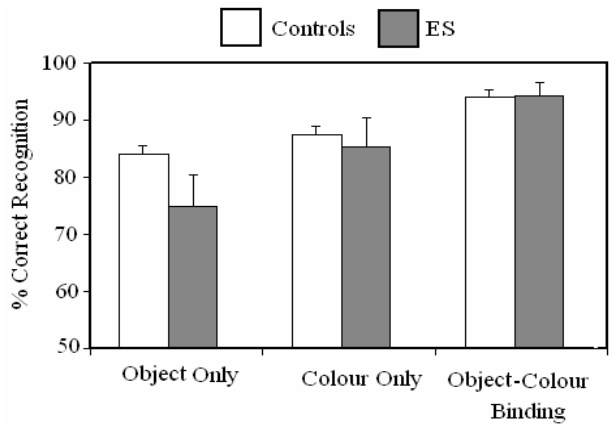

Figure 4.5. Percentage of correct recognition for ES and controls in Experiment 9 (Error bars represent the standard error of the mean).

4.5.4 Comments

ES without difficulty was able to use verbal codes to retain information on bound features that were visually presented. This suggests that ES is specifically unable to hold conjunctions of information in visual short-term memory. If this were the case, using visual information in both the study and test phases (instead of words as recognition clues) would elicit the same pattern of results observed in Experiment 7. This hypothesis was assessed in the following experiment.

4.6 Experiment 10

4.6.1 Aims

Experiment 10 addressed memory in ES and matched controls for nameable features and conjunctions of these features using a task that required the

maintenance of this information in short-term memory relying mainly on visual codes.

4.6.2 Methods

4.6.2.1 Participants

The same participants who undertook Experiment 9 entered Experiment 10.

4.6.2.2 Task Design

The same stimuli used in Experiment 9 were used in Experiment 10. For Experiment 10 the study arrays were the same as described in Experiment 9. However, the test arrays presented objects rather than words (see Figure 4.6). In the condition assessing memory for single features (i.e., object only and colour only), probe arrays presented twice as many items presented in the study array. Probe arrays consisted of the same studied items (50%) plus new items not presented in the study phase (50%). In the test phase, participants were requested to select, using the mouse, the objects or colours they had seen in the study array. In the condition assessing memory for the binding of objects with colours (i.e., object-colour binding), the test display presented two separate arrays of items. One array consisted of the same objects previously seen plus the same number of objects not presented at the study, and the second array consisted of the same colours previously seen plus the same number of colours not presented at the study. Participants were requested to select, using the mouse, the objects they had seen in the study array with their corresponding colours. The selected combinations were shown at the bottom of the screen. The task consisted of 18 trials per experimental condition (9 trials per array size).

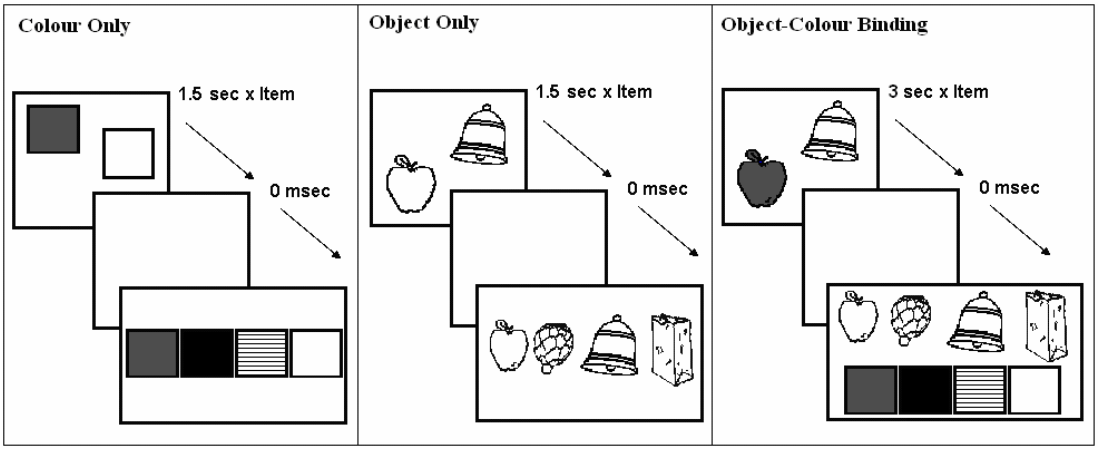

Figure 4.6. Experimental conditions and trial sequence used in Experiment 10 (the actual set sizes used in this experiments were 4 and 6 for colour and object only and 2 and 3 for object-colour binding).

4.6.3 Results

Figure 4.7 shows mean performance in Experiment 10. ES had no difficulties in remembering objects [PS = 29.32, t = -0.57, p = n.s.] or colours [PS = 41.30, t = -0.23, p = n.s.] presented as individual features. However, ES's memory for these features integrated into objects was impaired [PS = 0.05, t = -5.41, $p < 0.01$] (Figure 4.7A). When her performance in the condition assessing memory for bound features was analyzed across set sizes (see Figure 4.7B), these differences fell short of significance [2 items: PS = 8.37, t = -1.54, p = 0.08; 3 items: PS = 8.39, t = -1.54, p = 0.08]. The discrepancy analysis showed that 0.23% of the population (t = -4.09) would be poorer than ES when memory for the binding of objects with colours was compared to her average performance. In contrast, 94.54.0% (t = 1.83) and 97.06% (t = 2.25) of the population would perform poorer than ES when performance in conditions assessing memory for object only and colour only respectively, are compared to her average performance.

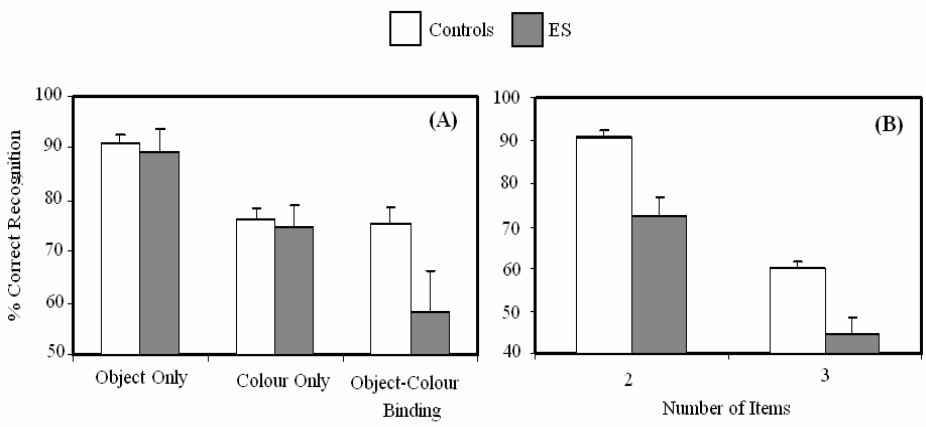

Figure 4.7. **(A)** Percentage of correct recognition for ES and controls in Experiment 10. **(B)** Performance split across array sizes for the condition assessing object-colour binding (Error bars represent the standard errors of the mean).

4.6.4 Comments

Taken together, the results of Experiments 7 to 10 suggest that ES's impairments reflect an inability to represent bound information in visual short-term memory while her memory for visual unbound information and for verbal bound and unbound information remains intact. The previous experiments assessed recognition memory for verbal and non-verbal information therefore, it would also be interesting to investigate whether the selective deficit shown by ES in memory for objects would replicate when recall is used as the retrieval strategy.

Experiment 11 and 12 were devised to investigate memory for bound and unbound information using a free recall paradigm. Experiment 11 investigated free recall of single and bound words that were aurally presented. Experiment 12 investigated free recall of shapes and colours that were visually presented as individual or combined features.

4.7 Experiment 11

4.7.1 Aims

If ES verbal short-term memory for features and objects is intact, she would perform well in tasks assessing memory for single and bound features that are presented aurally.

4.7.2 Methods

4.7.2.1 Participants

The same participants who participated in Experiment 10 entered into this experiment.

4.7.2.2 Task design

For this experiment lists consisting of two or three syllable words that corresponded to the name of pictures taken from the same database used in Experiments 9 and 10 were created. Objects which naming frequencies were above 100 were selected. Additionally, a list of adjectives which were selected on the basis of their semantic relation to the objects chosen was constructed (see Appendix 6 for the stimuli used in this experiment). Lists of 4 or 6 nouns (noun only condition), 4 or 6 adjectives (adjective only condition), or 2 or 3 combinations of nouns and adjectives (noun-adjective binding condition) were presented aurally using loud speakers. The presentation rate was 1 word per sec (2 sec for the pairs) with an interval of 1 sec between words or combinations. Participants were requested to

remember these words and to recall them in any order. The task consisted of 18 trials per experimental condition (9 trials per array size).

4.7.3 Results

Figure 4.8 shows mean performance in Experiment 10. ES had no difficulties in recalling nouns [PS = 65.39, t = 0.41, p = n.s.], adjectives [PS = 63.02, t = 0.35, p = n.s.], or combination of nouns with adjectives [PS = 85.13, t = 1.13, p = n.s.].

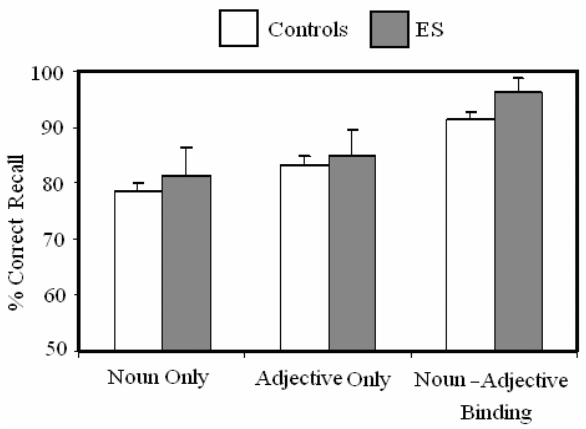

Figure 4.8. Percentage of correct recall for ES and controls in Experiment 11 (Error bars represent the standard errors of the mean).

4.7.4 Comments

The finding of preserved short-term memory for bound verbal information observed in the recognition task of Experiment 9 was replicated in this recall experiment. Note that Experiment 11 extends this finding not only to a new retrieval strategy (i.e., recall) but also to a new modality as the stimuli were aurally presented. These results suggest that whenever ES can rely on verbal codes to assist her memory for bound features she can remember this information as well as controls.

4.8 Experiment 12

4.8.1 Aims

If the impairment in ES for visual binding extends to memory recall, she should perform poorly on tasks assessing visual recall (i.e., by drawing) of bound visual features while she would perform well in tasks assessing visual recall of single visual features.

4.8.2 Methods

4.8.2.1 Participants

The same participants who entered Experiment 11 took part in Experiment 12.

4.8.2.2 Task design

In this experiment the stimuli used were nameable shapes and colours. Figure 4.9 shows the experimental conditions and trial sequences used in Experiment 12. A set of 8 nameable shapes (Square, Triangle, Circle, Diamond, Rectangle, Oval, Arch, and Cross) and a set of 8 colours (Red, Pink, Blue, Turquoise, Green, Yellow, Orange, and Brown) were used to construct arrays for this task. Arrays of 2 or 4 shapes (shape only condition), 2 or 4 colours (colour only condition), or 1 or 2 combinations of shapes with colours were presented in the initial display. The display was presented for 1.5 sec per features as in Experiment 8 and 9. Participants were instructed to remember as many items as possible. In conditions assessing memory for

shape or colour only once the study array disappeared, participants were provided with a booklet and a pencil for the shape only condition or 8 colouring pencils for the colour only condition (pencils corresponding to the colours used in the task). Participants were requested to draw the shapes seen before or lines in the colours that were presented in the study array.

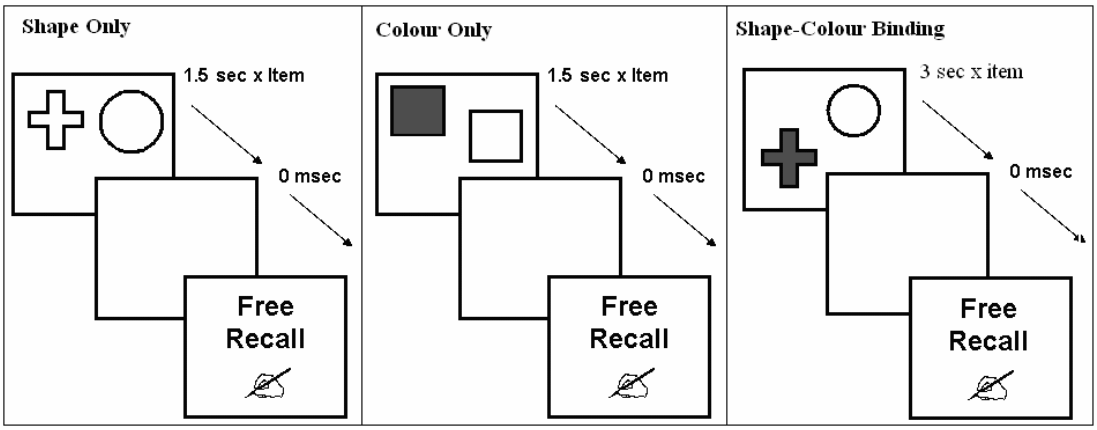

Figure 4.9. Experimental conditions and trial sequences used in Experiment 12.

For the condition assessing the binding of shapes with colours, two different procedures were used. As the specific deficit shown by ES in holding bound information in visual short-term memory vanishes whenever she can use verbal labels for rehearsing, ES and controls were first asked to study the coloured shapes visually and to draw them down as soon as the initial display had disappeared (this block was called "without verbal aid"). Then a second block of coloured shapes was presented but in this occasion ES and controls were asked to name them aloud when they were studying them and to keep rehearsing them until they had drawn them on the booklet (this block was called "with verbal aid"). In both blocks, participants were provided with a booklet and a set of eight colouring pencils and they were requested to select the colours of the shapes previously seen and to draw the corresponding shapes as soon as the study display disappeared. Six trials (3

trials per array size) were used for each experimental condition, including the two blocks of stimuli used in the binding condition.

4.8.3 Results

Figure 4.10 (A and B) shows mean performance in Experiment 12. Analysis carried out on data collected during the "without verbal aid" block showed that ES had no difficulties in recalling shapes [PS = 19.41, t = -0.92, p = n.s.] or colours [PS = 38.88, t = -0.29, p = n.s.] presented as individual features. However, ES memory recall for these same features integrated into objects was impaired [PS = 2.4, t = -2.39, $p < 0.05$] (Figure 4.10A).

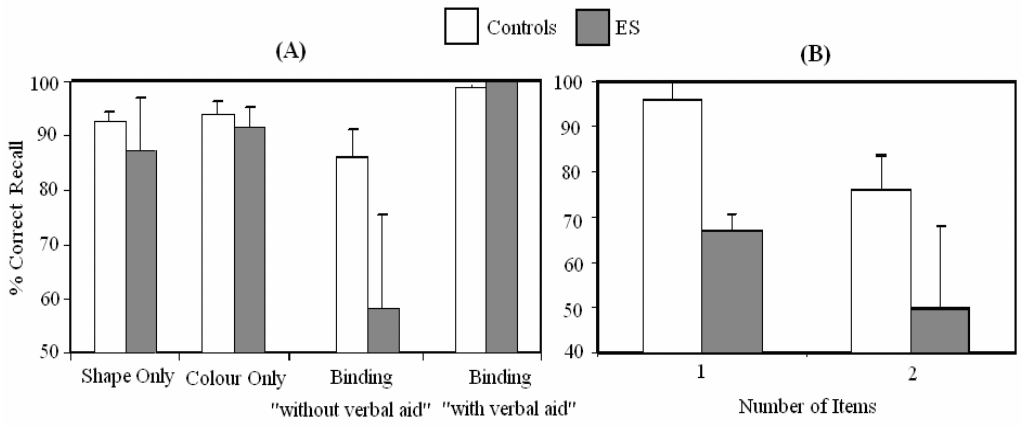

Figure 4.10. **(A)** Percentage of correct recall for ES and controls in Experiment 12 (Error bars represent the standard errors of the mean). **(B)** Performance split across array sizes for the condition assessing the binding of shapes and colours "without verbal aid".

When ES's performance in the condition assessing memory for bound features was analyzed across set sizes, she was significantly poorer than controls at set size 1 [PS = 2.62, t = -2.33, $p < 0.05$] but this difference did not reach significance for set size 2 [PS = 8.52, t = -1.53, p = n.s.] (Figure 4.10B). The discrepancy analysis showed that 9.42% of the population (t = -1.46)

would be poorer than ES when memory for the binding of objects with colours was compared to her average performance. In contrast, 62.99% (t = 0.35) and 84.86% (t = 1.1) of the population would perform poorer than ES's when performance in conditions assessing memory for shapes only and colours only respectively, were compared to her average performance.

When participants were requested to use verbal codes to rehearse the combinations of shapes and colours (block called "with verbal aid"), ES difficulties to recall bound features disappeared [PS = 72.38, t = 0.64, p = n.s.]. Analysis of the discrepancy of ES performance in this block showed that 94.7% of the population (t = 1.90) would have a lower score than ES when memory recall for bound features was compared to her average performance.

4.8.4 Comments

The results of Experiment 12 further support previous findings that ES displays an inability to hold in short-term memory bound information processed within the visual domain while her visual short-term memory for single information as well as for verbal information is preserved. The finding that ES could not hold in visual short-term memory 1 coloured shape without verbal aid is striking. It might be argued that in this situation the binding between features may have not been required as there was no need to remember the combination to succeed in this task. However, even in a condition as simple as this, ES lost information from her visual short-term memory. Further exploration of this deficit showed that information lost could be either of shape or colour without showing any preference for any type of feature.

4.9 Assessing dissociations in ES

The results presented in this series of experiments, reveals that ES exhibits two types of dissociations. One involves short-term memory for visual bound versus verbal bound information and the other involves visual short-term memory for single versus bound features. Together these dissociations suggest that ES verbal short-term memory is intact while her visual short-term memory for object representations but not for individual features is impaired. In order to assess whether this pattern of performance meets criteria for classical dissociation, the methodology devised by Crawford and Garthwaite (2005) was implemented. This methodology permits the investigation of whether this differential impairment in visual short-term memory for complex objects reliably dissociates from the other forms of short-term memory assessed in ES.

To investigate dissociations in ES's, performance in Experiments 9 and 10 was compared. These experiments only differed in the retrieval stage as Experiment 9 used the recognition of words (in which the participants needed to translate the visual information into verbal codes), while Experiment 10 required recognition of visual objects. By comparing performance in conditions assessing memory for bound features in Experiments 9 and 10 it would be possible to investigate whether the selective impairment observed in ES' visual short-term memory for bound information dissociates from her short-term memory for verbal bound information. By comparing performance in the conditions assessing memory for single objects or single colours with performance in the condition assessing memory for objects bound with colours of Experiment 10, it would be possible to assess whether the differential impairment observed in ES's memory for visual objects as compared to memory for visual features also finds the criteria for classical dissociation.

The method proposed by Crawford and Garthwaite (2005) requires that all inputs use the same metric. All the experiments presented here used percentage of correct responses as dependent variables. However, the chance level for these experiments differed. In Experiment 9 participants made their recognition on test displays where 50% of the items were the correct object-colour pairs while the other 50% were old objects repaired with new colours (25% of the times) or new objects repaired with old colours (25% of the times). Therefore, chance performance in this condition was 50%. In Experiment 10 the test phase was different. Participants' recognition was based on two new sets of colours and objects each double the number of objects presented in the study display. Participants were instructed to select each object with its corresponding colours. As 2 or 3 objects were presented in the condition assessing memory for bound features the probability of choosing the correct objects would be $p = \Sigma\, n\, /(\, 2 \times \text{no. of study objects} - i * 2 \times \text{no. of study colours} - i)$ (with n ranging from 1 to set size and i from 0 to set size -1). Therefore, when 2 objects were presented on the study display the probability of correct object recognition was $p = 1/(4 * 4) + 1/(3 * 3) = 0.0625 + 0.11 = 0.1736$ (17.36%). When 3 objects were presented the probability for correct object recognition was $p = 1/(6 * 6) + 1/(5 * 5) + 1/(4 * 4) = 0.027 + 0.04 + 0.0625 = 0.1295$ (12.95%). The total probability of correct recognition for the condition assessing memory for bound features was 30.31%. The percentage of correct responses above this probability (chance) was then used for calculation.

According to this analysis ES's corrected short-term memory performance (% above chance) for verbal features bound into objects (Experiment 9) was M = 45.37 and for visual features bound into objects (Experiment 10) was M = 28.01. Controls corrected short-term memory performance for verbal features bound into objects (Experiment 9) was M = 44.79, SD = 3.76 and for visual features bound into objects (Experiment 10) was M = 45.04, SD = 2.97. These

statistics were entered into the program (Crawford & Garthwaite, 2005) and the results were significant [PS = 0.05, t = -5.406, p < 0.001]. Therefore, when verbal and visual short-term memory were analyzed in the comparison of ES and controls, the patient's pattern of performance fulfilled the criteria for a classical dissociation.

To test the dissociation between objects and features the corrected memory performance obtained in the Experiment 10 was used. In this case, performance in conditions assessing memory for features (performance in colour and object only conditions was collapsed for such purpose) and memory for objects (i.e., the binding) was compared. Performance was corrected for chance level which was 50% for single features and 30.31% for the binding of these features (as it was shown in the calculation above). According to this analysis ES's corrected visual short-term memory performance for features was M = 32.18 and for objects M = 28.01. Controls corrected visual short-term memory performance for features was M = 33.79, SD = 3.96 and for objects was M = 45.04, SD = 2.97. These measures were entered into the program (Crawford & Garthwaite, 2005) and the results mirrored those found in the previous analysis [PS = 0.05, t = -5.406, p < 0.001]. Therefore when visual short-term memory for features and objects were analyzed, ES's pattern of performance fulfilled the criteria for a classical dissociation.

Summarizing these results, ES presented with a selective impairment of visual short-term memory for multi-feature objects while her visual short-term memory for single features as well as her verbal short-term memory were intact.

4.10 General Discussion

4.10.1 Implications of ES' results for the functionality of working memory

The selective impairment in visual short-term memory for bound information found in ES had not been reported in the literature to date. Specifically, there are three issues emerging from ES's performance that may have implications for the organization of working memory. The first relates to the selective impairment of visual short-term memory for objects only with preserved verbal short-term memory. The fact that ES showed preserved verbal short-term memory for information presented in single and bound formats while she has impaired visual short-term memory for bound information fits well into the two segregated components subserving verbal-phonological information (phonological loop) and visual information (visuo-spatial sketchpad). The implications of ES's performance for the current models of short-term memory will be discussed more thoroughly in Chapter 8 where evidence accrued in this thesis will be taken together. The contribution of executive problems in ES was ruled out as although she showed a slight increase in perseverative responses on the Wisconsin Card Sorting Test, she performed well on all other measures of executive functions. Furthermore, Allen et al. (2006) recently found that holding bound information in visual short-term memory could rather be an automatic process which places little or no demand on the central executive.

The second issue relates to the functional interrelations of the working memory components. When ES was encouraged to transfer visual information into verbal codes (Experiment 9 and Experiment 12 in the block "with verbal aid"), her impairment in remembering bound visual features was compensated. One other case also showing the interrelatedness of these

short-term memory components is patient MJK (Best & Howard, 2005), who could use a visually based code to remember visually presented verbal items but could not re-code these items phonologically. The authors observed that MJK substituted visually similar items for one another, her performance was better with visual than auditory stimuli, and she was able for example, to remember numbers (e.g., 8) better than written words. The pattern of performance observed in ES supports the view that short-term memory components (i.e., verbal and visual) are relatively independent systems but with strong functional interrelations. These interrelations may provide the mechanism whereby compensatory strategies can be developed after selective damage to short-term memory components and which may explain why this specific difficulty had never been noted by ES before.

The third issue is the paradoxical relation between left brain damage observed in a right handed patient with impaired visual and preserved verbal short-term memory. The majority of publications concerning memory and brain laterality converge in that verbal memory functions seem to be subserved by the left brain hemisphere while visual memory functions rely on the right brain hemisphere (Milner, 1971; Milner, 1982; Milner & Taylor, 1972). There is however alternative evidence to this left-verbal/right-nonverbal dichotomy. For example, Smith and Jonides (1995) reported activation on the left ventro-lateral frontal cortex during a task involving short-term memory for abstract objects. In addition, MacLeod, Buckner, Miezin, Petersen, and Raichle (1998) found activation on the right frontal region (BA10) using a semantic monitoring working memory task. It is worth noticing that ES's impairments reflect an inability restricted to store bound information in visual short-term memory while she can store other types of information (visual and verbal) without difficulties.

These results suggest that a trans-hemispheric functional reorganization takes place after brain damage. This reorganization may be seen as the biological aid underpinning the development of compensatory strategies. Additionally, these results suggest that the left-verbal/right-nonverbal approach extensively reported in memory literature may represent a limited view of the functional scope of the cerebral hemispheres.

4.10.2 Implications of ES's results for the current debate on the capacity of visual short-term memory

The memory deficit displayed by ES for bound visual features with intact memory for individual features suggests that visual short-term memory for objects and features may be subserved by separate mechanisms. In their seminal paper, Vogel et al. (2001), suggested that the unit of capacity of visual short-term memory seems to be determined by the number of objects rather than by the number of features, features being stored in visual short-term memory within integrated objects representations. According to ES's performance, it seems unlikely that features are stored in visual short-term memory within integrated objects as she could remember individual features without difficulties while she was less able to remember objects composed of the same number and types of features. It is worth noticing that ES's problems for holding bound information in visual short-term memory did not reflect a capacity limitation as she could remember individual features as well as controls during conditions assessing memory for single and bound information. Additionally, ES showed a normal visual span as assessed by the Visual Pattern Test (Della Sala et al., 1999) as well as completely normal perceptual binding functions. Her problem seems to reflect a limitation to hold in visual short-term memory the relatedness between features.

Therefore, this suggests that the way features are integrated into objects, that is, the binding, represents an additional piece of information and that this information seems to be processed by mechanisms distinct to those responsible for feature processing. This new evidence in a brain damage individual provides further support to those arguments presented in Chapters 2 (Experiment 3) whereby holding integrated objects in visual short-term memory consumed more capacity than holding the same number of individual features. This does not rule out that the final outcome of these processes may result in objects represented as a whole in visual short-term memory. However, it does suggest that to reach this object-based representation, different parallel mechanisms should work attuned.

In summary, ES has a specific deficit in visual short-term memory for visual objects defined by bound features while her memory for individual visual features as well as her verbal memory (for objects and features) remains intact. These findings are consistent with the suggestion that individual features and bindings are maintained by separated brain mechanisms.

4.11 Leading Ideas

The series of experiments presented in this chapter provide strong evidence on the involvement of visual short-term memory in processing complex events. This investigation across memory domains (i.e., verbal and visual), types of information (i.e., abstract and nameable), and retrieval processes (i.e., recall and recognition), has shown that there may be differential vulnerability of binding operations to brain damage. Furthermore, these results have also corroborated previous findings presented in Chapter 2 suggesting the additional operations required to retain information about the relatedness between features in short-term memory and in Chapter 3 which

suggested that healthy older participants conserve the ability to represent integrated objects in their short-term memory.

This study was not devised to assess age-related changes in visual short-term memory, however, performance along the series of experiments presented here support for the claim that healthy older adults remember multi-feature objects as well as the individual features composing these objects (as shown in Chapter 3 and reported by Brockmole et al., 2008). This spared functionality allowed for separating ES's performance from the performance of healthy older controls who were matched to her in age and years of education. Following this evidence, the next chapters of this thesis will address the assessment of older people who are affected by the most common age-related neurodegenerative disorders, namely Alzheimer's Disease. As healthy older people have proved normal in performing tasks presented in this and previous chapters (e.g., Chapters 3), this provides a favourable context to investigate memory binding deficits in Alzheimer's Disease using tasks that are not sensitive to the effects of age.

CHAPTER 5

Verbal short-term memory binding deficits in Alzheimer's Disease: evidence from a recall paradigm

5.1 Introduction

Evidence discussed in Chapter 1 (Part I) suggests that binding information in memory may depend on the connectivity between brain regions responsible for processing different aspects of sensory inputs (e.g., colours, shapes, locations). Damasio (1989) suggested that it seems to be unlikely that one single anatomical site subserves the integration of memory and motor processes and that a single store represents the meaning of entities or events. In fact, the results presented in Chapter 4 further support this statement as ES showed a selective impairment in holding bound features in visual short-term memory while she could perfectly hold individual features. This suggests that at some level in her visual short-term memory there should be a break down of processes responsible for representing the information that enables the association (i.e., the binding) of features processed in different dimensions (i.e., what object shape went with what colour). This in turn suggests poor connectivity across feature dimensions.

Hence, binding is a cognitive process that may be at the base of the integrative functions and which heavily depends on the effectiveness of brain connectivity. It would be therefore expected to find deficits of this cognitive function in patients suffering from neurodegenerative disorders in which brain regions are progressively disconnected. One example of these disorders is Alzheimer's Disease, the most common neurodegenerative condition of

old age which main pathological outcomes are neuronal death and brain disconnection (Braak et al., 1999; Braak & Braak, 1996; Kavcic, Ni, Zhu, Zhong, & Duffy, 2008; Zhou, Dougherty, Jr., Hubner, Bai, Cannon, & Hutson, 2008).

As was discussed in Section 1.9.3, these pathological changes in Alzheimer's Disease might hamper memory binding functions. For example, these changes may help to explain why early in the disease patients suffering from this condition have a great deal of impairment in representing different attributes of stimuli together in memory (e.g., objects and locations) (Swainson et al., 2001). This chapter describes experimental work carried out to investigate whether or not there are short-term memory binding deficits in Alzheimer's Disease.

5.1.1 Why is it important to investigate short-term memory binding in Alzheimer's Disease?

1) As was discussed in Section 1.9.1 of Chapter 1 (Part II), patients with Alzheimer's Disease have problems learning associations or "bindings" between items. However, their ability to hold these bindings for a short time in memory has not been investigated to date.

2) Evidence discussed in Section 1.5.5 of Chapter 1 (Part I) suggests that associative learning and short-term memory binding should be seen as functions subserved by different mechanisms (Colzato et al., 2006; Logie et al., 2009; Treisman, 2006). Therefore, the fact that Alzheimer's Disease patients have shown deficits in the former function may not predict they will have deficits in the latter.

3) The literature on early detection of Alzheimer's Disease has presented the Paired Associate Learning Tasks as tools that may aid the assessment of Alzheimer's Disease patients (Buschke et al., 1999; O'Connell et al., 2004; Swainson et al., 2001). However, these tasks were not designed to assess memory binding functions explicitly. The reason for this statement was discussed in detail in Chapter 1 (Section 1.9.1 and 1.9.4, Part II).

4) As was shown in Chapter 4, short-term memory binding functions can be selectively impaired after brain damage. Taking together findings of Chapter 4 with the fact that it is still unknown whether the associative memory deficits found in Alzheimer's Disease are over and above memory deficits for unrelated events, it would be worth investigating this function in Alzheimer's Disease patients as a possible account of memory impairments observed in sufferers from this disease.

5) Finally, the results presented in Chapter 3 led to the suggestion that processes responsible for binding features into objects in short-term memory are not differentially affected by age (see also Brockmole et al., 2008). Hence, should this function be affected by Alzheimer's Disease, this would be the first empirical evidence of memory binding deficits in this neurodegenerative disorder and of a task that could reliably separate Alzheimer's Disease from normal ageing.

Two experiments were carried out aimed at investigating whether the process of binding information in short-term memory is affected in patients with Alzheimer's Disease. To this end, a verbal task was devised that explicitly assesses binding in short-term memory.

5.2 Experiment 13

5.2.1 Aims

The main aim of this experiment was twofold: First, to investigate whether patients with Alzheimer's Disease have problems in holding bound information in verbal short-term memory and second, to investigate whether memory for items bound into complex events is impaired in patients with Alzheimer's Disease to a greater extent than is their memory for the individual features composing these complex items.

5.2.2 Methods

5.2.2.1 Participants

Participants entering this experiment were 23 healthy elderly and 23 patients diagnosed as suffering from mild to moderate Alzheimer's Disease. Alzheimer's Disease patients and healthy elderly did not significantly differ in age (Healthy elderly: M = 69.78, SD = 6.47; Alzheimer's Disease patients: M = 73.26, SD = 6.09; $t(44) = -1.87$, p = n.s.) and years of education (Healthy elderly: M = 7.08, SD = 2.81, Alzheimer's Disease patients: M = 6.39, SD = 3.34; $t(44) = 0.76$, p = n.s.). Patients with Alzheimer's Disease were diagnosed according to the diagnostic criteria established by the DSM-IV-TR and NINCDS-ADRDA group (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984). In addition, Alzheimer's Disease patients and healthy elderly were excluded if they had problems with colour vision as assessed by the Colour Blindness Test (Dvorine, 1963). All participants gave their signed consent to take part in this study. The general neuropsychological profile of patients entering this experiment is shown in Table 5.1.

Table 5.1. Neuropsychological profile of Alzheimer's Disease patients entering Experiments 13 and 14.

		Experiment 13 (n = 23)			Experiment 14 (n = 21)		
	Cut-off score	Mean ± SD	Range	N. of patients performing below cut-off	Mean ± SD	Range	N. of patients performing below cut-off
MMSE	> 24 (1)	18.70 ± 3.40	14 - 24	21	18.60 ± 3.3	14 – 24	21
GDS	>= 5 (2)	5.61 ± 0.50	5 – 6	23	5.5 ± 0.5	5 - 6	21
VOSP - Shape detection	< 15 (3)	19.2 ± 1.2	16 – 20	0	19.3 ± 1.1	16 - 20	0
Delayed Prose Recall	4.5 (4)	0.5 ± 1.4	0 – 5	21	0.6 ± 1.3	0 – 5	19
Digit Forward Span	2.75 (5)	4.2 ± 0.8	3 - 6	0	4.2 ± 0.8	3 – 6	0
Raven Progressive Matrices	14.75 (4)	17.7 ± 4.6	6 – 24	5	18.4 ± 5.1	10 – 24	6
Trial Making Test B-A	185 (6)	250.7 ± 84.6	102 – 464	17	254.8 ± 98.4	102 - 464	15
Category Fluency	7.0 (4)	11.0 ± 6.8	0 – 25	7	12.4 ± 8.0	0 – 25	6

GDS : Global Deteriorating Scale; MMSE: Mini Mental State Examination; VOSP: Visual Objects and Space Perception Battery; (1): Folstein et al. (1975); (2): Reisberg, Ferris, de Leon, and Crook (1982); (3): Warrington and James (1991); (4): Spinnler and Tognoni (1987); (5): Orsini, Grossi, Capitani, Laiacona, Papagno, and Vallar (1987); (6): Giovagnoli, Del, Mascheroni, Simoncelli, Laiacona, and Capitani (1996); (4, 5, and 6): Cut-off scores equal the inferred 5-centile of the population distribution.

5.2.2.2 Stimuli and Apparatus

Participants were assessed using a PC running an E-prime script (Psychology Software Tools Inc., 1996) generated ad hoc for the study. The program presented participants with arrays of items on the PC screen. The number of items in these arrays varied between healthy elderly and Alzheimer's Disease patients and between conditions assessing memory for single features and memory for bound features. Healthy elderly were presented with arrays of 6 items in conditions assessing memory for single features and arrays of 3 items in the condition assessing the binding of these features in memory. Alzheimer's Disease patients were presented with arrays of 4 items in conditions assessing memory for single features and of 2 items in the condition assessing the binding of these features in memory. These arrays sizes were selected on the basis of the results from a pilot study which

suggested that at this level of memory load, floor and ceiling effects would be avoided in both groups.

Items used in these arrays (i.e., objects and colours) were those used in Experiment 9 and described in Section 4.5.2.2 (Experiment 9).

5.2.2.3 Task Design

Each trial consisted of an initial screen which presented participants with the study array, with a presentation time of 1.5 sec [9] per feature (i.e., per colour or object). Immediately after the study array had disappeared, a new screen requested participants to recall verbally (i.e., by naming them aloud) the items they had just seen in no particular order. Participants' responses were recorded using a scoring sheet.

Four conditions were devised for this task (Figure 5.1). Three assessed memory for single features and one assessed memory for the binding of these features. *Memory for colours:* In this condition the study array consisted of coloured squares. Each square was presented in a different colour. Participants were instructed to remember these colours and to recall them when requested. *Memory for objects*: In this condition the study array consisted of common objects. Objects were outlined figures. Participants were instructed to remember these objects and to recall them when requested.

[9] As this task assessed the recall of verbal information, the presentation time was long enough to allow Alzheimer's Disease patients and healthy elderly to encode the studied materials verbally. By presenting arrays for 1.5 sec per feature, the presentation time was equated across conditions according to the total amount of information to-be-remembered (as determined by the number of features).

Memory for objects and colours unbound: In this condition the study array consisted of colours and objects presented as separate entities. Half of the items were coloured squares and the other half were outlined figures of common objects. Participants were instructed to remember the colours and the objects separately. Immediately after the initial presentation, participants were requested to recall the colours and the objects separately. *Memory for object-colour binding*: In this condition the study array consisted of different objects filled with different colours. These coloured objects were constructed by randomly combining objects with colours from the two sets. Participants were requested to remember the combinations of objects with colours. Immediately after the initial presentation, participants were requested to recall these coloured objects. Arrays in this condition displayed half of the items presented in conditions assessing memory for individual items. The purpose of this procedure was to keep constant the number of features across conditions. This would allow investigating the extent to which memory for bound features is impaired above memory for individual features once memory load (as defined by the total amount of features) was controlled.

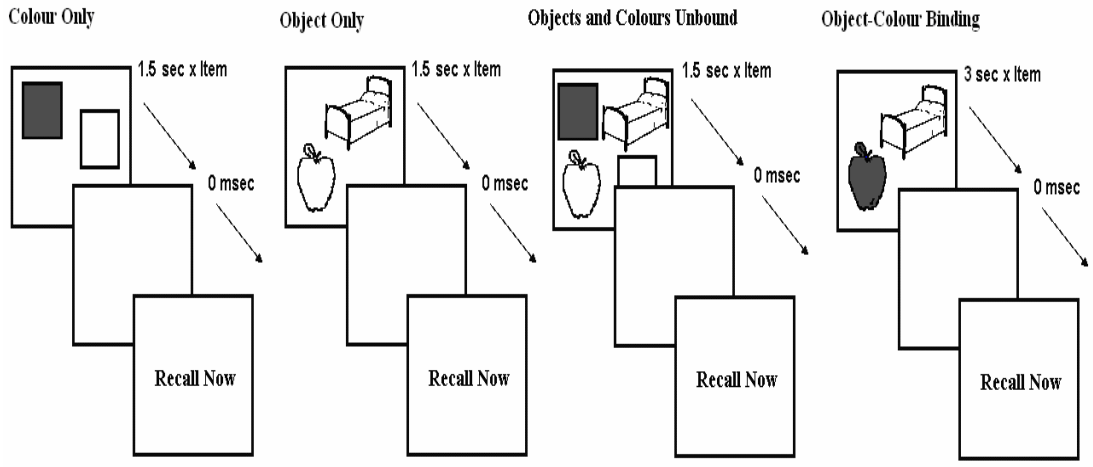

Figure 5.1. Experimental conditions and trial sequences of the task of Experiment 13.

Colours and objects were evenly used across the different experimental conditions. Individual or bound features could be repeated within condition but not within trial. Additionally, identical arrays were never repeated within any experimental condition.

5.2.2.4 Procedure

At the beginning of the experiment, participants were presented with two separate arrays one consisting of 22 colours and another one consisting of 22 objects. These arrays presented the same colours and objects used in the experiment plus new colours and new objects intermixed within the arrays. Participants were requested to name each of the colours and the objects. This procedure ensured that each participant could readily name all the colours and the objects used (see Appendix 5 for the arrays used in this screening test). Participants were then presented with a script which explained the task in detail (see Appendix 7). After these instructions, the different experimental conditions were delivered in separate blocks and in a counterbalanced order. Each experimental condition consisted of 6 trials that were fully randomized across participants.

5.2.3 Results

Performance was analysed with a two (Group = healthy elderly vs. Alzheimer's Disease patients) by four (Condition = object only vs. colour only vs. objects and colours unbound vs. object-colour bindings) mixed-ANOVA. Mean performance levels across groups and conditions are shown in Figure 5.2. As expected, Alzheimer's Disease patients showed poorer overall memory performance than healthy elderly as shown by a significant main effect of Group [$F(1,44) = 50.38$, $p < 0.001$] and Condition [$F(3,132) =$

10.47, p < 0.001]. The interaction was also significant [F(3,132) = 5.47, p < 0.01].

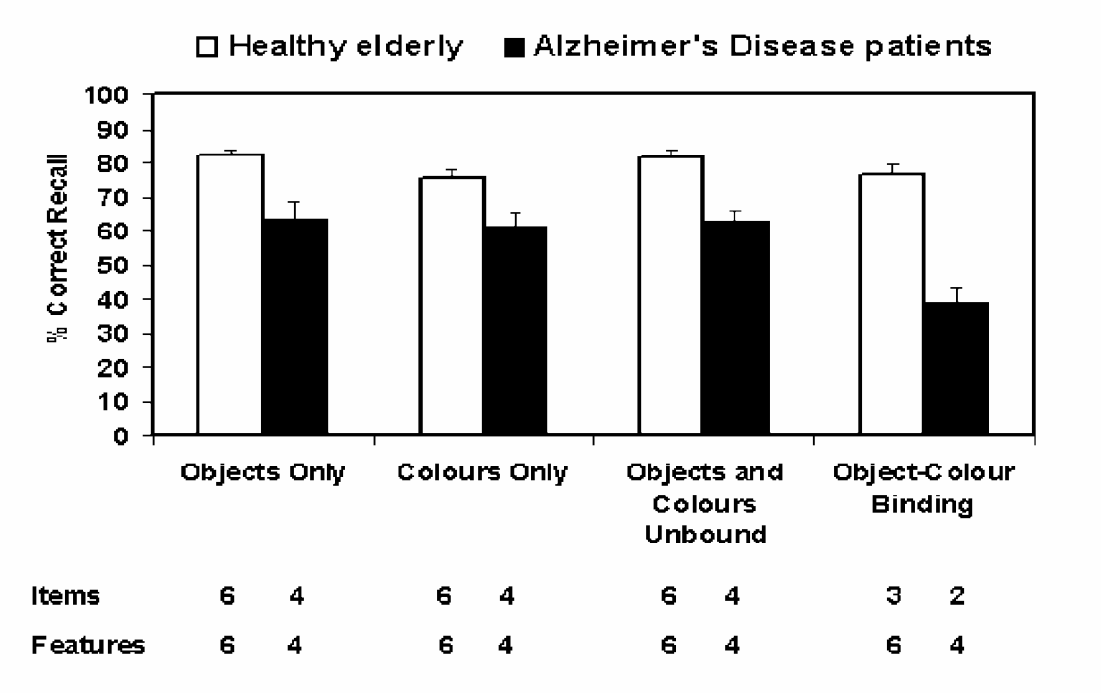

Figure 5.2. Percentage of correct recall in the Group by Condition analysis of Experiment 13 (Error bars represent the standard errors of the mean).

Pairwise comparisons were carried out between groups for each of the four experimental conditions separately (4 contrasts), and across conditions for each group separately (4 x 2 = 8 contrasts). Hence, with a total of 12 pairwise comparisons the alfa threshold was set at 0.004. Comparisons with p-values below this threshold were assumed to reflect significant differences.

These pairwise comparisons showed that Alzheimer's Disease patients performed more poorly than healthy elderly in conditions assessing memory for objects only [MD = 18.36, SE = 5.20, p = 0.001], objects and colours unbound [MD = 19.20, SE = 3.84, p < 0.001], and object-colour binding [MD = 37.20, SE = 5.58, p < 0.001]. Alzheimer's Disease patients and healthy elderly did not significantly differ in the condition assessing memory for colours only [MD = 14.37, SE = 4.80, p = n.s.].

Further pairwise comparisons across conditions showed that Alzheimer's Disease patients' performance in the object-colour binding condition was significantly poorer than in conditions assessing memory for objects only [MD = 24.64, SE = 5.79, $p < 0.001$], colours only [MD = 22.10, SE = 5.92, $p < 0.001$], and objects and colours unbound [MD = 23.55, SE = 4.96, $p < 0.001$]. None of the other contrasts carried out in Alzheimer's Disease patients across conditions assessing memory for single or unbound features resulted in significant differences. There were no significant differences in any of the contrasts carried out with the healthy elderly's performances.

5.2.3.1 Analysis of errors

As Alzheimer's Disease patients performed significantly more poorly in memory for object-colour binding than in the other conditions, an analysis of errors was carried out to assess whether Alzheimer's Disease patients were less able to retrieve colours or objects. This analysis was possible because in the condition assessing memory for objects and colours unbound I scored memory for the whole array and for objects and colours separately. In the condition assessing memory for object-colour binding, I scored the recall of objects, colours, and of the combination. Therefore, the percentage of objects and colours recalled as single entities in the two conditions was entered in this analysis. Within group, dependent sample t-tests were carried out to assess if memory for each feature in the condition assessing object-colour binding differed from memory for each feature in the condition assessing memory for objects and colours unbound (Figure 5.3). No differences were found in the healthy elderly group when memory for objects and colours were compared across conditions [Objects: MD = 5.79, t = -1.49, p = n.s.; Colours: MD = 4.34, t = -1.57, p = n.s.]. Alzheimer's Disease patients recalled more objects in the object-colour binding condition than in the unbound

condition [MD = 16.66.9, t = -2.45, $p < 0.05$]. Alzheimer's Disease patients were less able to retrieve colours in the condition assessing memory for object-colour binding than in the condition assessing memory for unbound features [MD = 14.49, t = 2.64, $p < 0.05$].

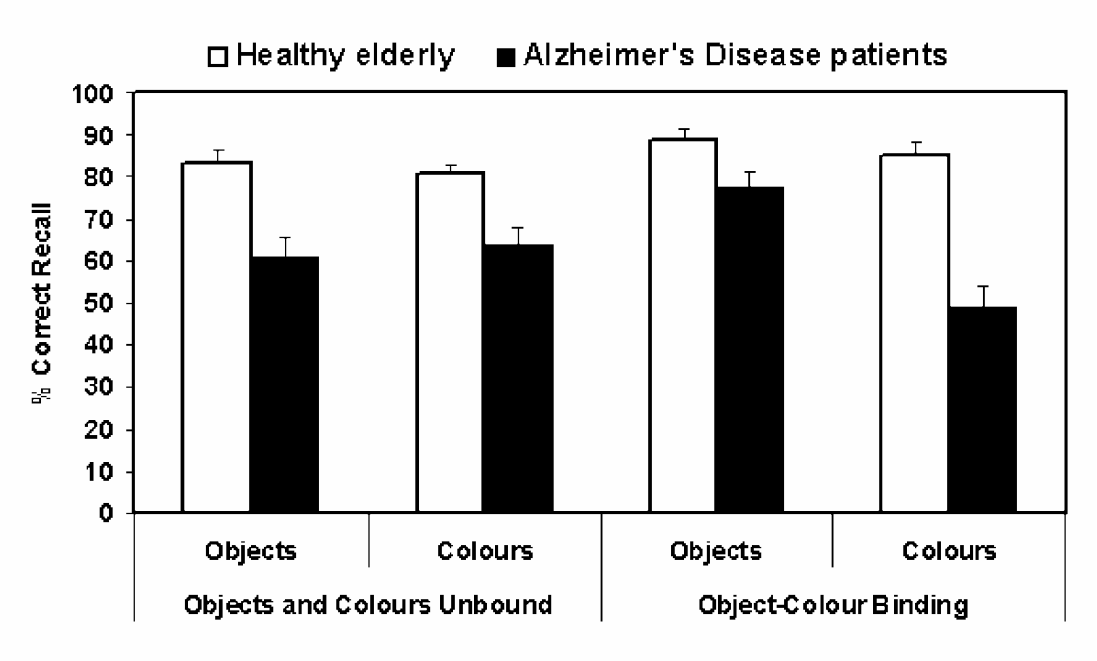

Figure 5.3. Percentage of features correctly recalled in conditions assessing memory for objects and colours unbound and object-colour binding of Experiment 13 (Error bars represent the standard errors of the mean).

5.2.4 Discussion

The results of Experiment 13 showed that Alzheimer's Disease does impair verbal short-term memory for bound information. Moreover, Alzheimer's Disease patients' impairment in recalling bound features was significantly greater than their difficulties in recalling individual features.

The analysis of errors suggests that patients with Alzheimer's Disease are particularly impaired in retaining in memory features bound together over

short period of times. Retaining colours within bound items seems to be more vulnerable than retaining objects. This finding fits well with the results by Lloyd-Jones (2005), whereby patients with Alzheimer's Disease were found less able to use colour-based than object-based information when recognizing coloured objects. This is the first empirical evidence suggesting that Alzheimer's Disease also impairs processes responsible for holding bound information in short-term memory when this information is processed within the verbal domain.

The paramount drop in memory performance for objects bound with colours observed in Alzheimer's Disease patients contrasts with a preserved memory for this type of complex information in healthy elderly. The process of binding features in visual short-term memory in healthy younger and older adults was investigated in Chapter 3. Healthy older adults were found to have poorer overall memory performance for abstract shapes and colours; however, their ability to hold these surface features bound in visual short-term memory was not affected more than their ability to hold individual features (e.g., shapes). It was suggested that age spares those processes responsible for binding surface features (i.e., shapes and colours) into integrated objects. The current experiment was not designed to investigate age effects on memory binding; however, the finding that healthy elderly had equivalent memory for bound and unbound features supports those previous observations of Chapter 3. This also suggests that the binding deficit appears to be specific to Alzheimer's Disease.

A possible caveat to Experiment 13 is that memory performance of the two groups was significantly different in conditions assessing memory for objects or colours only and for objects and colours unbound as well as for bound features. Therefore, the significant interaction observed in Experiment 13 could have been driven by a preserved ability of healthy elderly to perform a

task that did not demand enough cognitive effort. It is known that older people's impairments are more likely to show in tasks that demand greater amounts of cognitive effort (Kester et al., 2002). In order to claim specificity of these binding deficits in Alzheimer's Disease, it is important to demonstrate that under increased cognitive demands, as imposed by high memory load, the differences between Alzheimer's Disease patients and healthy elderly in the condition assessing memory for bound items persists. This issue was addressed in Experiment 14.

5.3 Experiment 14

5.3.1 Aims

Experiment 14 investigated whether the memory impairment observed in Alzheimer's Disease patients could be due to general difficulty or to a specific binding deficit. For the aims of this experiment, memory load was increased for the healthy elderly so as to reduce the differences found in conditions assessing memory for single or unbound features between groups.

5.3.2 Methods

5.3.2.1 Participants

Participants entering Experiment 14 were 20 healthy elderly and 21 Alzheimer's Disease patients diagnosed as suffering from mild to moderate Alzheimer's Disease. Out of the 20 healthy elderly, 15 were participants who had entered Experiment 13 while 5 were new participants. Out of the 21

Alzheimer's Disease patients, 16 had entered Experiment 13 and 5 were new patients. It is worth noticing that all participants who took part in both experiments went through the same number of sessions and performed the same number of experimental conditions following counterbalanced procedures. Alzheimer's Disease patients and healthy elderly entering this experiment did not significantly differ in age (Healthy elderly: M = 69.35, SD = 6.02; AD: M = 73.33, SD = 6.71; t(39) = -1.97, p = n.s.) and years of education (Healthy elderly: M = 7.25, SD = 2.97, Alzheimer's Disease patients: M = 6.81, SD = 3.66; t(46) = 0.42, p = n.s.). The same inclusion and diagnostic criteria used in Experiment 13 applied to Experiment 14. All participants gave their signed consent to take part in this study. The general neuropsychological profile of patients entering this experiment is shown in Table 5.1.

5.3.2.2 Procedure

For Experiment 14 the same task described in Experiment 13 was used. However, the size of the stimuli arrays was changed for healthy elderly. In conditions assessing memory for objects only, colours only and objects and colours unbound, healthy elderly were presented with 8 items. In the condition assessing memory for object-colour binding, healthy elderly were presented with 4 items. The other task parameters remained the same.

5.3.3 Results

Performance was analysed with a two (Group = healthy elderly vs. Alzheimer's Disease patients) by four (Condition = objects only vs. colours only vs. objects and colours unbound vs. object-colour binding) mixed-ANOVA. Mean performance levels across groups and conditions are shown in Figure 5.4. Main effects were significant for Group [$F(1,39) = 29.61$, $p <$

0.001], Condition [$F(3,117) = 18.82$, $p < 0.001$], and for the interaction [$F(3,117) = 7.35$, $p < 0.01$].

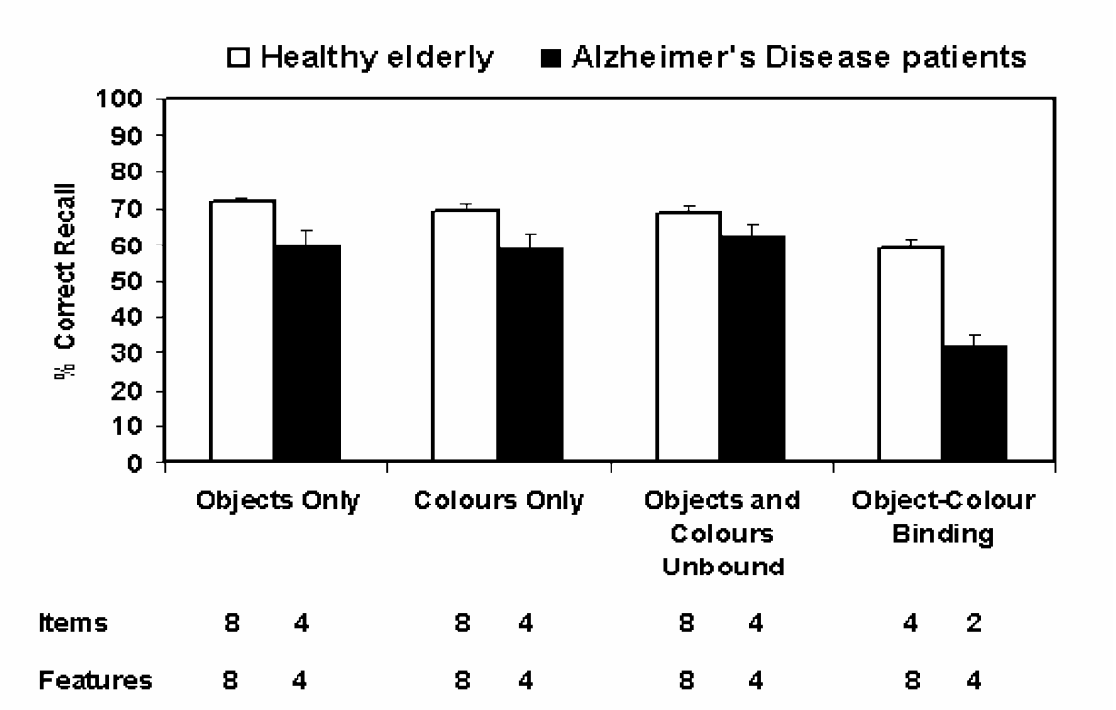

Figure 5.4. Percentage of correct recall in the Group by Condition analysis of Experiment 14 (Error bars represent the standard errors of the mean).

Pairwise comparisons performed across groups showed that Alzheimer's Disease patients performed more poorly than healthy elderly in the condition assessing memory for object-colour bindings [MD = 37.20, SE = 4.29, $p < 0.001$]. None of the other comparisons resulted in significant differences.

Pairwise comparisons performed across conditions showed that Alzheimer's Disease patients' performance in the object-colour binding condition was significantly poorer than in conditions assessing memory for objects only [MD = 28.17, SE = 5.13, $p < 0.001$], colours only [MD = 27.38, SE = 5.75, $p = 0.001$], and objects and colours unbound [MD = 30.95, SE = 4.67, $p < 0.001$]. None of the other contrasts carried out in Alzheimer's Disease patients across

conditions assessing memory for single or unbound features resulted in significant differences. There were no significant differences in any of the contrasts carried out in healthy elderly.

The results show that even when healthy elderly and Alzheimer's Disease patients had non significantly different performance in the conditions assessing memory for single and unbound features, Alzheimer's Disease patients were less able to retain in short-term memory the relatedness between items as compared to healthy elderly.

5.3.3.1 Analysis of errors

As for Experiment 13, an analysis of errors was carried out in Experiment 14. Dependent sample t-tests were performed to examine if memory for each feature in the condition assessing object-colour binding differed from memory for each feature in the condition assessing memory for objects and colour unbound (Figure 5.5). No differences were found in healthy elderly when memory for objects and colours were compared across conditions [Objects: MD = 4.17, t = -1.04, p = n.s.; Colours: MD = 0.42, t = -0.11, p = n.s.].

Alzheimer's Disease patients recalled fewer objects in the condition assessing memory for unbound features than in the condition assessing memory for bound features, however this comparison fell short of significance [MD = -14.29, t = -2.0, p = n.s.]. Alzheimer's Disease patients recalled more colours in the condition assessing memory for objects and colours unbound than in the condition assessing memory for objects bound with colours [MD = 22.22, t = 4.64, $p < 0.001$].

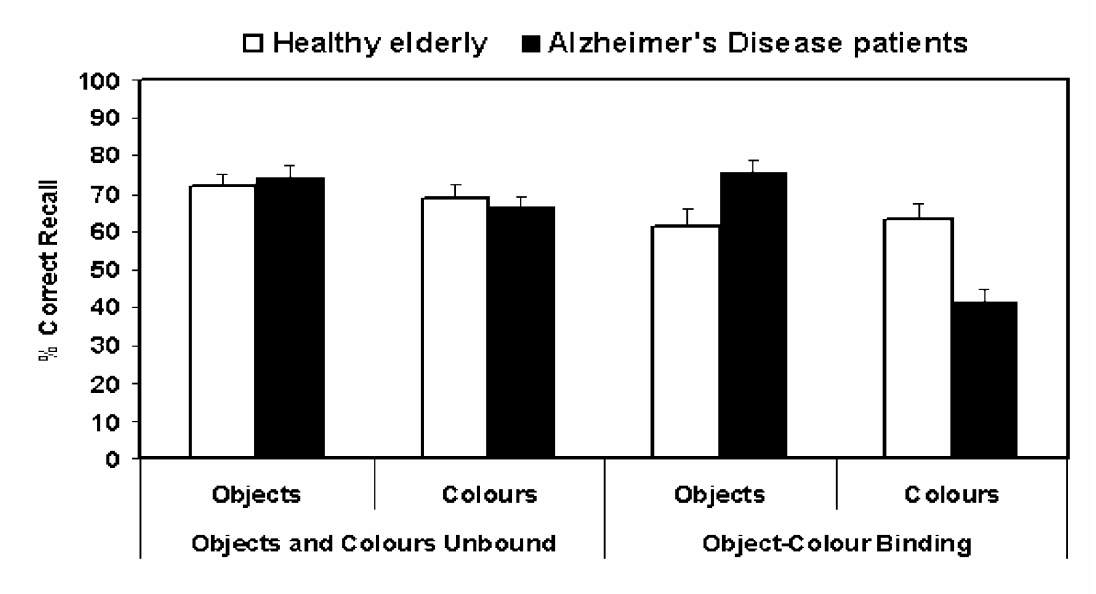

Figure 5.5. Percentage of features correctly recalled in conditions assessing memory for objects and colours unbound and object-colour binding in Experiment 14 (Error bars represent the standard errors of the mean).

Finally, given that the procedures in the two experiments were comparable participants who took part in both experiments were selected and a three-way mixed-ANOVA with Group (Healthy elderly vs. Alzheimer's Disease patients) as the between-subjects factor and Experiment (Experiment 13 vs. Experiment 14) and Condition (objects only vs. colours only vs. objects and colours unbound vs. object-colour binding) as the within-subjects factors was carried out. A total of 18 healthy elderly and 19 Alzheimer's Disease patients entered this further analysis designed to investigate the extent to which the experimental manipulation introduced in Experiment 14 had any differential impact on the overall pattern of results observed in Experiment 13.

There were significant main effects for Experiment [$F(1,35) = 19.84$, $p < 0.001$], for Group [$F(1,35) = 64.61$, $p < 0.001$], and Condition [$F(3,105) = 14.86$, $p < 0.001$]. Significant interactions were found in the analysis of Experiment by Group [$F(1,35) = 19.84$, $p < 0.001$], suggesting that healthy elderly's performance was impacted by the experimental manipulation, and in the

analysis of Group by Condition [$F(3,105) = 6.98$, $p < 0.001$], whereby the impact that the condition assessing memory for bound features versus single or unbound features had on performance in Alzheimer's Disease patients was present across experiments. The other interactions, including the three-way interaction, were non-significant, suggesting that the experimental manipulation did not impact differentially on the performance pattern across conditions. That is, the Alzheimer's Disease group showed a drop in binding performance compared with the other conditions, while the healthy elderly group did not, and this differential effect for the Alzheimer's Disease group was present in both experiments.

5.3.4 Discussion

Increasing the task demands in terms of memory load resulted in a drop in memory performance in healthy elderly to the extent that the differences between this group and the Alzheimer's Disease group observed in Experiment 13 in conditions assessing memory single or unbound features were removed. This notwithstanding, the main outcome of Experiment 13 was replicated (i.e., Alzheimer's Disease patients showed a paramount impairment in binding information in verbal short-term memory).

The analysis of errors also confirmed the findings from Experiment 13. Patients with Alzheimer's Disease were less able to retrieve colour-based than object-based information. Therefore, in two separate experiments additional support for the findings by Lloyd-Jones (2005) was provided, who suggested that Alzheimer's Disease patients can use shape but not colour when remembering coloured objects. However, in two experiments presented here, this finding has been extended to binding in verbal short-term memory.

The finding that memory for single or unbound features and memory for bound features is not significantly different in healthy elderly in both experiments suggests that memory for bound features is equivalent to memory for the same type and amount of individual features that are presented separately. This finding is consistent with results reported in Chapter 3. This also supports the suggestion that age *per se* does not affect those processes responsible for integrating features in short-term memory. Finally, the three-way ANOVA suggested that the experimental manipulation had an overall effect on performance in healthy elderly, that is it decreased to the level at which differences were removed between groups in conditions assessing memory for single or unbound features, but this manipulation did not modify the pattern of results observed in Experiment 13. That is, Alzheimer's Disease's selective binding deficit.

5.4 General discussion

The results of the experiments presented here support the hypothesis that the deficit in binding information in verbal short-term memory in patients with Alzheimer's Disease is more pronounced than their memory impairment for unrelated information. In both experiments, patients with Alzheimer's Disease performed significantly more poorly when they had to recall bound information than when they had to remember individual or unbound features. Swainson et al. (2001) reported that patients with Alzheimer's Disease performed more poorly than healthy older adults when they had to recall associations of patterns with locations during a learning paradigm. Although not acknowledged by the authors, this suggests that binding information may be impaired by Alzheimer's Disease. However, they did not assess whether this deficit was due to a difficulty in holding in memory the association of patterns with locations or just to a difficulty in holding

locations in memory. This caveat of the Paired Associates Learning Test of CANTAB was discussed in Sections 1.9.1 and 1.9.4. The results of the current experiments help to disentangle memory for bindings from memory for features. With this methodology it was shown that these deficits apply to temporary binding in verbal short-term memory in Alzheimer's Disease patients.

There are two methodological characteristics of the experiments presented in this chapter that make the finding of impaired memory for bound information in Alzheimer's Disease relevant. First, memory load was controlled across conditions by keeping constant the number of features. Additionally, the memory load for Alzheimer's Disease patients was kept within their capacity by presenting 2 objects in the condition assessing memory for bound information as compared to 3 or 4 objects presented to healthy elderly in Experiments 13 and 14 respectively. This allowed equating overall memory performance between the Alzheimer's Disease and healthy elderly groups for the single feature and unbound memory conditions. Using this experimental manipulation, patients with Alzheimer's Disease presented with a paramount memory deficit for bound information, in particular, in recalling colour-based information within bound colour-object items. By equating performance for conditions assessing memory for single and unbound features, this memory binding difficulty cannot be attributed to an overall memory impairment.

It might be argued that the task presented here could have tapped long-term memory as visual arrays were composed of highly nameable features (with strong semantic representations) and were presented for relatively long periods of times (e.g., 9 sec when 6 features were shown). However, when constructing arrays of coloured objects, colours and objects were randomly combined, with colours and objects repeated across trials in different

combinations. This made it unlikely that the pairing of features would be semantically based. Secondly, objects and colours were evenly repeated across conditions; but there was not repetition of individual or bound features within trials nor was there repetition of particular combinations of features or objects in specific locations. Memory traces for a given trial would therefore be overwritten by the array presented in the following trial, making it less likely that any long-term representation of these arbitrary and rapidly changing associations could be formed (for a discussion on learning and binding during short-term memory tasks see Section 1.5.5).

Given that we specifically avoided semantic associations between objects and colours, our task was not devised to address the issue on whether Alzheimer's Disease patients had an inability to over-ride typical semantic associations (e.g., yellow-banana). However, the results from previous studies also assessing memory for object-colour combination (Della Sala et al., 2000; Lloyd-Jones, 2005) suggest that it does not seem to be the content of these bindings or the availability of semantic clues that determines the breakdown of these binding operations in Alzheimer's Disease. Therefore, we suggest that the difficulties observed in patients with Alzheimer's Disease represent a genuine deficit in holding in verbal short-term memory associations or "bindings" of different types of features in unified representations.

This is the first empirical evidence reporting that Alzheimer's Disease affects the process of binding information in short-term. Also, the procedures used in these experiments allowed for the separation of the contribution of memory for individual items and for bound items in recalling complex events. Therefore, the results provide reliable evidence of the contribution of memory for unrelated or related information to the overall memory impairment observed in patients with Alzheimer's Disease.

5.5 Leading Ideas

The present findings have demonstrated a deficit in binding in Alzheimer's Disease for information which can easily be verbalised, with bindings between verbal labels. However, verbal short-term memory and visual short-term memory seem to operate under different principles when it comes to binding operations (see Section 1.5.3 of Chapter 1 for differences in binding semantic and arbitrary information, and Section 1.5.5 where the role that semantic cues may play in the interaction between short- and long-term memory is discussed). Furthermore, as was shown in Chapter 4, ES presented with a selective deficits in holding in visual short-term memory integrated objects while she could hold in verbal short-term memory the same objects without difficulties. Therefore, it would be worth investigating whether those processes responsible for binding visual features difficult to encode verbally in short-term memory are also impaired by Alzheimer's Disease. The next chapter presents the results of two experiments aimed at investigating this hypothesis.

CHAPTER 6

Memory binding in the detection and the differential diagnosis of Alzheimer's Disease: evidence from a visual short-term memory change detection task

6.1 Introduction

The results presented in Chapter 5 suggest that processes responsible for binding information in short-term memory are affected by Alzheimer's Disease. However, as the results presented in Chapter 3 showed, these functions may be preserved in older adults. These findings might open new possibilities for the assessment of Alzheimer's Disease as the neuropsychological tasks that have been claimed to be particularly sensitive to detecting Alzheimer's Disease (e.g., Paired Associate Learning Tasks) (Swainson et al., 2001) have also been performed poorly by healthy elderly (de Jager et al., 2002). However, the tasks presented in Chapter 3 assess recognition in visual short-term memory whereas Alzheimer's Disease patients in Chapter 5 were investigated using verbal recall in a short-term memory task. There is evidence suggesting that recall and recognition are retrieval processes mediated by different brain functions and regions (Bastin et al., 2004; Holdstock, Mayes, Gong, Roberts, & Kapur, 2005; Lowndes & Savage, 2007; Mayes et al., 2007). As was discussed in Section 1.4.3 of Chapter 1 (Part I), abundant literature has been delivered reporting the value of recognition tasks for the assessment of short-term memory binding functions. As recognition is mediated by two separate mechanisms, recollection and familiarity (Daselaar et al., 2006; Davidson & Glisky, 2002; Lowndes & Savage, 2007; Opitz & Cornell, 2006; Pashler, 1988; Ranganath,

Yonelinas, Cohen, Dy, Tom, & D'Esposito, 2004; Yonelinas et al., 1999), it has been suggested that this retrieval process may provide a better understanding of how visual short-term memory works during change detection tasks involving bound information (see Section 1.4.3 for a comprehensive review of this subject). Therefore, as healthy older adults performed these change detection tasks assessing memory for bound information no differently than they performed tasks assessing memory for single information (Chapter 3), and considering that patients with Alzheimer's Disease presented with paramount difficulties in performing free recall tasks assessing short-term memory for bound information, a question that follows would be: Do patients with Alzheimer's Disease also present with short-term memory binding deficits when recognition is the retrieval process assessed?

This new chapter addresses the recognition of visual information presented in single and bound format in patients with Alzheimer's Disease, Depression, and healthy elderly using a change detection task. By demonstrating that binding in short-term memory is a function impaired in Alzheimer's Disease patients and that this impairment does not depend on the type of visual material or the retrieval processes, it will be possible to argue that short-term memory binding deficits are universal features of Alzheimer's Disease. It would also be possible to extend the usefulness of memory binding tasks to a new memory domain (i.e., visual) and to a new retrieval process (i.e., recognition). It is worth noticing that visual short-term memory for bound information was found to be preserved in healthy elderly (Chapter 3). It would be therefore an important step forward to investigate this process in Alzheimer's Disease as short-term memory binding may be the one and only memory function that would allow separating healthy older adults from Alzheimer's Disease patients reliably, providing by this means a potential

solution to one important problem we face today for the early detection of Alzheimer's Disease in clinical settings.

One other problem in the area of the diagnosis of Alzheimer's Disease concerns the differential diagnosis between this disease and Depression. Depression is a major problem in old age and it frequently overlaps or accompanies Alzheimer's Disease in its early stages (Buerger et al., 2003; Swainson et al., 2001). Depression is indeed the most common confounding disease when geriatricians have to decide in which particular diagnostic category their older patients fall (Buerger et al., 2003; Hill & Spengler, 1997). Aware of this issue, Swainson et al. (2001) investigated which memory tasks would be more useful for the differential diagnosis of Alzheimer's Disease and depression. In their study the authors assessed this question in a group of patients with Alzheimer's Disease , a group of depressed patients, and a group of patients classified as questionable dementia (a form of Mild Cognitive Impairment), as the early detection of Alzheimer's Disease was another issued tackled by this study.

The authors found that the Paired Associates Learning Task of the CANTAB was the task that separated Alzheimer's Disease from depressed patients more accurately than any other task. In fact when performance of depressed patients and controls was collapsed and compared to that of Alzheimer's Disease patients, the percentage of overlapping responses between these groups was 7%. If this result is compared to the result of the Warrington SRMT for words**,** which had 99% of overlapping responses, one may suggest that associative memory tasks may be a tool to aid in the differential diagnosis of Depression and Alzheimer's Disease. However, the Paired Associates Learning Task of the CANTAB is a long-term memory task. The tasks proposed in the current research are short-term memory tasks. As was discussed in Chapter 1, binding or forming associations in long-term and

short-term memory seem to be functions mediated by different mechanisms. Hence it is important to assess whether the potential value of these tasks for separating Alzheimer's Disease patients from healthy elderly (as it was shown in Chapter 5) may also apply for separating Alzheimer's Disease patients from depressed patients. In addition, the Paired Associates Learning Task of the CANTAB does not separate the contribution of item memory (e.g., patterns only or location only) and memory for the binding between items (e.g., patterns and locations) to memory performance.

This new chapter further investigates the processes responsible for binding information in short-term memory in Alzheimer's Disease patients and focuses on three issues: (1) the recognition (rather than recall) of bound information, (2) the use of visual non-nameable materials (rather than the highly nameable stimuli used in Chapter 5), and, moreover (3) the study investigates the value of assessing short-term memory binding in terms of the differential diagnosis of Alzheimer' Disease and Depression.

6.2 Experiment 15

6.2.1 Aims

The aim of Experiment 15 was twofold. Firstly, it further investigated the short-term memory binding deficits observed in Alzheimer's Disease patients with a change detection task which assesses visual short-term memory for non-nameable features. If Alzheimer's Disease affects processes responsible for binding information in short-term memory in a non-material specific way, this new task would produce a pattern of results similar to that observed in Chapter 5 that is, patients with Alzheimer's Disease would present paramount difficulties for remembering bound information while

their memory for individual items would be impaired to a lesser extent. Secondly, Experiment 15 investigated whether performance in short-term memory binding tasks would be able to separate Alzheimer's Disease patients from depressed patients. If the preserved long-term associative memory functions observed in depressed patients using the Paired Associate Learning Task of the CANTAB (Swainson et al., 2001) extend to short-term memory binding functions, the performance of depressed patients should not differ from that of healthy elderly using the tasks proposed here but it should be different from that of Alzheimer's Disease patients.

6.2.2 Methods

6.2.2.1 Participants

Thirteen healthy elderly, 10 depressed patients, and 11 patients with mild to moderate Alzheimer's Disease were recruited into this experiment. Patients were diagnosed following the criteria described in Chapter 5. None of these patients suffered from other neurological or psychiatric disorder. Diagnosis was done by consultant geriatricians and psychiatrists. All patients and controls consented to take part in the study.

A one way ANOVA confirmed that patients and controls entering this experiment were not significantly different in age (Healthy elderly: M = 71.15, SD = 4.14; Depression: M = 73.5, SD = 7.76; Alzheimer's Disease patients: M = 75.0, SD = 5.69; $F(2,31) = 1.31$, p = n.s.), education (Healthy elderly: M = 15.54, SD = 3.45; Depressed: M = 13.80, SD = 3.26; Alzheimer's Disease patients: M = 13.64, SD = 3.75; $F(2,31) = 1.10$, p = n.s.), and Verbal IQ (Wechsler, 2002) (Healthy elderly: M = 107.38, SD = 14.92; Depressed: M = 108.50, SD = 5.07; Alzheimer's Disease patients: M = 105.33, SD = 5.45; $F(2,31)$

= 0.20, p = n.s.). The neuropsychological profile of patients entering this study is presented in Table 6.1.

Table 6.1. Results of the neuropsychological assessment of Alzheimer's Disease and depressed patients entering Experiment 15.

	Alzheimer Patients		Depressed Patients		t (p)
	M ± SD	Range	M ± SD	Range	
ACE (/100)	63.6 ± 12.5	(40 – 79)	90.4 ± 5.0	(82 – 95)	5.70 (0.000)
MMSE (/30)	23.3 ± 3.1	(17 – 27)	28.4 ± 1.1	(27 – 30)	6.42 (0.000)
VOSP- Object Decision (/20)	15.2 ± 2.3	(12 – 18)	17.4 ± 1.5	(15 – 19)	5.06 (0.000)
TMT B-A	220.9 ± 147.1	(42 – 483)	77.3 ± 37.9	(19 – 121)	2.37 (0.030)
Verbal Fluency (animals)	8.1 ± 4.6	(2 – 14)	18.0 ± 4.6	(9 – 24)	5.17 (0.001)
Verbal Fluency (FAS)	24.2 ± 13.2	(8 – 50)	44.4 ± 10.2	(32 – 59)	4.63 (0.000)
Rey Figure – Copy (/36)	25.0 ± 12.7	(4 – 36)	34.5 ± 1.2	(33 – 36)	2.23 (0.039)
Rey Figure – Delayed (/36)	3.9 ± 5.2	(0 – 13)	7.9 ± 8.2	(0 – 25)	2.47 (0.033)
Prose Recall (A)- Immediate	3.6 ± 3.5	(0 – 10)	15.6 ± 3.9	(9 – 20)	7.01 (0.000)
Prose Recall – Delayed	0.7 ± 1.6	(0 – 5)	12.3 ± 3.7	(7 – 19)	9.26 (0.000)
Word List – Immediate	9.2 ± 6.5	(2 – 20)	30.3 ± 4.3	(21 – 34)	9.27 (0.000)
Word List – Delayed Recall	0.1 ± 0.3	(0 – 1)	6.5 ± 2.9	(2 – 11)	7.99 (0.000)
Word List – Delayed Recognition	13.7 ± 3.1	(7 – 18)	22.5 ± 1.8	(19 – 24)	7.10 (0.000)
Visual Recognition Test - Copy	95.8 ± 10.7	(69 – 104)	101.6 ± 3.3	(94 – 104)	1.48 (0.157)
Visual Recognition Test – Recall	3.5 ± 8.1	(0 – 24)	39.0 ± 22.2	(10 – 70)	4.45 (0.000)
Visual Recognition Test – Recognition	27.8 ± 6.7	(19 – 39)	39.9 ± 5.2	(30 – 46)	4.25 (0.001)

ACE: Addenbrooke's Cognitive Examination; MMSE: Mini Mental State Examination; VOSP: Visual Object and Space Perception Battery; TMT: Trial Making Test.

As can be seen in Table 6.1 Alzheimer's Disease and depressed patients significantly differed in most of the functions assessed in the neuropsychological assessment with the exemption of the the copy phase of the Visual Recognition Test.

6.2.2.2 Stimuli and Apparatus

The stimuli and apparatus used in this experiment are the same described in Section 2.2.2.2. The task consisted of three experimental conditions: shape only, colour only, and shape-colour binding. These conditions were the same as those described in Section 3.2.2.2. For this new experiment the study display presented 3 items to healthy elderly and depressed patients and 2

items to Alzheimer's Disease patients. Previous pilot analysis carried out in healthy elderly suggested that these array sizes would avoid ceiling and floor effects. Further piloting suggested that these array sizes would also allow comparative performance of patients and controls under conditions in which differences across groups in tasks assessing memory for individual features would be minimized. Thus, this may enable the investigation of the cost of holding in visual short-term memory bindings between features when memory performance for individual features was kept at a similar level across groups. The other task parameters were the same as described in Section 3.2.2.2.

6.2.2.3 Procedures

Participants entering this experiment underwent a general screening phase whereby their colour vision was assessed using the Colour Blindness Test (Dvorine, 1963). Participants who scored more than 2 in the test were excluded from the study. They then performed a perceptual binding task which was given to rule out possible perceptual binding problems. As was discussed in Section 1.9.2, perceptual binding deficits have been found in patients with Alzheimer's Disease. To differentiate this perceptual/memory binding problems the perceptual tasks described in Experiments 4 and 5 (see Appendix 2 – I A and B) were given to patients and controls entering this experiment. Only patients with Alzheimer's Disease, Depression, and healthy elderly with performance above 90% on this task (9 out of 10 trials per type of binding should be performed correctly) were assessed further.

After the colour vision and perceptual tasks a general instruction script was presented which informed participants of the task requirements (see Appendix 2 – II). Then, each experimental condition was preceded by a specific instruction script which also included 15 practice trials. During the

task, participants were requested to take time to make their decisions as their responses were not to be timed. Several breaks were provided along the task. The entire task took 30 to 45 minutes to complete.

6.2.2.4 Statistical analysis

For the experiments presented in this chapter the Signal Detection Theory was also applied. As for Chapter 3, it was investigated whether the other response components underpinning performance in change detection tasks would differ across groups. The usefulness of the Signal Detection Theory for analysing performance during change detection tasks was discussed in Section 1.4.3 of Chapter 1 (Part I). Therefore, the dependent variables for this experiment were percentage of correct recognition, sensitivity for change detection (A'), and Response Bias (β).

6.2.3 Results

Percentage of correct recognition: The percentage of correct recognition was entered in a two-way mixed-ANOVA with Group (Healthy elderly vs. Alzheimer's Disease patients vs. Depressed patients) as the between-subjects factor and Condition (shape only vs. colour only vs. shape-colour binding) as the within-subjects factor. A significant main effect was found for Group [$F(2,31) = 19.81$, $p < 0.001$]. As the Mauchly's test of sphericity was found to be significant, the Greenhouse-Geisser correction factor was applied for the within-subjects factor analysis. After this correction a significant main effect was found for Condition [$F(1.34,41.43) = 57.02$, $p < 0.001$] as well as for the interaction [$F(2.67,41.43) = 7.72$, $p < 0.001$] (Figure 6.1A).

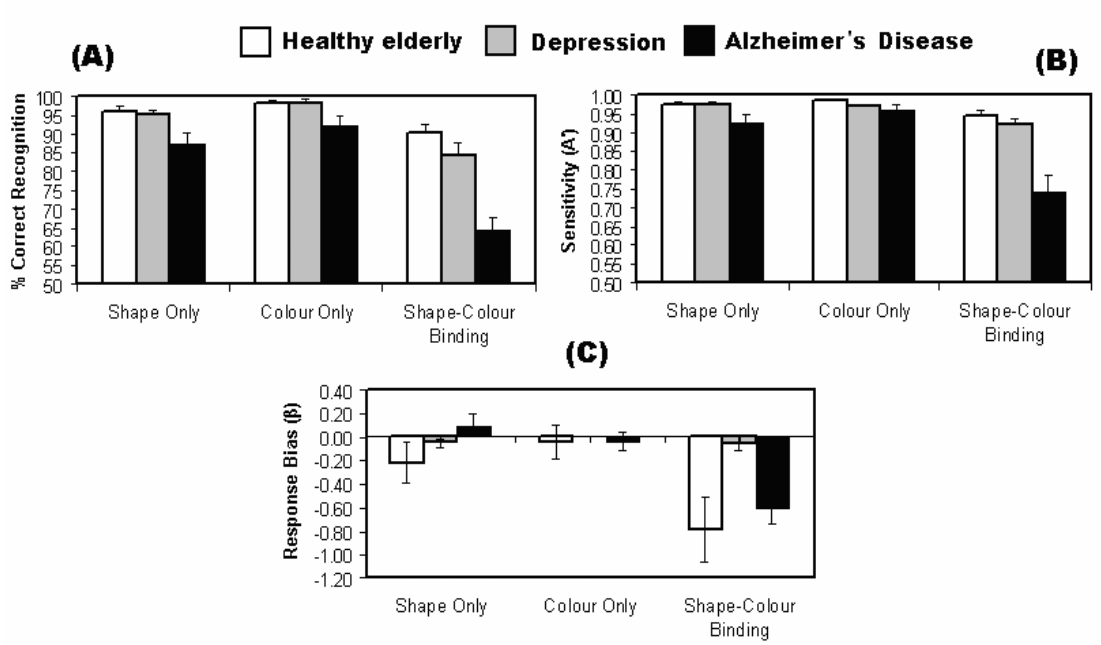

Figure 6.1. (A) Percentage of correct recognition above chance (50%), **(B)** Sensitivity (A'), and **(C)** Response Bias (β) for the three experimental conditions in healthy elderly, depressed and Alzheimer's Disease patients in Experiment 15 (Error bars represent the standard errors of the mean).

Post-hoc tests performed across Group using Bonferroni corrections showed that healthy elderly and depressed patients did not differ [MD = 2.16, SE = 2.32, p = n.s.]. Alzheimer's Disease patients however performed significantly more poorly than both healthy elderly [MD = 13.50, SE = 2.25, $p < 0.001$] and depressed patients [MD = 11.34, SE = 2.41, $p < 0.001$]. Additional post-hoc tests, also using Bonferroni corrections, were carried out across the three groups for each condition separately what resulted in 9 pairwise comparisons (alfa = 0.0055). This analysis showed that healthy elderly and depressed patients did not differ in any of the experimental conditions. Alzheimer's Disease patients, healthy elderly, and depressed patients' performance did not differ significantly in conditions assessing memory for shape or colour only. In the shape-colour binding condition however, Alzheimer's Disease patients performed significantly more poorly than

healthy elderly [MD = 25.75, SE = 3.98, $p < 0.001$] and than depressed patients [MD = 19.87, SE = 4.25, $p < 0.001$].

Pairwise comparisons using Bonferroni corrections were carried out across conditions for each group separately. Using the same alfa threshold set above, this analysis showed that healthy elderly's performance did not differ significantly in any contrast performed across conditions. For Alzheimer's Disease patients, memory performance for shape-colour binding was poorer than performance for shape only [MD = 22.71, SE = 4.13, $p < 0.001$] and than for colour only [MD = 27.84, SE = 4.38, $p < 0.001$]. Performance in these two last conditions in Alzheimer's Disease patients did not differ. For depressed patients memory performance in the condition assessing memory for shape-colour binding was poorer than for colour only [MD = 14.06, SE = 2.95, $p = 0.003$]. No other contrast in this group was found to be significant.

A': A significant main effect was found for Group [$F(2,31) = 16.24$, $p < 0.001$]. The test of sphericity was found significant hence the Greenhouse-Geisser correction was applied. For the within-subjects factor analysis a significant main effect was found for Condition [$F(1.15,35.57) = 28.87$, $p < 0.001$] as well as for the interaction [$F(2.29,35.57) = 8.96$, $p < 0.001$] (Figure 6.1B).

Post-hoc tests across Group using Bonferroni corrections showed that healthy elderly and depressed patients did not differ [MD = 2.16, SE = 2.32, p = n.s.]. Alzheimer's Disease patients however showed significantly poorer sensitivity than both healthy elderly [MD = -0.09, SE = 0.017, $p < 0.001$] and depressed patients [MD = -0.08, SE = 0.018, $p < 0.001$]. Additional post-hoc tests were carried out across groups for each condition separately using the alfa threshold mentioned above. This analysis showed that Alzheimer's Disease patients had less sensitivity than healthy elderly [MD = -0.204, SE = 0.039, $p < 0.001$] and depressed patients [MD = -0.18, SE = 0.042, $p < 0.001$]

only in the condition assessing memory for shape-colour binding. None of the other contrasts resulted in significant effects.

Pairwise comparison using Bonferroni corrections were carried out across conditions for each group separately. No contrasts performed across conditions in the healthy elderly group showed significant effects. For Alzheimer's Disease patients, sensitivity for changes in shape-colour binding was poorer than for shape only [MD = -0.18, SE = 0.048, p = 0.001] and than for colour only [MD = -0.216, SE = 0.051, $p < 0.001$]. Sensitivity in these two last conditions did not differ. For depressed patients none of the contrasts performed across conditions showed significant effects.

Beta: Significant main effects were found for Group [$F(2,31) = 4.18$, p = 0.025] and for Condition [$F(2,62) = 7.54$, $p < 0.01$] but not for the interaction [$F(4,62) = 1.75$, p = n.s.] (Figure 6.1C).

Pairwise comparisons using Bonferroni corrections carried out across Group showed that no contrast resulted in significant effect. Pairwise comparisons carried out across Condition showed significantly more response bias toward "same" response in the condition assessing memory for shape-colour binding than in shape only [MD = -0.43, SE = 0.15, p = 0.028] and colour only [MD = -0.45, SE = 0.125, $p < 0.01$]. Response bias in the condition assessing memory for shape only or colour only did not differ.

6.2.4 Discussion

Concerning the hypotheses for Experiment 15 it can be concluded that Alzheimer's Disease does impair those processes responsible for holding in visual short-term memory bound features into integrated objects, extending

by this mean previous findings of Chapter 5 showing short-term memory binding deficits in Alzheimer's Disease patients but in the verbal domain.

Whereas Alzheimer's Disease patients' performance in conditions assessing memory for single features did not differ from that of healthy elderly and depressed patients, in the condition assessing memory for shape-colour binding, Alzheimer's Disease patients' performance was significantly poorer than that of healthy elderly and depressed patients. This suggests that short-term memory binding deficits in Alzheimer's Disease are over and above deficits for single features. This fits with the suggestion made in Chapter 5 in which the recall of bound verbal features was found to be impaired in Alzheimer's Disease patients to a much greater extent than their recall of individual objects or colours. The fact that healthy elderly and depressed patients did not differ in any experimental condition suggests that this deficit seems to be specific to Alzheimer's Disease. Therefore, short-term memory binding deficits may help to differentiate Alzheimer's Disease from healthy elderly as it was shown in Chapter 5 and in the current experiment, and from depressed patients as the results of the present experiment suggest. The Signal Detection Theory analysis suggested that poor sensitivity may explain why Alzheimer's Disease patients were less able to detect changes in shape-colour bindings as compared to healthy elderly and depressed patients. However, preferences for choosing a particular response (i.e., response bias) did not account for these differences.

One other result from this experiment which supports previous findings presented in Chapter 3 is that healthy elderly can retain in visual short-term memory information about shapes and colour bound in an object-based representational format. Remembering bindings between shapes and colours was not more difficult for healthy elderly than remembering shapes only or colour only, a finding that has been consistently shown across different

experiments of this thesis. Depressed patients' memory performance was better for colour only than for shape-colour binding. As for healthy elderly, for depressed patients it was not more difficult to remember shapes bound with colours than shape only. These new findings are consistent with previous findings suggesting that colour is a feature easy to remember and that shape seems to drive memory for the binding between these features. They also suggest that binding functions are preserved in patients with depression. Alzheimer's Disease however, seems to disrupt this representational format as for these patients it was more difficult to remember the binding between features than each feature presented as a single entity. Between-groups contrasts showed that differences in performance between healthy elderly and depressed patients in the condition assessing memory for shape-colour binding was non significant while it was paramount between both groups and Alzheimer's Disease patients. This suggests that Alzheimer' Disease profoundly impairs those processes responsible for holding in visual short-term memory bindings between different types of features.

The task used in Experiment 15 investigated the binding in visual short-term memory of different types of features. In Chapter 3 however, it was suggested that binding the same type of feature (i.e., colour) in visual short-term memory was also a process not affected by age. The following experiment investigated whether such colour-colour binding would also help to differentiate between healthy elderly, depressed, and Alzheimer's Disease patients with similar efficiency as was observed in Experiment 15.

6.3 Experiment 16

6.3.1 Aims

This new experiment was aimed at investigating whether the short-term representation of bindings made of the same feature type in memory was affected in patients with Alzheimer's Disease and whether it could also help to differentiate between healthy elderly, depressed, and Alzheimer's Disease patients. If the integrative processes underlying short-term memory functions responsible for binding across feature dimensions are shared with those responsible for binding within dimension, the results of Experiment 15 should be replicated in this new experiment.

6.3.2 Methods

6.3.2.1 Participants

The same participants recruited into Experiment 15 took part in this experiment.

6.3.2.2 Task design

The task for this experiment used three experimental conditions: colour only, colours unbound, and colour-colour binding. These conditions were the same as described in Experiment 5. The only difference is that in the current experiment healthy elderly and depressed patients were presented with arrays of 3 items and Alzheimer's Disease patients were presented with arrays of 2 items. The reasons for selecting these array sizes were the same

given in Experiment 15. The other task parameters remained as for Experiment 5.

6.3.2.3 Procedures

The same procedures described in Experiment 15 were used in this experiment.

6.3.2.4 Statistical analysis

The same methodology for processing and interpreting the results described in Experiment 15 was used in this new experiment.

6.3.3 Results

Percentage of correct recognition: A significant main effect was found for Group [$F(2,31) = 10.26$, $p < 0.001$]. The Greenhouse-Geisser correction was applied for the within-subjects factor analysis. After this correction a significant main effect was found for the type of experimental Condition [$F(1.27,39.53) = 94.22$, $p < 0.001$]. The effect of the interaction was found to be marginal [$F(2.55,39.53) = 2.44$, $p = 0.05$] (Figure 6.2A).

Post-hoc analysis across groups using Bonferroni corrections showed that healthy elderly and depressed patients did not differ [MD = 2.66, SE = 2.44, p = n.s.]. Alzheimer's Disease patients however performed more poorly than both healthy elderly [MD = 10.51, SE = 2.38, $p < 0.001$] and depressed patients [MD = 7.85, SE = 2.54, $p = 0.012$]. Additional post-hoc tests were carried out across groups for each condition separately. This analysis showed that healthy elderly and depressed patients did not differ in any of the experimental conditions. In the condition assessing memory for colour-

colour binding Alzheimer's Disease patients performed more poorly than healthy elderly [MD = 9.36, SE = 2.02, $p < 0.001$] but not than depressed patients [MD = 6.52, SE = 2.16, p = n.s.].

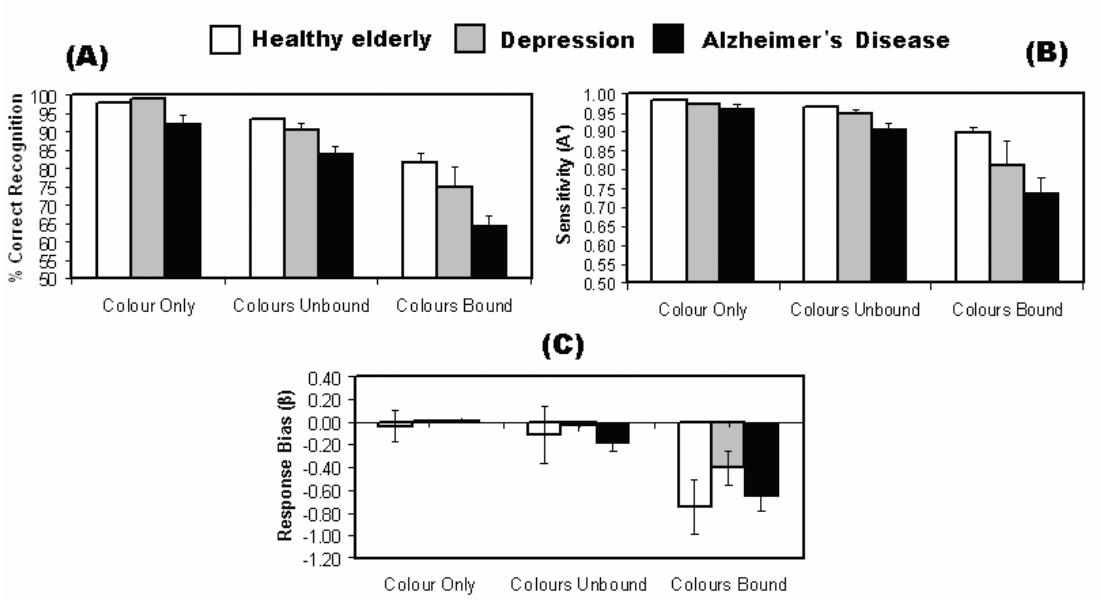

Figure 6.2. (A) Percentage of correct recognition above chance (50%), **(B)** Sensitivity (A'), and **(C)** Response Bias (β) for the three experimental conditions in healthy elderly, depressed, and Alzheimer's Disease patients in Experiment 16 (Error bars represent the standard errors of the mean).

Pairwise comparisons were carried out across conditions for each group separately. These contrasts showed that healthy elderly's memory performance in the condition assessing memory for colour-colour binding was poorer than in conditions assessing memory for colours unbound [MD = 11.91, SE = 3.05, $p < 0.01$] and colour only [MD = 19.11, SE = 2.49, $p < 0.001$]. Memory performance in colours unbound condition was poorer than in colour only [MD = 4.20, SE = 1.12, p = 0.014]. For Alzheimer's Disease patients, the drop in memory performance in the condition assessing memory for colour-colour binding as compared to colours unbound was significant [MD = 19.70, SE = 2.46, $p < 0.001$] and much larger than that of

healthy elderly. The same was observed for the contrasts between colour-colour binding and colour only [MD = 28.21, SE = 3.16, $p < 0.001$] and between colours unbound and colour only [MD = 8.51, SE = 1.84, $p < 0.001$]. For depressed patients, performance in the condition assessing memory for colour-colour binding was poorer than that for colours unbound [MD = 15.63, SE = 3.95, $p = 0.001$] and than for colour only [MD = 24.06, SE = 5.37, $p < 0.001$]. Memory performance for colours unbound was poorer than that for colour only [MD = 8.43, SE = 1.62, $p < 0.001$].

A': A significant main effect was found for Group [$F(2,31) = 6.33$, $p < 0.01$]. After correcting the degrees of freedom using the Greenhouse-Geisser epsilon, a significant main effect was found for Condition [$F(1.07,33.10) = 41.09$, $p < 0.001$] but not for the interaction [$F(2.14,33.10) = 2.66$, p = n.s.] (Figure 6.2B).

Post-hoc tests across groups using Bonferroni corrections showed that healthy elderly and depressed patients did not differ [MD = 0.037, SE = 0.022, p = n.s.]. Alzheimer's Disease patients showed significantly poorer sensitivity for change detection than healthy elderly [MD = 0.08, SE = 0.022, $p < 0.01$] but not than depressed patients [MD = 0.04, SE = 0.023, p = n.s.].

Pairwise comparison using Bonferroni corrections were carried out across conditions. These contrasts showed that sensitivity for change detection in the condition assessing memory for colour-colour binding was worse than sensitivity for colours unbound [MD = 0.13, SE = 0.021, $p < 0.001$] and than for colour only [MD = 0.16, SE = 0.023, $p < 0.001$]. Sensitivity for change detection in colours unbound was worse than for colour only [MD = 0.032, SE = 0.005, $p < 0.001$].

Beta: No effect of group was found for response bias [$F(2,31) = 0.56$, p = n.s.]. There was a significant main effect of the type of experimental condition [$F(2,62) = 13.45$, $p < 0.01$] but there was no interaction between these factors [$F(4,62) = 0.40$, p = n.s.] (Figure 6.2C).

Pairwise comparisons carried out across conditions showed significantly more response bias toward "same" response in the condition assessing memory for colour-colour binding than in colours unbound [MD = -0.49, SE = 0.11, $p < 0.001$] and colour only [MD = -0.60, SE = 0.14, $p < 0.001$]. Response bias in the condition assessing memory for colours unbound and colour only did not differ.

6.3.4 Discussion

The overall pattern of results observed in Experiment 15 was replicated in this new experiment. Alzheimer's Disease patients once again performed more poorly on the task and there was a significant effect of condition with worse scores for the binding condition and the interaction strongly tended towards significance. Alzheimer's Disease patients performed significantly worse than the healthy elderly in the colour-colour binding condition, and depressed patients performance fell in between performance of healthy elderly and Alzheimer's Disease patients. However, this drop in memory performance observed in depressed patients did not reach the threshold of significance when it was compared to performance of healthy elderly. In fact post-hoc contrasts proved that healthy elderly and depressed patients performed equivalently in the three experimental conditions whereas performance of both groups differed significantly from that of Alzheimer's Disease patients overall. However, the initial suggestion of depressed patients' performance in colour-colour binding condition falling in between the other two groups was corroborated by further post-hoc tests which

showed that depressed patients' memory performance in the colour-colour binding condition did not differ from that of Alzheimer's Disease patients nor from that of healthy elderly. The results of the Signal Detection Theory suggest that sensitivity for change detection was poorer overall in Alzheimer's Disease patients but it did not interact with the type of experimental conditions hence, it does not explain the larger drop in memory performance in the condition assessing memory for colour-colour binding observed in Alzheimer's Disease patients. As for Experiment 15, response bias did not account for any of these differences.

Experiment 16 also corroborated previous findings presented in Chapters 2 and 3 as well as by other authors (Olson & Jiang, 2002; Wheeler & Treisman, 2002; Xu, 2002) suggesting that remembering bicoloured objects with colours bound is a more difficult task than remembering bicoloured objects with colours unbound or than remembering unicoloured objects. This was true for the three groups assessed here, but it was significantly greater for Alzheimer's Disease patients, suggesting that Alzheimer's Disease may impair those processes responsible for integrating colours in visual short-term memory more severely.

6.4 General discussion

The results of Experiments 15 and 16 further support the claim that Alzheimer's Disease impairs processes responsible for holding bound features in visual short-term when these features are processed either across dimensions (Experiment 15) or within dimension (Experiment 16). The results of this chapter allow extending previous findings of Chapter 5 to a new memory domain (i.e., visual short-term memory) and to a new retrieval process (i.e., recognition). This suggests that Alzheimer's Disease may impair

binding functions in short-term memory in a more general fashion which does not depend on a particular type of material or retrieval process. Furthermore, visual short-term memory binding functions seem to differentiate between Alzheimer's Disease patients from depressed patients, especially when bindings comprise different types of features such as shapes and colours.

These findings fit well with those reported by Swainson et al. (2001). In their study they used a task that tapped the process of forming long-lasting associations between different types of information (i.e., objects and locations). Although they did not assess memory for each feature separately, they found that remembering the combination (i.e., object + location) was extremely difficult for Alzheimer's Disease patients, resulting in an impairment in relation to both healthy elderly and depressed patients. Similar differences between Alzheimer's Disease patients and healthy elderly have been reported by other authors using the same tasks (Fowler et al., 2002; O'Connell et al., 2004). However, the results of the experiments presented in this chapter indicate that binding deficits may be underpinning these associative memory difficulties observed in Alzheimer's Disease patients whereas tasks used in these earlier studies cannot provide this evidence. Recent reports suggest that binding in short-term and long-term memory may be functions subserved by different mechanisms (Colzato et al., 2006; Logie et al., 2009; Treisman, 2006). Hence, the results of Experiment 15 and 16 suggest that further research will be required to assesses whether these long-term associative memory deficits observed by other authors in Alzheimer's Disease patients (Lindeboom et al., 2002; Swainson et al., 2001) may also be accounted for by defects in binding different items into single units or in remembering each items individually.

In addition to having demonstrated a deficit for bound as compared with unbound or single features in Alzheimer's Disease patients, an issue currently neglected by Paired Associates Learning Tasks, the tasks presented here have also proved to be insensitive to the effects of age. Therefore, the deficit reported here reflects an impairment associated to the development of the disease as healthy older adults have no difficulties in performing these tasks (see Chapter 3 for evidence about this preserved ability in normal ageing). It is worth noting that other response components assessed through the Signal Detection Theory suggested that poor sensitivity for change detection may underlie poor performance in Alzheimer's Disease patients especially when these changes occurred between features of different types. However, Alzheimer' Disease seems not to impact differentially on response bias during memory for single or bound features.

One other finding of these experiments is that tasks assessing memory for the binding of different types of features seem to be more effective at differentiating Alzheimer's Disease and Depression than tasks assessing memory for the binding of the same feature type. There is evidence in the literature on neurocognition and Depression suggesting that depressed patients, even when correctly medicated, have memory problems and that these memory problems have been found to be associated to impairments in medial temporal lobe structures (Gualtieri, Johnson, & Benedict, 2006). These memory impairments seem to involve deficits in encoding or retrieval and in recall or recognition (Brand, Jolles, & Gispen-de, 1992; Burt, Zembar, & Niederehe, 1995). However, they have been found to be more evident when the effort required by tasks is greater (e.g., recall tasks). As was shown in Chapter 2, binding information within the same feature dimension seems to be more resource demanding than binding features across dimensions. This claim is supported by the Multiple Resources Theory which suggests that binding the same type of feature would result in greater interference due to

competition within a single dimension (Olson & Jiang, 2002). It might be possible that this greater interference due to within-dimension binding could have resulted in this memory impermanent described in depressed patients. Other possible reasons behind this poor performance could be the use of medication and the severity of the depression. None of the patients entering this experiment was using tricyclic antidepressants by the time of the assessment, drugs that are known to have more impact on cognitive performance. The average score in the Geriatric Depression Scale was 15.3 (SD = 5.7). The standard deviation of the Geriatric Depression Scale was big and this was due to one depressed patient scoring 6 in this scale (the other scores were between 10 and 21). This patient however, showed a neuropsychological background within the range of the group and was on Selective Serotonin Reuptake Inhibitors by the time of the assessment (i.e., Sertraline). The average Geriatric Depression Scale however suggests a severe form of Depression. This observation in addition to the difficulty of the task may explain why within-dimension binding may be a function more affected by Depression hence less specific for differentiating between Alzheimer's Disease and depressed patients. Finally, it may be argued that the small sample of depressed patients may have hampered between groups comparisons. Future research is required to investigate whether this effect of depression on short-term memory binding of features of the same type persists when increasing the number of patients.

6.5 Leading Ideas

Results presented in Chapter 5 and 6 have confirmed the hypothesis that Alzheimer's Disease impairs selectively those functions responsible for binding information in short-term memory regardless of the type of material (i.e., verbal or nonverbal) and the retrieval process (i.e., recall or recognition).

These short-term memory binding tasks proved to be sufficiently sensitive to separate Alzheimer's Disease patients from healthy older adults and to differentiate them from depressed patients particularly when features of different types were bound together. One question arising from these finding is whether short-term memory binding tasks may also be sensitive enough to detect cognitive changes in the course of Alzheimer's Disease well before other traditional memory tasks, which are part of the neuropsychological assessment currently used for detecting this neurodegenerative disorder. One useful approach to investigate this possibility would be assessing carriers of gene defects that lead to the development of Alzheimer's Disease and who are still asymptomatic. This approach was employed in Chapter 7.

CHAPTER 7

Could tasks assessing binding in visual short-term memory detect memory changes in Alzheimer's Disease in its asymptomatic stages?

7.1 Introduction

Long-term memory binding seems not to be the only associative memory function that is impaired by Alzheimer's Disease in its early stages. As was shown in Chapters 5 and 6, short-term memory binding seems to be impaired by Alzheimer's Disease in a more specific fashion. This specificity arises from the fact that healthy elderly have been found to have preserved short-term memory binding functions, as it was shown in Chapter 3 and throughout Chapters 4, 5 and 6. This suggests that short-term memory binding tasks may help to differentiate between healthy older adults from those with Alzheimer's Disease.

This new chapter aims at providing further support to the claim that short-term memory binding tasks would aid in the detection of Alzheimer's Disease. To accomplish this goal, individuals suffering from a genetic disorder that leads to the development of Alzheimer's Disease were assessed using the short-term memory tasks devised for this project. The main aim of this chapter was to investigate whether short-term memory binding functions could also help to distinguish, behaviourally, between carriers of a gene defect that leads to the development of Alzheimer's Disease from relatives who do not carry this genetic defect. If this hypothesis proves valid,

the claim that short-term memory binding tasks may aid in the early detection of Alzheimer's Disease would be supported.

As this chapter concerns the sensitivity of short-term memory binding tasks for the detection of cognitive changes in Alzheimer's Disease, I would direct the attention of readers to Chapter 1 (Section 1.9.1, Part II) where a thorough review of this subject was presented. In this introduction I will rather focus on the general features of this genetic form of Alzheimer's Disease and on the value of investigating the genetic forms of the neurodegenerative diseases to explore the physiopathological mechanisms underlying these disorders. I shall then present the results of one experiment which addressed two main issues. One concerned the usefulness of short-term memory binding tasks in the early detection of Alzheimer's Disease. The second investigated the age at which short-term memory binding problems can be detected in this form of Alzheimer's Disease in its asymptomatic stages (i.e., asymptomatic Carriers).

7.2 Genetic and neuropathological features of Alzheimer's Disease due to the mutation E280A found in Antioquia, Colombia

Alzheimer's Disease E280A is an autosomic-dominant genetic disorder in which 50% or more of offspring will develop the disease. Figure 7.1 shows a genealogy of 13 families studied in this population in which the high inheritance of the genetic defect can be observed along 8 generations.

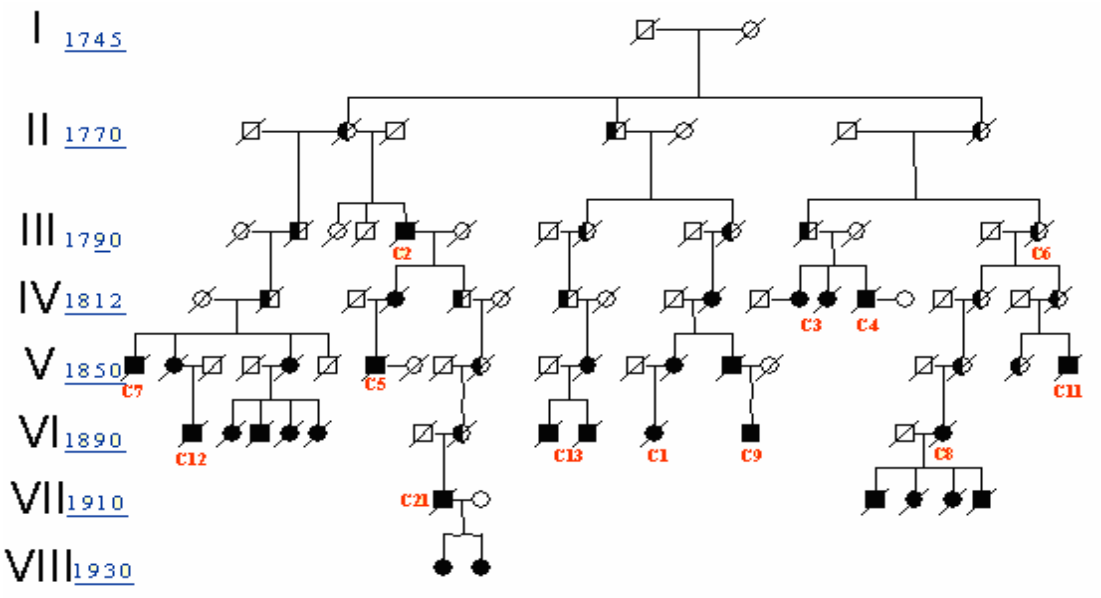

Figure 7.1. Genealogical tree of 13 families (C1 – C13) with E280A associated Alzheimer's Disease. Filled items means affected with the mutation. The diagonal line crossing the items means death. Roman numbers are generations and the Arabic numbers are years (see also Lopera et al., 1997 for other family trees and a more thorough description of this disorder).

It is considered an early-onset variant as the average age of onset has been found to be 46.8 even though it ranges from 34 to 62 (Lopera et al., 1997). The disease results from the abnormal expression of the codon 280 of the Preseniline-1 gene in the chromosome 14. This abnormal expression results from a mutation characterized by a Glutamic Acid to Alanine (two genetically coded amino acids) substitution (Glu280Ala) (Lemere et al., 1996). As a consequence, an abnormal increase in the overall proteolytic activity of the amyloid precursor protein (APP) elicits the production of Aβ peptides in the central nervous system, more specifically of Aβ42 (this peptide can be found increased in cerebrospinal fluid and this is considered a biomarker of Alzheimer's Disease) (Rachakonda, Pan, & LE, 2004). This Aβ peptide forms plaques in the brain as the disease progresses. These amyloid deposits are present in the hallmark lesions of Alzheimer's Disease (i.e., neuritic plaques

and neurofibrillary tangles), and are thought of as the responsible pathological mechanisms for the neuronal death (see Appendix 8 for slides of the hippocampus showing the neuronal death in E280A associated Alzheimer's Disease) (Caputo & Salama, 1989; Caputo, Scott, Sobel, Sygowski, Wischik, & Brunner, 1992). The detection of Aβ42 in cerebrospinal fluid is considered a biological marker for Alzheimer's Disease (Mayeux et al., 1999; Rachakonda et al., 2004). The neuropathological findings on brains of sufferers from this disease have met the criteria for Alzheimer's Disease (Lopera et al., 1997; Velez, Arellano, Cardona, Jimenez , Lopera, & Felipe, 2004). This suggests that despite this being an early-onset genetic variant of the disease, its pathological outcomes do not differ from those described in the late-onset sporadic Alzheimer's Disease (see Lopera et al., 1997 for a detailed description of these neuropathological findings).

This specific disorder was described in Antioquia, a province of Colombia, South America, where approximately 25 families encompassing between 2000 and 3000 members have been screened (Lopera et al., 1997). This has been considered the largest kindred of genetic Alzheimer's Disease studied to date (see Appendix 9 for the geographic distribution of these families in Antioquia, Colombia).

7.3 Clinical features of Alzheimer's Disease E280A

Among the clinical manifestations presenting in this hereditary disorder, memory problems are considered the earliest and most common symptoms. These are followed by personality and behavioural changes, language difficulties, depression, headache, and by the end of the disease gait disturbances and seizures (Lopera et al., 1997). Although the clinical features of this familial variant do not differ substantially from those described in the

sporadic Alzheimer's Disease, the neurodegenerative process in this genetic condition seems to be more rapidly deteriorating than in the non-familial form. For example, while the average survival period of patients with sporadic Alzheimer's Disease is 10 years after the diagnosis, patients with this genetic variant survive for approximately 8 years (although it may vary depending on the age of detection).

Among those carriers of this gene defect who have not yet reached criteria for Alzheimer's Disease, there are some who complain about memory problems even years before the disease becomes clinically detectable. Based on these early memory complaints carriers have been split in those with and without memory symptoms (Ardila et al., 2000). The neuropsychological assessment of these subgroups has shown that in fact there are significant cognitive changes in carriers who complain of memory impairments. These carriers with memory symptoms are those in a stage of the disease that may correspond to the Mild Cognitive Impairment phase described in the sporadic form of Alzheimer's Disease (Petersen, 2004). This suggests that the brain deterioration begins well before the clinical picture fulfils criteria of Alzheimer's Disease.

Studies have shown that carriers who complain about memory problems perform significantly more poorly than their healthy relative non-carriers in the following neuropsychological tests: Mini-Mental State Examination, Naming Test (Low Frequency), Memory of Words Test, Recall of Drawings, Wechsler Memory Scale (Logical Memory, Associative Learning, and Total Score), Rey-Osterrieth Complex Figure (Immediate Recall Condition), Boston Diagnostic Aphasia Examination (Complex Ideational Material Subtest), Memory of Three Phrases Test, Serial Verbal Learning (maximum score and Delayed Recall), Knopman Test (First Trial, Second Trial, and Recall after 5 Minutes), Digit Symbol, and Visual "A" Cancellation Test (Additions). These

results supported the hypothesis that memory complaints represent the earliest symptom of familial Alzheimer's Disease, suggesting by this mean that as for the sporadic Alzheimer's Disease, the genetic form of the disease also presents primarily as an amnesic syndrome. Among other minor cognitive impairments found were mild anomia, concentration difficulties and defects in the understanding of complex verbal material (Ardila et al., 2000).

Important social characteristics of this population are low education and high familiar interbreeding. The high interbreeding has been considered one important factor underpinning the propagation of the gene defect across large clusters of individuals within these families (Lopera et al., 1997). As an autosomal dominant disease it is expected that approximately 75% of offspring would be affected. However, as Figure 7.1 shows, in the VI generation some families had 100% of offspring affected. This unexpectedly high proportion suggests that other factors may modify the inheritance pattern of this variant of Alzheimer's Disease. The low education has been considered a disease-modifying factor which affects directly the age of onset (the higher the education the earlier the detection as more educated individuals seek for help first) but inversely the survival (less educated people, who live in rural areas, live longer) (Lopera et al., 1997; Pastor et al., 2003). These features of the disease are relevant to this study as well, as the impact that a low socio-cultural background (e.g., low education) has on neuropsychological testing has been well documented in previous studies (Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology, 2001).

7.4 Advantages of the genetic forms of neurodegenerative diseases

There seems to be a consensus in that more effort should be addressed to detect Alzheimer's Disease earlier. This stems from the fact that the earlier the detection of the disease the wider the scope for actions that can be implemented to modify its devastating course. In line with this aim, researchers working on this area have focused on conditions whose sufferers are more likely to convert to Alzheimer's Disease. In doing so, several different classifications have been postulated such as Mild Cognitive Impairment (MCI), Age Associated Memory Impairments (AAMI), Age-Associated Cognitive Decline (AACD), Age-Related Cognitive Decline (ARCD), or Benign Senescent Forgetfulness (BSF) (Crook, Feher, & Larrabee, 1992; Petersen & Negash, 2008; Petersen, Smith, Waring, Ivnik, Tangalos, & Kokmen, 1999; Small, 2001; Small, Stern, Tang, & Mayeux, 1999; Stoll, Hafner, Pohl, & Muller, 1994).

Among these forms, the amnestic Mild Cognitive Impairment is the one that have been associated to the highest risk for developing Alzheimer's Disease (Petersen, 2004; 2006; 2007; Petersen et al., 1999; Petersen et al., 2001; Petersen & Knopman, 2006; Petersen & Negash, 2008). Therefore, more effort has been allocated to investigate what mechanisms underlie the conversion of amnestic Mild Cognitive Impairment to Alzheimer's Disease. These efforts have been worthwhile as they have contributed to shedding light into the physiopathology of Mild Cognitive Impairment as well as to improving the theoretical constructs of tasks aimed at detecting Alzheimer's Disease. However, and fortunately, the rate of conversion from Mild Cognitive Impairment to dementia is 10% to 15% per year (Petersen, 2004; Petersen & Knopman, 2006) reaching up to 21.9% over a period of 3 years (Gabryelewicz et al., 2007). This suggests that although Mild Cognitive Impairment is a

condition that may give insights about the mechanisms leading to Alzheimer's Disease and that it provides a favourable scenario to assess the reliability of tasks aimed at detecting early this disorder, the potential value of this condition for such purposes is still limited as a great deal of Mild Cognitive Impairment patients will never develop Alzheimer's Disease (e.g., those labelled non-converter MCI; Fowler et al., 2002).

However, bringing those hypotheses drawn upon Mild Cognitive Impairment patients to individuals suffering from a genetic deficit that invariably leads to Alzheimer's Disease will help to override these limitations. This may be seen as an advantage of the genetic diseases as they provide a favourable biological scenario wherein hypotheses about physiopathological mechanisms underlying these diseases could be reliably tested.

In addition, a genetic variant of Alzheimer's Disease would provide a good model to investigate if tasks proposed for this study would be useful for detecting cognitive changes in Alzheimer's Disease well before it becomes clinically detectable by traditional neuropsychological tasks (Albert, 1996; Cosentino et al., 2008; Evans et al., 1997; Lerner, Friedland, & Whitehouse, 1992). This would further support the claim that short-term memory binding tasks may be considered sensitive tools for the early detection of Alzheimer's Disease.

7.5 Experiment 17

7.5.1 Aims

Experiment 17 addressed one main question that was: Do asymptomatic carriers and Alzheimer's Disease patients with the genetic defect E280A

present with short-term memory binding deficits? It was also investigated whether these deficits could be detected before the disease can be diagnosed on the basis of traditional clinical procedures (i.e., clinical and neuropsychological criteria).

7.5.2 Methods

7.5.2.1 Participants

To assess these hypotheses, three groups of participants were entered in the experiment. One group consisted of fifteen patients diagnosed as mild Alzheimer's Disease according to the diagnostic criteria described in Chapter 5. A second group consisted of twenty two asymptomatic carriers of the gene defect E280A. For the third group, twenty healthy relatives of patients and carriers who do not carry any genetic defect were included. All participants consented to take part in the study. The demographic characteristics of participants in the three groups are shown in Table 7.1.

Before the experiment, participants underwent a general screening in which their colour vision and perceptual functions were assessed. Colour vision problems were assessed using the Colour Blindness Test (Dvorine, 1963). Perception for shape-colour and colour-colour bindings was assessed using the perceptual tasks described in Experiments 3-6, 8, 15 and 16 (see Appendix 2 – I A and B). For these screening tasks, the same cut-off scores described in Experiment 3 were used.

Table 7.1. Age and years of education of participants entering Experiment 17.

		Mean (SD)	Range
Age	Carriers *	35.5 (6.7)	(23-45)
	Alzheimer' Disease patients	43.8 (5.1)	(32-52)
	Family non-Carriers	42.3 (10.5)	(25-58)
Years of Education	Carriers	9.0 (4.0)	(2-16)
	Alzheimer' Disease patients	8.5 (4.3)	(1-18)
	Family non-Carriers	9.1 (2.7)	(4-13)

* Carriers were younger than AD patients ($p < 0.01$) and than Family non-Carriers ($p < 0.05$). However, considering that the short-term memory binding functions assessed here were not sensitive to the effects of age (Chapter 3), and that further analysis using age as a covariable did not modified the relevant outcomes of the statistical analysis, this difference was not considered relevant in this experiment.

7.5.2.2 Task design

For this experiment two tasks were used. One task assessed short-term memory binding of shapes and colours and the second task assessed the binding of colours into bicoloured objects in short-term memory. These tasks were the same tasks described in Experiment 14 and 15 of Chapter 6 respectively. In this new experiment Alzheimer's Disease patients were presented with two items on each array whereas Carriers and Family non-Carriers were presented with three items. The reasons for selecting these set sizes were the same as those given in Chapter 5 Section 5.2.2.3. The dependent variable used for the analysis was the percentage of correct recognition and the sensitivity for change detection (A') calculated through the Signal Detection Theory (see Section 2.2.2.5 of Chapter 2 for a description of this variable). As previous experiments showed that response bias does not account for the poor performance observed in Alzheimer's Disease patients, this variable was not calculated for this experiment.

7.5.2.3 Statistical Analysis

For comparing performance of the three groups in the different experimental conditions a two-way mixed-ANOVA was used. The between-subjects factor was Group (Family non-Carriers vs. Carriers vs. mild Alzheimer's Disease patients) and the within subjects factors was Condition (Different feature types: shape only vs. colour only vs. shape-colour binding; Same type of feature: colour only vs. colours unbound vs. colour-colour binding). The analysis for shape-colour and colour-colour binding was performed separately. Post-hoc comparisons were carried out across groups for each condition separately (9 contrasts) and across conditions for each group separately (3 x 3 = 9). Therefore, a total of 18 pairwise comparisons were performed. The Bonferroni corrected alfa level was set at 0.003. Post-hoc comparisons resulting in p values below this threshold were considered significant.

7.5.3 Results

The results of the neuropsychological assessment of participants entering this experiment are shown in Table 7.2. Alzheimer's Disease patients had poorer memory performance than both Family non-Carriers and Carriers as shown by the Paired Associate Learning Task (adapted to Spanish speakers from the Paired Associate Learning Task of Weschler, 1997) and the delayed recall of the Rey Figure. Executive functions also proved poorer in Alzheimer's Disease patients than in Family non-Carriers and Carriers as suggested by the Verbal Fluency Test and the number of category reached in the Wisconsin Card Sorting Test (WCST) (a short version with 48 cards version from Berg, 1948). These neuropsychological findings suggest that this genetic variant of Alzheimer's Disease in its initial stages presents as an amnesic and dysexecutive syndrome resembling the pattern of behaviour described for

the sporadic form of Alzheimer's Disease (Greene, Hodges, & Baddeley, 1995). It is worth noticing that the average performance of Alzheimer' Disease patients in the Paired Associate Learning Task significantly differ from that of Family non-Carriers and from Carriers. This supports previous suggestions about the value of the Paired Associate Learning Tasks for separating Alzheimer' Disease from non-demented individual (O'Connell et al., 2004). Finally, Carriers and Family non-Carriers did not differ in any of the neuropsychological tasks used in this assessment.

Table 7.2. Results of the neuropsychological assessment of participants entering the experiment.

		Family non-Carriers (n = 20)		Carriers (n = 22)		Mild Alzheimer's Disease (n = 15)	
		Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
MMSE		28.15 (5.80)	(24-30)	28.86 (1.70)	(25-30)	25.60 (3.54)	(18-30)
PAL	¥ *	12.66 (3.81)	(5-19)	12.24 (4.95)	(4.5-20)	7.71 (3.65)	(3-13.5)
FAS		13.05 (5.24)	(7-29)	12.91 (6.25)	(2-29)	10.00 (3.32)	(3-16)
REY-Copy	*	25.30 (6.47)	(5-33)	26.73 (6.37)	(5.5-34)	20.20 (8.74)	(4-31)
REY-Recall	¥ *	16.13 (6.22)	(1-25.5)	14.80 (7.40)	(2.5-26)	3.50 (4.81)	(0-18.5)
Verbal Fluency	¥ *	21.30 (4.27)	(12-27)	19.57 (6.25)	(9-32)	14.40 (4.39)	(4-21)
TMT - A	¥	51.06 (19.03)	(31-99)	81.37 (65.13)	(31-290)	106.21 (47.38)	(54-210)
WCST Categories	¥ *	3.50 (1.54)	(1-6)	3.24 (1.61)	(0-6)	1.64 (1.01)	(0-3)
WCST – CI		10.78 (7.59)	(6-37)	11.80 (8.13)	(2-37)	17.54 (16.34)	(6-44)

MMSE: Mini Mental State Examination (Folstein et al., 1975); FAS: Phonological Fluency; REY-Copy and Recall: copy and recall of the Complex Figure of Rey; TMT - A: Part A of the Trial Making Test (Reitan, 1958); WCST – CI: Conceptualization Index is defined as the average number of trials required to detect that a change in the sorting criterion is required; ¥: Family non-Carriers vs. Mild AD different at $p < 0.05$; *: Carriers vs. Mild AD different at $p < 0.05$.

7.5.3.1 Short-term memory binding of shapes and colours

The percentage of correct recognition was entered in a two-way mixed-ANOVA. The analysis of Group tended towards a significant main effect

[F(2,54) = 2.76; p = 0.072]. The analysis of the within-subjects main effects showed significant effect of Condition [F(2,108) = 180.73; p < 0.001] and of the interaction of Group by Condition [F(4,108) = 9.84; p < 0.001] (Figure 7.2A).

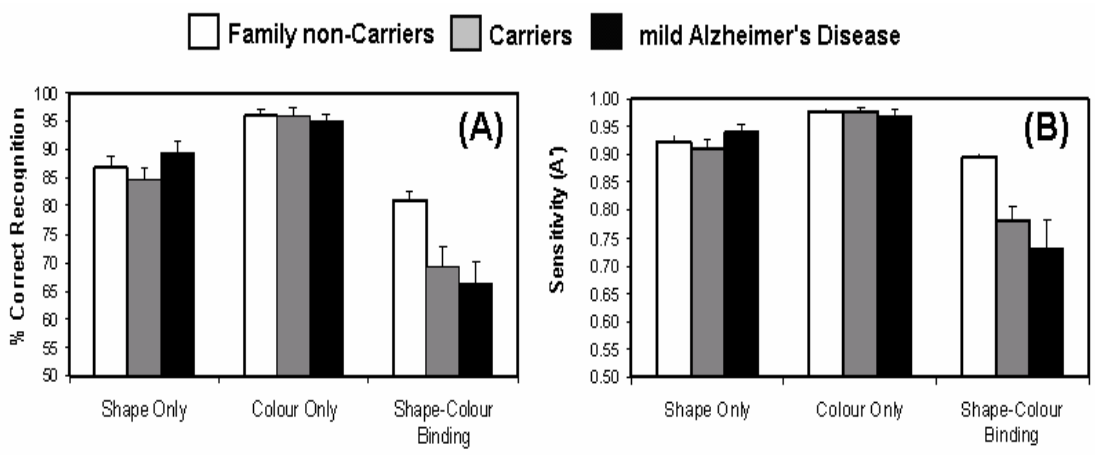

Figure 7.2. (A) Percentage of correct recognition and **(B)** Sensitivity (A′) in Family non-Carriers, Carriers, and Alzheimer's Disease patients in the three conditions of the task assessing memory binding of shapes and colours (Error bars represent the standard errors of the mean).

Post-hoc comparisons across groups showed that Alzheimer's Disease patients, Carriers, and Family non-Carriers did not show significant differences in any of the contrasts performed in the conditions assessing memory for shape only or colour only. However, Alzheimer's Disease patients performed significantly worse than Family non-Carriers (but not than Carriers) in the condition assessing memory for shape-colour binding [MD = 14.76, SE = 3.75, p = 0.001]. Carriers also performed more poorly than Family non-Carriers in the condition assessing memory for shape-colour binding [MD = 12.05, SE = 3.39, p = 0.002].

The analysis across conditions showed that Alzheimer's Disease patients performed more poorly in the condition assessing memory for shape-colour

binding than in the condition assessing memory for shape only [MD = 23.07, SE = 2.76, p < 0.001] and than in the condition assessing memory for colour only [MD = 28.60, SE = 3.59, p < 0.001]. Alzheimer's Disease patients' memory performance in the condition assessing memory for shape only was not significantly different than in the condition assessing memory for colour only [MD = 5.53, SE = 1.49, p = n.s.]. Carriers performed more poorly in the condition assessing memory for shape-colour binding than in the condition assessing memory for shape only [MD = 15.45, SE = 1.60, p < 0.001] and than in the condition assessing memory for colour only [MD = 27.04, SE = 2.03, p < 0.001]. Carriers' memory performance in the condition assessing memory for shape only was poorer than in the condition assessing memory for colour only [MD = 11.59, SE = 1.99, p < 0.001]. Hence, these results suggest that the overall pattern of performance of Carriers and Alzheimer's Disease patients was similar. For Family non-Carriers, memory performance in the condition assessing shape-colour binding was poorer than in colour only [MD = 14.95, SE = 1.66, p < 0.001] but not than in the condition assessing shape only [MD = 5.65, SE = 2.41, p = n.s.]. Family non-Carriers performed more poorly in the condition assessing memory for shape only than for colour only [MD = 9.30, SE = 1.70, p < 0.001].

When A' was entered in a two-way mixed-ANOVA, a significant main effect was found for Group [$F(2,54) = 3.87$, p = 0.027]. The assumption of sphericity was violated hence the Greenhouse-Geisser epsilon was used to correct the degrees of freedom. This yielded significant main effects for Condition [$F(1.29,69.88) = 97.41$, p = 0.027] and for the interaction of Group by Condition [$F(2.58,69.88) = 10.09$, p < 0.001] (Figure 7.2B).

Post-hoc comparisons carried out across groups showed that Alzheimer's Disease patients, Carriers, and Family non-Carriers did not show significant differences in sensitivity in any of the contrasts performed in the conditions

assessing memory for shape only or colour only. Alzheimer's Disease patients proved to be significantly less sensitive than Family non-Carriers to detect changes in the condition assessing memory for shape-colour binding [MD = 0.16, SE = 0.04, p = 0.001]. No other contrast performed across groups in the condition assessing memory for shape-colour binding resulted in significant effects.

The analysis across conditions showed that Alzheimer's Disease patients' sensitivity was lower in the condition assessing memory for shape-colour binding than in the condition assessing memory for shape only [MD = 0.21, SE = 0.04, p < 0.001] and than in the condition assessing memory for colour only [MD = 0.24, SE = 0.04, p < 0.001]. Alzheimer's Disease patients' sensitivity in the condition assessing memory for shape only and colour only was not significantly different [MD = 0.03, SE = 0.01, p = n.s.]. Carriers' sensitivity for change detection in the condition assessing memory for shape-colour binding was significantly lower than in conditions assessing memory for shape only [MD = 0.13, SE = 0.017, p < 0.001] and colour only [MD = 0.20, SE = 0.025, p < 0.001]. Carriers' sensitivity for change detection in shape only was lower than in colour only [MD = 0.08, SE = 0.013, p < 0.001]. For Family non-Carriers, the sensitivity in the condition assessing shape-colour binding was poorer than in colour only [MD = 0.08, SE = 0.01, p < 0.001] but not than in the condition assessing shape only [MD = 0.026, SE = 0.016, p = n.s.]. Family non-Carriers showed lower sensitivity in the condition assessing memory for shape only than for colour only [MD = 0.057, SE = 0.012, p < 0.001].

7.5.3.2 Short-term memory binding of colours

The percentage of correct recognition was entered in the same ANOVA model which yielded a non significant main effect of Group [$F(2,54) = 0.51$; p

= 0.601]. After correcting the degrees of freedom using the Greenhouse-Geisser epsilon, significant mains effects were found for Condition [$F(1.31,71.15) = 84.20$; $p < 0.001$], and for the Group by Condition interaction [$F(2.63,71.15) = 7.62$; $p < 0.001$] (Figure 7.3A).

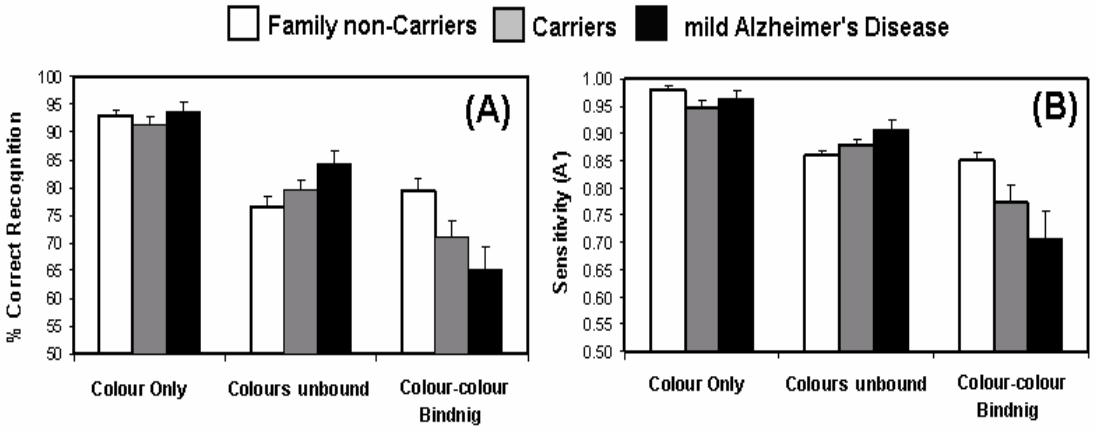

Figure 7.3. (A) Percentage of correct recognition and **(B)** Sensitivity (A') in Family non-Carriers, Carriers, and Alzheimer's Disease patients in the three conditions of the task assessing memory binding of colours (Error bars represent the standard errors of the mean).

Post-hoc contrasts carried out using the same threshold set above showed that none of the pairwise comparisons across groups yielded significant effects. Post-hoc tests performed across conditions for each group separately showed that Alzheimer's Disease patients' performance in the condition assessing memory for colour-colour binding was poorer than in the condition assessing memory for colours unbound [MD = 19.20, SE = 4.36, p = 0.002] and colour only [MD = 28.53, SE = 3.36, p < 0.001]. Alzheimer's Disease patients performed more poorly in the condition assessing memory for colours unbound than for colour only [MD = 9.33, SE = 1.86, p = 0.001]. For Carriers the post-hoc tests showed that their performance in the condition assessing memory for colour-colour binding was poorer than for colour only [MD = 20.11, SE = 2.51, p < 0.001] but not than in colours

unbound [MD = 8.57, SE = 3.03, p = n.s.]. Remembering colours unbound resulted in a poorer memory performance in Carriers than remembering colour only [MD = 11.54, SE = 1.75, p < 0.001]. Family non-Carriers' memory performance in conditions assessing colour-colour binding and colours unbound did not differ [MD = 2.08, SE = 3.45, p = n.s.]. They performed however more poorly in the condition assessing memory for colour-colour binding than in colour only [MD = 13.64, SE = 2.39, p < 0.001], which was also better than colours unbound [MD = 16.45, SE = 1.59, p < 0.001]. Hence, the interaction found during the analysis of memory binding for colours suggests that it was the performance of the group of Alzheimer's Disease patients in the condition assessing memory for colour-colour binding that drove the significant main effect of the Group by Condition interaction (as memory for bound colours versus memory for unbound colours resulted in significant differences in Alzheimer's Disease patients only).

When A' was entered in this analysis, no effect of Group was found [$F(2,54) = 1.58$; p = n.s.]. Significant mains effects were found for Condition [$F(1.35,72.94) = 63.46$; p < 0.001], and for the interaction between these factors [$F(2.70,72.94) = 5.41$; p = 0.003] (Figure 7.3B).

Post-hoc tests performed across groups resulted in non significant pairwise comparisons. Post-hoc comparisons carried out across conditions showed that Alzheimer's Disease patients' sensitivity for change detection in colour-colour binding did not significantly differ from sensitivity for colours unbound [MD = 0.19, SE = 0.49, p = n.s.] but it was lower than for colour only [MD = 0.25, SE = 0.045, p < 0.001]. Changes in colours unbound condition were detected by Alzheimer's Disease patients no differently than changes in colour only [MD = 0.056, SE = 0.015, p = n.s.]. Hence, it does not seem to be a problem of sensitivity that underlies the poorer memory for colours bound versus colours unbound observed in Alzheimer's Disease patients. For

Carriers the sensitivity was found lower in the colour-colour binding condition than in colour only [MD = 0.175, SE = 0.031, $p < 0.001$]. No other contrast resulted in a significant effect. For Family non-Carriers the sensitivity was lower in the colour-colour binding condition than in colour only [MD = 0.130 SE = 0.019, $p < 0.001$] which was better than for colours unbound [MD = 0.122, SE = 0.015, $p < 0.001$]. The sensitivity for colour-colour binding and colours unbound did not significantly differ [MD = 0.009 SE = 0.025, p = n.s.].

7.5.4 Discussion

These results extend the previous finding of short-term memory binding deficits observed in the sporadic Alzheimer's Disease to a familial form of the disease due to the mutation E280A of the gene of the Preseniline-1. This also suggests that memory binding deficits may be seen as a feature common to Alzheimer's Disease in both its early and late onset variants. Previous reports suggest that there may be behavioural, cognitive, and neuropathological differences (i.e., different phenotypical expressions) across different genotypic defects of the same gene (Lopera et al., 1997). However, from the results presented here it is possible to conclude that memory binding functions are impaired by Alzheimer's Disease to a much greater extent than memory functions responsible for processing single events (i.e., colours only or shapes only), and that this is true for both the early and late onset variant of Alzheimer's Disease. This is in line with the first hypothesis proposed for this experiment.

Although Alzheimer's Disease patients and Carriers remembered shapes only or colour only no differently than Family non-Carriers, participants in the first two groups could not remember the binding between these features

to the same extent as Family non-Carriers. These binding deficits observed in Alzheimer's Disease patients and Carriers gain more value if we consider that they appear in the condition where all groups remembered the same number of single features with an equivalent level of accuracy. This rules out the possibility that binding deficits in Alzheimer's Disease patients were due to memory load. Furthermore, patients with Alzheimer's Disease were presented with only 2 items whereas Carriers and Family non-Carriers were presented with 3, which further reduces the potential impact of memory load *per se*. These findings suggest that binding deficits are a particular feature of Alzheimer's Disease which are distinguishable from other impairments due to memory load and reduced span.

Analysis across conditions assessing memory for shapes and colours bound and unbound showed that the pattern of performance for both Alzheimer's Disease patients and Carriers was very similar and in the form of memory for binding < memory for shapes < memory for colours. This was not the case for Family non-Carriers in whom the pattern was in the form of (memory for binding = memory for shape) < memory for colours. This supports previous findings suggesting that short-term memory stores shapes and colours bound in an object-based format (Chapter 2).

In no condition assessing memory for single features did the three groups of participants differ. It was only the condition assessing memory for shape-colour binding in which Carriers and Alzheimer's Disease patients differed from Family non-Carriers but not from each other. Of note, when the neuropsychological background was analyzed Carriers and Family non-Carriers did not differ from each other in any tasks and both were different from Alzheimer's Disease patients in several tasks assessing memory and executive functions. This is an outstanding finding suggesting that short-term memory binding tasks can detect neurodegenerative changes in the

course of Alzheimer's Disease much earlier than other neuropsychological tasks traditionally used for such purpose. It is also of note that among these neuropsychological tasks a Paired Associate Learning Task was used. It has been claimed that the Paired Associate Learning tasks are highly sensitive for detecting Alzheimer's Disease in the early stages (Fowler et al., 2002; O'Connell et al., 2004; Swainson et al., 2001). From this perspective, it may be argued that short-term memory binding tasks would accomplish this aim more effectively and reliably as these tasks are performed by older people without difficulties (Chapters 3, 5, and 6 of this thesis present results supporting this statement).

In the case for short-term binding between features of the same type (i.e., colours bound into bicoloured objects), Alzheimer's Disease patients, Carriers, and Family non-Carriers showed differential abilities. Whereas patients with the genetic Alzheimer's Disease were less able to hold colours bound in short-term memory as compared to colours unbound, Carriers and Family non-Carriers showed no such differences when they were compared across these conditions. These findings have two main implications. One, concerns the aim of the current study which was assessing the usefulness of short-term memory binding tasks for detecting Alzheimer' Disease. From this perspective it may be suggested that tasks assessing the binding of features in memory of the same type would separate Alzheimer's Disease patients from healthy individuals acceptably but they would be less efficient in detecting those who, among these still healthy individuals (e.g., asymptomatic carriers), will develop the disease. The other implication concerns the unit of storage of short-term memory. In Experiments 5, 6, and 16 it has been found that remembering objects defined by colours bound was a more demanding task than remembering objects defined by colours unbound. In the current experiment this was not the case for Carriers and Family non-Carriers who showed equivalent performance in these

conditions. Although the instructions given to participants were precise, the strategies they used to perform the task were not monitored. It might be possible that participants of this study were binding colours within patterns in both colours unbound and colours bound condition even though they were instructed not to do so. This possibility seems to be more likely than the possibility that they there were not binding in any condition because the Alzheimer's Disease patients were more impaired in the colours bound condition only. This suggests that participants were actually binding colours and that Alzheimer's Disease patients were the only patients who encountered difficulties in accomplishing this task.

Summing up, the results of this experiment confirmed that patients with the genetic form of Alzheimer's Disease due to the mutation E280A of the Preseniline-1 gene do present with deficits in binding information in short-term memory and that these deficits are greater than memory deficits for individual features. This further supports previous finding presented in Chapter 5 and 6 and extends these findings to a new form of Alzheimer's Disease, the genetic variant. Additionally, the results presented here suggest that short-term memory binding tasks, and more specifically those assessing the binding between different feature types, can be considered sensitive tools for detecting the onset of the neurodegenerative changes of Alzheimer's Disease years before the disease can be detected by traditional clinical procedures. One question that follows from these results is when these short-term memory binding deficits occur.

In order to investigate this question a new analysis was carried out including Carriers and Family non-Carriers and adding age as a new between-subjects factor. Two subgroups were defined. One group encompassed participants under 35 years old while the second group encompassed participants with age equal or above 35 years. This age cut-off was chosen based on previous

reports which suggest that asymptomatic carriers of this gene defect with an average age of 34.5 years who did not complain of memory impairment outperformed carriers who did complain of memory problems in neuropsychological tasks such as Logical Memory, Associative Learning, Recall of Rey-Figure, Boston Diagnostic Aphasia Examination, Memory for Three Phrases, Serial Verbal Learning, Digit Symbol, and TMT-A (Ardila et al., 2000). This suggests that memory problems seem to be the earliest symptom of this form of Alzheimer's Disease. As the average age of the symptomatic carriers in this earlier study was 41.50 (approximately 5 years younger than the average age of onset of the disease = 46.8) it was hypothesised that the age limit selected for the present analysis may allow us to assess whether younger asymptomatic carriers who have also been found to perform normally in a wide range of cognitive tasks would show short-term memory binding deficits using the tasks devised for this project.

Other authors have reported similar findings to those by Ardila et al. (2000) in the sporadic form of Alzheimer' Disease, suggesting that subtle behavioural changes can be present in these still asymptomatic individuals many years before the disease becomes detectable (Backman, Small, & Fratiglioni, 2001; Small, Mobly, Laukka, Jones, & Backman, 2003). In support of this claim, an unpublished study by the Neuroscience Group of Antioquia, Colombia, reported that a carrier of the gene defect E280A who was 20 years old showed a pattern of brain reorganization which consisted of increased signals (fMRI) in the hippocampus and parahippocampal regions during a memory task involving visual images. This suggests that very early in this neurodegenerative disorder (perhaps decades), there seems to be functional reorganization which underlies brain changes resulting from the expression of this genetic mutation. Bassett et al. (2006) demonstrated more intense and extensive fMRI activation in the frontal and temporal lobes including the hippocampus during memory encoding in 95 asymptomatic offspring (50-75

years of age) of late-onset familial Alzheimer's Disease (see also Fukuyama, 2006 for evidence on functional brain reorganization in Mild Cognitive Impairment patients, or Fleisher et al., 2005 for similar changes in individuals with high risk for Alzheimer's Disease due to Apolipoprotein-E epsilon-4 genotype). Pariente et al. (2005) also reported fronto-parietal activation in Alzheimer's Disease patients but not in controls in a face-name associative memory tasks. The authors suggested that this network reflects compensatory strategies for failing associative memory in Alzheimer's Disease patients. This set of evidence suggests that the neurodegenerative process of Alzheimer's Disease induces functional and structural brain changes and that these changes start developing years before the disease can be detected behaviourally by the current available methods.

7.6 Analysis of the age of onset of short-term memory binding deficits in asymptomatic Carriers of the gene defect E280A

Twenty four asymptomatic carriers entered this new analysis. Out of this 24, 22 took part in the previous analysis and two were new participants. The second group consisted of twenty Family non-Carriers who also entered the previous analysis. Both groups were split according to age using 35 as the cut-off criterion. This resulted in four subgroups, one group of 13 Carriers with age below 35 (Age: M = 28.69, SD = 4.15; Education: M = 10.38, SD = 4.44) and another group consisted of 8 Family non-Carriers with age below 35 (Age: M = 30.25, SD = 4.15; Education: M = 11.63, SD = 1.51) (Age: MD = 1.55, t(19) = 0.37, p = n.s.; Education: MD = 1.2, t(19) = 0.76, p = n.s.). A third group consisted of 11 Carriers with age equal or above 35 (Age: M = 40.64, SD = 2.42; Education: M = 9.09, SD = 3.5) and the fourth group consisted of 12 Family non-Carriers with age equal or above 35 (Age: M = 45.17, SD =

5.13; Education: M = 8.83, SD = 2.62) (Age: MD = 4.53, t(21) = 2.66, p = 0.014; Education: MD = 0.26, t(21) = 0.21, p = n.s.).

Table 7.3. Neuropsychological assessment of Carriers and Family-non Carriers entering the analysis of the age of onset of short-term memory binding deficits.

	< 35 years				>= 35 years			
	Family non-Carriers (n = 8)		Carriers (n = 13)		Family non-Carriers (n = 12)		Carriers (n = 11)	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
MMSE	29.00 (1.51)	(26-30)	29.00 (1.83)	(25-30)	27.25 (7.41)	(24-30)	28.82 (1.47)	(26-30)
PAL	14.00 (3.04)	(9-18)	14.67 (4.23)	(6-20)	12.17 (4.11)	(5-19)	10.68 (4.83)	(4.5-19)
FAS	13.63 (4.53)	(7-19)	12.00 (6.78)	(2-29)	13.33 (5.76)	(8-29)	13.36 (5.50)	(7-24)
REY-Copy	27.63 (4.14)	(19-32)	27.35 (7.43)	(5.5-34)	24.88 (7.51)	(5-33)	25.55 (4.48)	(17-32)
REY-Recall	16.56 (6.30)	(5.5-25.5)	15.19 (7.66)	(3-26)	16.08 (6.42)	(1-23)	13.27 (7.16)	(2.5-23)
Verbal Fluency	21.25 (3.65)	(17-27)	17.83 (6.09)	(9-28)	21.33 (4.16)	(14-27)	21.00 (5.78)	(12-32)
TMT - A	57.29 (20.65)	(31-186)	75.58 (70.51)	(34-290)	50.45 (24.55)	(21-99)	73.89 (52.56)	(31-186)
WCST Categories	4.13 (1.73)	(1-6)	3.25 (1.36)	(1-5)	3.10 (1.37)	(1-5)	3.18 (1.78)	(0-6)
WCST – CI	10.63 (8.31	(6-31)	10.75 (8.71)	(6-37)	11.00 (9.39)	(6.00-37)	10.70 (6.27)	(2-26)

See footnotes of Table 7.2. None of the independent sample t-tests carried out across groups resulted in significant differences.

As the previous analysis showed that was the shape-colour binding the only condition in which Carriers and Family non-Carriers performed significantly different, and further analysis involving performance (i.e., accuracy) in conditions assessing memory for shape or colour only carried out with Carriers and Family non-Carriers across the different age groups showed no effect of Group [F(1,40) = 0.32, p = n.s.] and no Group by Age interaction [F(1,40) = 1.87, p = n.s.], this current analysis focused on performance on the condition assessing short-term memory for shape-colour binding only.

For this analysis the percentage of correct recognition was entered in a two-way factorial ANOVA with Group and Age as the between-subjects factors

and percentage of correct recognition as the dependent variable. Significant main effects were found for Group [$F(1,40) = 11.08$, $p = 0.002$], Age [$F(1,40) = 7.45$, $p = 0.009$], and for the interaction between these factors [$F(1,40) = 7.30$, $p = 0.010$] (Figure 7.4A).

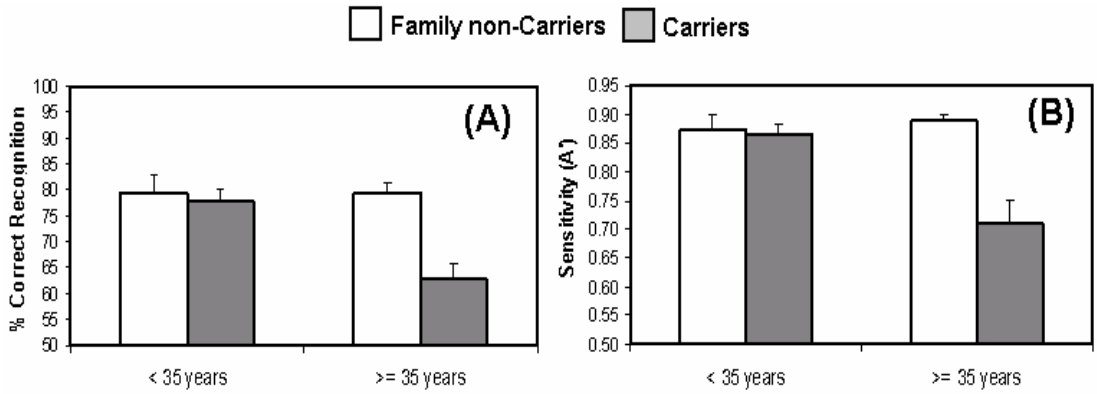

Figure 7.4. (A) Percentage of correct recognition and **(B)** Sensitivity (A') in the condition assessing memory for shape-colour binding in Family non-Carriers and Carriers across the two age groups (Error bars represent the standard errors of the mean).

Four post-hoc contrasts were carried out across Age (2 levels) and Group (2 levels). The alfa threshold was therefore corrected at 0.0125. The analysis across groups showed that Carriers below the age of 35 did not differ from Family non-Carriers of the same age group [MD = 1.73, SE = 4.03, p = n.s.]. Carriers of age equal or above 35 performed significantly more poorly than Family non-Carriers of the same age group [MD = 16.59, SE = 3.74, $p < 0.001$]. The analysis across Age showed that Carriers >= 35 performed significantly more poorly than Carriers < 35 [MD = 14.95, SE = 3.68, p = 0.001]. Family non-Carriers did not show differences across age groups [MD = 0.08, SE = 4.08, p = n.s.].

When A' was entered in the same ANOVA model, significant main effects were found for Group [$F(1,40) = 12.87$, $p = 0.001$], Age [$F(1,40) = 6.94$, p =

0.009], and for the interaction between these factors [$F(1,40) = 10.97$, $p = 0.002$] (Figure 7.4B). Post-hoc tests carried out across Groups showed that Carriers below the age of 35 did not differ from Family non-Carriers of the same age group [MD = 0.007, SE = 0.37, p = n.s.]. Carriers of age equal or above 35 showed less sensitivity for change detection in shape-colour bindings than Family non-Carriers of the same age group [MD = 0.18, SE = 0.035, $p < 0.001$]. The analysis across Age showed that Carriers >= 35 performed significantly more poorly than Carriers < 35 [MD = 0.15, SE = 0.034, $p < 0.001$]. Family non-Carriers did not show differences across age groups [MD = 0.017, SE = 0.038, p = n.s.].

Therefore, the results of this analysis suggest that when Carriers reach the age of 35 or more (as average), they will not remain asymptomatic as short-term memory binding deficits, although unperceived by these patients, will be detected by the tasks proposed in this project.

This is in agreement with previous observations made based on clinical reports which suggested that this genetic form of Alzheimer's Disease seems to commence its phenotypical expression at ages around 35 (Ardila et al., 2000). However, the literature delivered to date had not reported any kind of abnormal behaviour in carriers of this gene defect who still remain completely asymptomatic. As table 7.3 shows, these carriers in fact remain normal according to the neuropsychological assessment what is in line with previous reports (Ardila et al., 2000). From this perspective it is possible to argue that short-term memory binding tasks could be considered tasks which are able to detect cognitive changes in the neurodegenerative course of Alzheimer's Disease years before the disease becomes clinically apparent. More precisely, it can be posited that short-term memory binding problems may be detected by the neuropsychological tasks proposed here an average of 11.8 years before the disease becomes clinically evident (46.8 being the

average age of onset according to Lopera et al., 1997). If we also consider the report by Ardila et al. (2000) who suggested that the neuropsychological profile of this genetic variant of Alzheimer's Disease does not differ substantially from that observed in the sporadic form of the disease, we may argue that tasks here proposed are likely to detect these changes in the late onset and sporadic variants of Alzheimer's Disease early. Future research should address this hypothesis.

7.7 General Discussion

In this new chapter the short-term memory binding problems reported in Alzheimer's Disease patients in Chapter 5 and 6 have been replicated. This new evidence suggests that memory binding problems are distinctive features of Alzheimer's Disease in its early/genetic and late/sporadic forms. These new results provide further support of the validity of the genetic forms of the neurodegenerative diseases in investigating the new tools aimed at detecting these disorders early.

Taken together the results presented in this chapter with the evidence accrued throughout this dissertation it may be possible to posit that: 1) Alzheimer's Disease impairs short-term memory for bound information more dramatically than it impairs memory for single or unrelated information; 2) This short-term memory binding problem seems to be specific to Alzheimer's Disease as it does not appear in healthy older adults (which is relevant to the late onset variants of the disease) or in relatives of patients with genetic Alzheimer's Disease who do not carry the gene defect. 3) These short-term memory binding problems could signal the onset of the disease much earlier than any other neuropsychological task currently available in clinical settings. 4) It seems to be that the binding in memory of

information of different types is the function more vulnerable to the neurodegenerative changes accompanying Alzheimer's Disease in its early stages.

One outstanding finding of this chapter is that of the poorer performance of Carriers of the gene defect when they were compared with Family non-Carriers. It is worth noticing that this pattern of results appears over a completely normal neuropsychological background. This suggests that those mechanisms subserving binding operations in short-term memory are targeted by the neurodegenerative processes of Alzheimer's Disease earlier than those responsible for other cognitive functions which are assessed by traditional neuropsychological tasks. These include for example those functions responsible for forming long lasting associations between items as it happens in the Paired Associate Learning Tasks. The Paired Associate Learning Task used in this study involves the formation of association between words whereas the task used by O'Connell et al. (2004) and Swainson et al. (2001) (see Chapter 1, Section 1.9.1, Part II) involves the association between visual (i.e., patterns) and spatial (i.e., location) information. There is evidence suggesting that Alzheimer's Disease impairs visuo-spatial memory earlier than other forms of memory (Ricker, Keenan, & Jacobson, 1994; Sahgal et al., 1992). This may explain why carriers of the gene defect performed the Paired Associate Learning Task used in this study without difficulties as it involves verbal information. However, other authors have suggested that Paired Associate Learning Tasks involving the semantic and meaningful associations between words are also highly sensitive for detecting Alzheimer's Disease (Buschke et al., 1999; Buschke et al., 1997; Grober, Buschke, Crystal, Bang, & Dresner, 1988).

This may have important implications for our current understanding of cognitive changes in Alzheimer's Disease as to date, the formation of

associations in long-term memory have been considered one of the earliest functions affected by Alzheimer's Disease (Fowler et al., 2002; Granholm & Butters, 1988; Swainson et al., 2001). As was discussed above, the mechanism responsible for these long-term memory deficits is the damage to the hippocampus observed early in the disease. Hence, if the formation of short-term bindings is affected earlier than the formation of long-lasting associations, this may imply that the hippocampus may not be the only structure targeted by Alzheimer's Disease in its early stages. The reason for this statement stems from the fact that short-term memory binding seems to be a function that does not rely on medial temporal lobe structures but mainly on neocortical structures (Prabhakaran et al., 2000; Xu, 2007) (also see in Table 1.2 the fMRI study by Piekema et al., 2006 which reported that the hippocampus was not activated by object-colour bindings).

Therefore, Alzheimer's Disease could affect these neocortical integrative processes earlier than those processes responsible for representing the association of information in long-term memory which, according to our current knowledge, are subserved by medial temporal lobe structures mainly the hippocampus (Lowndes & Savage, 2007; Mayes et al., 2007; Moses & Ryan, 2006). I shall discuss these issues in more depth in Chapter 8 of this thesis (Overview).

One other important finding of this experiment is the lack of differences between Carrier and Family non-Carriers in the task assessing short-term memory binding for the same type of feature (i.e., colour-colour binding). It might be argued that a lack of power was the reason behind this non significant effect. However, if we considerer the results of the comparisons carried out for the binding of shapes and colours, this possibility seems to be less likely. What would underlie this lack of differences for the binding of the same type of features? One possible reason may be found at a functional

level. Whereas binding shapes with colours implies bridging across cortical regions distantly located, binding colours with colours requires no such long connections. As was discussed above, Alzheimer's Disease in its progression disconnects brain regions. There is evidence suggesting that this disconnection involves long cortico-cortical pathways earlier than short cortico-cortical pathways (Calderon, Parra, Llibre, Fernandez, & Gongora, 1997; Calderon, Parra, Llibre, & Guitierrez, 2004). From these perspectives, these memory binding tasks may be seen as tools able not only to detect the beginning of the neurodegenerative process of Alzheimer's Disease but also to monitor the course of its progression.

In sum, results presented in this chapter convey the message that short-term memory binding tasks could be useful tools for detecting memory changes in the neurodegenerative course of Alzheimer's Disease as early as 11 years before the disease becomes clinically evident. With this new evidence, the sensitivity of short-term memory binding tasks for detecting Alzheimer's Disease have been further assessed and validated. This claim is consistent with previous reports where memory problems have been observed as early as 6 years before the onset of the disease (Backman et al., 2001). One other issue arising from these findings is the sensitivity of these memory binding tasks to separate Alzheimer's Disease patients from normal older individuals. Further research should address whether these tasks would also differentiate Alzheimer's Disease patients from patients with other non-Alzheimer dementia with similar efficiency.

7.8 Conclusions

1. The results presented in this chapter confirm previous findings of Chapters 5 and 6 suggesting that Alzheimer's Disease impairs

selectively and more pronouncedly memory encompassing complex events. These deficits in holding bound information in memory are well over and above memory deficits for single or unbound information.

2. Furthermore, the results of the experiment presented in this chapter extend previous findings from the sporadic form of Alzheimer's Disease to the genetic Alzheimer's Disease, suggesting that binding deficits may be considered universal features of the disease affecting its late-sporadic and early-genetic variants.

3. These deficits in holding bindings between features in memory seem to commence in Alzheimer's Disease years before the disease becomes clinically detectable. In this study it was shown that this time may be around 11 years.

4. Importantly, these memory binding deficits can be reliably detected using the tasks presented here. More specifically, short-term memory binding tasks seem to be promising tools for detecting memory changes early in the course of Alzheimer's Disease. This is true even when the neuropsychological assessment does not provide evidence of deterioration.

CHAPTER 8

Overview

8.1 Introduction

This thesis has addressed some crucial aspects concerning the functions and structure of short-term memory for related or bound information with a series of experiments. The main aim of this thesis was to assess short-term memory processing when the to-be-remembered information consisted of integrated objects or individual features and to investigate the impact of brain damage on these memory processes. Particular emphasis was given to the usefulness of short-term memory binding tasks in assisting the detection of Alzheimer's Disease.

In accomplishing these aims, five main contributions have been made. First, the results presented here may shed light into the structure and functions of memory in binding tasks. The current results offer valuable insights into how memory for complex episodes operates, the relation between short- and long-term memory, and the validity of some arguments underpinning the different memory models discussed in Chapter 1. A second area is the current debate about the unit of capacity of visual short-term memory. In six chapters evidence has been accrued suggesting that visual short-term memory is equipped with relatively independent mechanisms to process unrelated or single features and bound or related features. Furthermore, the results of this thesis suggest that the unit of storage of visual short-term memory (i.e., integrated objects or independent features) strongly depends

on the nature of the information encompassed by complex events (e.g., integrated objects).

One third area for which the results of this thesis are relevant is that concerning age-related memory changes. In Chapter 3, which was dedicated to the issue of age effects on short-term memory for bound information, and throughout the series of experiments presented in Chapters 4 to 7, it was consistently shown that aging does not disproportionally affect the short-term memory system responsible for storing integrated features into objects. Furthermore, (fourth contribution) taken together the results of the experiments presented in this thesis with the results of previous studies, it may be suggested that the effects of age on memory may vary depending on methodological and functional factors. Within the methodological factors, the type of material to be stored (e.g., items and locations vs. items and colours) and the duration for which these materials will be held in memory (i.e., short-term or long-term), seem to affect older people differently. Within the functional factors, age seems to affect the integrative process when the outcome of these binding operations does not lead to the representation of objects which features contribute to define their own identity (e.g., objects and locations). When features contribute to the object's identity (e.g., shape and colour), these binding processes seem to be spared in old age. These results suggest that short-term memory for bound features that define the identity of complex objects is not sensitive to the effects of normal ageing. This finding could form the basis for detecting pathological ageing.

One final area (fifth contribution) concerns the impact of brain pathology on memory for bindings. In one chapter assessing short-term memory binding in a patient with focal brain damage (Chapter 4), and in three chapters assessing this function in patients with Alzheimer's Disease (Chapter 5, 6, and 7), it was shown that short-term memory for complex objects and for

single items is subserved by separate processes. In the next Sections of this overview chapter I shall discuss each of these points in turn.

8.2 Implications for the structure and functions of memory and the current debate about the unit of capacity of visual short-term memory

8.2.1 How does short-term memory process complex episodes?

Some of the results presented in this thesis provide evidence that can be accounted for by the object-based hypothesis of visual short-term memory while other results are consistent with the feature-based hypothesis. One crucial observation concerning this issue is that it seems to be the nature of the information to-be-bound in memory that determines in which format this integrated information is stored. As long as objects comprise features of different types the process of binding would likely lead to the representation of unified objects in short-term memory (as it was observed in Chapter 2). In the series of experiments reported in this thesis it was consistently found that holding multi-feature objects (e.g., coloured shapes) in short-term memory and objects defined by one feature (e.g., shape only) did not result in significant differences in memory performance. This suggests that the process of feature integration is highly efficient in processing for different feature types (this was also found in Chapter 2 for shapes and orientations and for oriented coloured shapes). However, when objects comprise the same type of feature (e.g., bicoloured objects), integrative processes were found to be less efficient and these bound features did not appear to be represented in an object-based format. Hence, in this last case, the single features appear to be stored in short-term memory, and the binding between

these features (i.e., how features combine) is an additional piece of information which consumes extra memory capacity.

It was shown that this difference in the representational format of objects comprising the same and different features is, at least in part, a consequence of the interference arising when features compete for central resources (across or within feature dimensions). As this interference is less intense when features are drawn from different dimensions, the result of this integration would enable objects to be represented as single units without difficulty (as each dimension provides its own resources). However, the argument that this is a cost-free process as postulated by Luck and Vogel (1997) and Vogel et al. (2001) was not upheld by the outcome of Experiment 3 in Chapter 2. It was observed that as the number of multi-feature objects increased, memory capacity for these objects dropped more dramatically than for the same number of objects composed of one feature each. This finding provides further support to the Multiple Resources Theory.

The results of the assessment of case ES (Chapter 4) further support the above claim (i.e., fifth contribution). Only her visual short-term memory for bound features was impaired, while neither her visual short-term memory for single features nor her verbal short-term memory for features or objects were impaired. This suggests that for representing integrated objects in visual short-term memory, separate resources are required and these resources are not used for representing single features, nor for representing verbal information (i.e., features or objects). Summarising, these results suggest that: 1) objects defined by different feature types will more likely be represented in short-term memory as integrated objects in an object-based format. Objects defined by the same feature type will not be integrated in this format but in a rather feature-based format. 2) In neither of these situations

are these processes cost-free as extra memory capacity seems to be necessary to store the relatedness between these features into these complex objects.

8.2.2 The relation between short- and long-term memory

Although this thesis did not focus on long-term memory, there are two characteristics of the experiments presented which permit the discussions of some issues about the potential relation between short- and long-term memory for bound information. First, in Experiments 9-11, 13 and 14, stimuli were verbal and with strong semantic representations. Therefore, although they had to be retained for only short intervals, the possibility of accessing long-term representations of these stimuli (or their parts) cannot be disregarded. Second, the neuropsychological assessment carried out in various experiments of this research project included long-term memory tasks (see Section 4.2.2). With this neuropsychological background available it may be possible to determine relations between short-term and long-term memory functions in brain damaged and healthy individuals.

As was discussed in the review Chapter 1 (Section 1.5.3 and 1.5.5, Part I), whenever the to-be-remembered information can be represented using verbal codes, the retention of bound features in short-term memory is more stable. In this situation, the use of this information improves performance and the formation of long lasting representations from these complex events are not only more likely but also these representations are more stable and durable. If we consider the series of experiments presented in Chapter 4, there seems to be a clear advantage in memory for bound features when participants can use verbal codes rather than only visual features. In all experiments of Chapter 4 in which information could be directly represented as verbal codes (Experiments 9, 11, and 12 in the "with verbal aid" trials

blocks), participants performed significantly better in the binding conditions as compared to the single feature conditions. This was not the case when information was held in non verbal format. In Experiments 7, 10, and 12 in the "without verbal aid" trails blocks, remembering the bound features was not easier than remembering single features. It is more likely that verbal information can be held in short-term memory more efficiently because it can be linked to long-term memory representations, as expressed in Logie's workspace model (Logie, 2003; Logie & van der Meulen, 2009; see also Cowan, 2008). These verbal codes would in turn aid the retrieval of long-term traces of bound features resulting in better performance, as these long-term representations are more stable and less prone to interference. Notably, Allen et al. (2006), Logie et al. (2009), and Treisman (2006) reported that meaningless short-term memory bindings are more fragile and susceptible to interference.

A crucial example supporting this view could be taken from Experiment 12, reported in Chapter 4. In this experiment, when participants were explicitly asked to use verbal codes to aid visual short-term memory, not only did they perform better than when relying on visual codes, but ES no longer showed impairments. In the case of ES, it might be argued that she overcame her visual short-term memory impairment by bypassing information to verbal short-term memory before it reached any form of representational process in visual short-term memory (in which she was impaired). However, this explanation does not sufficiently explain why healthy controls performed better in the "with verbal aid" block (Experiment 12, Chapter 4). Here the reason may be the use of long-term memory representations when verbal codes were available. For example, using word pairs as stimuli in a serial-recall task, Cowan (2008) found that a rapid learning of these pairs occurs and that this impacts on performance during short-term memory tasks. Using pairs of shapes and colours arbitrarily combined Logie et al. (2009)

found that bindings formed during short-term change detection tasks are overwritten on every trial and no long-term traces of these items are recorded. Hence, there will be no impact of these previously presented items on short-term memory performance. Cowan (2008, Ch. 5) suggested that the possibility of learning this verbal material also impacts on the capacity limit of short-term memory. From this perspective chunking visual and verbal information would impact differentially on short-term memory capacity. Hence, these different impacts may reflect the differential access of these short-term representations to long-term engrams.

Therefore, the use of verbal codes may be seen as a way of bridging the content of short-term memory to long-term memory and this would help to explain the better memory performance when materials can be held using verbal codes as compared to when they are maintained in a visual format. These verbal codes, even if held for a short period of time, may be portraying an activated state of representations that are stored in long-term memory. This conveys the idea that when verbal codes are available to short-term memory, the unitary memory system hypothesis proposed by Cowan (1988) would be better supported, a suggestion that Cowan himself finds plausible (Cowan, 2008). However, this does not seem to be the case for unfamiliar stimuli that cannot be represented using verbal codes (e.g., abstract shapes). In this situation, the multi-component model, and particularly the visuo-spatial sketchpad, would subserve the representation of these inputs.

However, Logie's model (2003) would still encounter some limitations if it is used to offer an account for these memory operations. According to Logie's model, when stimuli are first viewed there would be activation of knowledge related to those stimuli stored in long-term memory. This then raises the question as to what would happen if no such knowledge is available in the case of novel abstract material. How this novel and meaningless information

could be effectively held and used in working memory if it leads neither to previous memories nor to the formation of new knowledge? Logie (2003) himself acknowledged this limitation and provided an alternative explanation as to account for this form of memory representation. The author suggested that: "*…when we are confronted by ambiguity, by implication this means that the knowledge activated by perception from the long-term store is insufficient. What knowledge is activated can be manipulated and transformed within working memory to help resolve the ambiguity. That is, working memory can generate new knowledge from old and as such would have significant evolutionary value*". That is why Logie (2003) sees working memory as a creative workspace.

However, I would like to reflect upon this suggested limitation of Logie's model together with two other issues: the demand of resources during short-term memory binding and the nature of the to-be-bound information aiming at shedding light into the structure of working memory and the role that the Episodic Buffer may play into this structure.

As is shown in Figure 1.1, when meaningless associations of common visual materials (e.g., lines and colours) are held in short-term memory (Figure 1.1A) no extra resources (i.e., the action of the central executive) seem to be required (Allen et al., 2006 had similar results with more common features such as circles, cross, triangles combined with colours). However, when lists of semantically unrelated words (Figure 1.1C) whose associations are also meaningless are presented, extra resources seem to be required to hold these bound verbal materials in working memory. Why is there a visual versus verbal discrepancy in working memory? The model of working memory proposed by Baddeley (2000) does not make assumptions or predictions about the efficiency of the visual and phonological buffers when the to-be-remembered information is complex in nature. I will use this new

opportunity to emphasize the differences between verbal and visual short-term memory for bound information and to propose some explanations which arise from the current and previous studies.

When information is entering working memory, mechanisms responsible for matching these inputs with previous representations will be activated as suggested by Logie's model (2003). The likelihood of activating these searching processes (and the strength of this activation) seems to depend on the probability of finding such previous representations. If the probability is very low (e.g., shapes and colours randomly combined as described in Allen et al., 2006; Logie et al., 2009; Treisman, 2006) these early processes would be aborted. The information would be removed from the Episodic Buffer and kept within the sketchpad where it will be held until new inputs arrive. As no previous representations were found nor will new representations be built from this information (see Logie et al., 2009, for a similar suggestion), these inputs will be very fragile and quickly overwritten (e.g., by a next trial in experimental settings). Because these active search processes were terminated early, a concurrent task could be performed at no extra cost because the central executive will not be engaged in the maintenance or representation of this information. This proposal would help to explain first, why Allen et al. (2006) found no effect of concurrent tasks on performance during short-term memory binding tasks involving meaningless associations; and second, why Logie et al. (2009), Treisman (2006), and Allen et al. (2006) found a remarkable fragility of these arbitrary bindings when they are held in working memory.

Therefore, the idea that the Episodic Buffer could be fed from the phonological loop and the sketchpad and from the central executive as suggested by Baddeley (2007e) seems to be upheld by these studies. The involvement of the central executive however may depend on the probability

of associating these recent inputs with previous engrams (i.e., long-term representations). If these previous representations are quickly found, this multimodal information is fed into the Episodic Buffer automatically. From there, it will be made available to working memory processing. If more effort has to be exerted to establish these links, more demands on the action of the central executive will be placed (more prompted to interference by concurrent tasks), but the outcomes would still be fed into the buffer (see Jefferies, Lambon, & Baddeley, 2004, for evidence supporting this view; also explained in Baddeley, 2007e). If these links are not found, the information would remain in the temporary memory buffers until new inputs reach working memory and overwrite these previous entries.

Note that in this proposal the ideas of Cowan (1988; 2008; 2009) of short-term memory as an activated subset of long-term memory, of Logie (2003) about long-term memory as a necessary early contact point for information before entering working memory, and of an Episodic Buffer (Baddeley 2000; 2007d and e) as the interface between working and long-term memory may find a favourable context. Future research seems to be required to investigate the extent of the involvement of the central executive (and the Episodic Buffer) in holding visual bound information in working memory when the probability that this complex information has previous long-term representations is higher than that of the shape-colour bindings used in the current and in earlier experiments (Allen et al. 2006; Logie et al, 2009; Wheeler & Treisman, 2002)) (see Figure 1.1A) but lower than that of the natural scenes used by Hollingworth (2005) (see Figure 1.1B).

Furthermore, evidence collected from ES suggests that short-term memory and long-term memory operate through separate processes, more specifically when it comes to binding operations. For example ES performed perfectly well in the Visual Reproduction Test including copy, immediate, and

delayed recall as well as in the recognition phase of the test. In these tasks different drawings ranging from very simple to more complex are presented for 10 seconds and participants are requested to remember them. When these drawing are removed, participants are requested to drawn them in a booklet provided. Considering the nature of the information presented in this test, some kind of binding operations are required in order to remember the way these figures are constructed as well as the relation between figures as in the designs D and E, both presenting two objects (see Appendix 4 for examples of items used in the Visual Reproduction Test). ES also performed well in the copy and delayed recall of the Rey's Figure, in the Doors and People Test, and in other long-term memory tasks.

These tests were not explicitly designed to assess memory binding but they do require binding operations for successful performance (see Section 4.2.2 for a discussion on this issue). However, ES could not hold in visual short-term memory a random polygon with its colour, or a canonical shape with colour, or a common object (e.g., an apple) with a semantically unrelated colour (e.g., pink).

Similarly, asymptomatic carriers of the gene defect E280A assessed in Experiment 17 of Chapter 7 showed totally preserved long-term memory functions. However, they performed significantly more poorly than their healthy relatives without the gene defect when tested for short-term memory binding. Taken together, the evidence discussed here suggests that short- and long-term memory are separate systems with very strong connections. One of these connecting mechanisms seems to be the use of verbal codes. Issues arising from this view are discussed in the next Section.

8.2.3 How valid are the arguments underpinning the different memory models?

Cowan's (1988) model suggests that short-term memory is a subset of long-term memory and that attention is the pointer responsible for selecting this subset. It could be difficult to explain some findings reported in this thesis using this model. For example, ES showed an entirely preserved long-term memory and normal attentional functions. She also showed normal short-term memory in a wide range of tasks. However, her visual short-term memory for bound features was dramatically impaired. This type of short-term memory deficit is left unaccounted by Cowan's model, as according to his view, there should be no reason to have deficits in short-term memory if long-term memory and attention are both preserved. In his chapter published in a recent book, Cowan & Chen (2009) acknowledged that his model runs into difficulties in accounting for those chunking processes involved in binding of visual features (e.g., shapes and colours) in short-term memory resulting in meaningless associations. If we consider that these types of binding were those used to assess ES's short-term memory, the limitations of Cowan's models to explain her impairments become obvious.

One other example suggesting dissociation between memory systems and also arguing against the unitary model could be derived from the carriers of the gene defect E280A whose assessment is reported in Chapter 7. These participants showed normal long-term memory and attention. However, their visual short-term memory for bound features was dramatically impaired. These results support the parallel hypothesis of short- and long-term memory, which suggests that there are also strong connections between these systems.

Early in this thesis it was pointed out that the results from the series of experiments presented would be more relevant for short-term memory than for working memory as the manipulation of information in memory was not explicitly addressed in this study. However, in the light of the findings discussed in these experiments, it may be possible to make some contributions to the discussion on the working memory model. Within the multi-component model of Baddeley and Hitch (1974), and more specifically in the revised version in which the Episodic Buffer was added (Baddeley, 2000), it may be suggested that the results presented in this thesis argue in favour of the existence of a buffer with such functional properties (i.e., feature integration). Just to mention some examples resulting from this thesis, I could point to case ES who showed a completely normal performance on neuropsychological background tests, completely normal verbal short-term memory and visual short-term memory for single features, but a dramatically impaired visual short-term memory for bound features. This suggests that visual short-term memory possesses separate mechanisms to process features integrated into unified representations (i.e., objects) and individual features. This statement is not far from that suggested by Baddeley on the functions of the Episodic Buffer (Baddeley, 2000). Unfortunately, in the current study concurrent tasks were not used (to assess the role of the central executive) nor did we use articulatory suppression (to disentangle the relative contribution of verbal short-term memory from visual short-term memory). These experiments in fact were not designed to contribute to the discussion of the model. However, they may still provide some insights about the existence of a buffer acting as a binding device. Another example in support of the existence of an Episodic Buffer is the finding that carriers of a gene defect (Chapter 7) were selectively impaired in short-term memory for bound features as this was their sole deficit. Furthermore, patients with Alzheimer's Disease assessed throughout the series of experiments showed short-term memory binding deficits which

were well beyond those expected from short-term memory deficits for single or unrelated information. This result supports the argument that short-term memory is equipped with independent functions to process integrated objects and single features.

One limitation of this account is the fact that as it was initially conceived, the buffer reflects the activity of a network aimed at integrating multi-modal information (i.e., visual and auditory, visual and verbal). However, it was recently found that information processed within the visual modality, also requires a buffer equipped with such functional properties. For example in the work by Allen et al. (2006), the authors used shapes and colours as single and bound features to investigate the functional properties of the Episodic Buffer. These results suggested that the buffer can carry out integrative functions that are not entirely cross-modal in nature. From the results reported in this thesis, the concept of an Episodic Buffer might have difficulty accounting for better performance with verbal binding than with visual binding tasks. In his recent book, Baddeley (2007a) suggested that perhaps the visuo-spatial sketchpad may also be equipped with integrative properties. This leaves open the possibility that the subsidiary systems of working memory (i.e., the visuo-spatial sketchpad and the phonological loop) may subserve integrative processes. However, further research is required to investigate this hypothesis.

8.2.4 Summarizing

1. The nature of the information to be integrated seems to affect the format in which objects are stored in short-term memory. Features of different types can be represented as integrated objects in short-term memory while features of the same type cannot.

2. Interference within or between feature dimensions seems to be a cardinal aspect underpinning the efficiency with which processes responsible for binding operations can function.
3. Shapes and colours used in the experiments presented here can be represented in an object-based format. However, as was shown in Chapter 2, the binding of these features in short-term memory does not seem to be a cost-free process. Representing coloured shapes in visual short-term memory required more capacity than representing shapes or colours only and this was more evident as the number of objects in the visual scene increased.
4. Features are not integrated into single objects in visual short-term memory in rigid structures. Rather it seems to be the binding between these features that is rigid. The fact that ES could remember perfectly well single visual features but she had paramount difficulties in remembering how these features combined into objects strongly supports this view. Therefore, features and the binding seem to be processed by separate mechanisms.
5. Binding occurs in both short-term and long-term memory. Processes responsible for this function in these memory systems however, seem separate and to operate differently. There is evidence for a strong connection between these memory systems. The availability of meaningful representations (i.e., verbal codes) seems to provide a way of strengthening memory representation, of increasing the efficiency of memory functions, and of bridging short- and long-term memory.
6. The new evidence accrued through memory binding research seems to provide valuables insights to continue refining memory models currently available. As has been discussed throughout this thesis, Baddeley's (Baddeley, 2000; 2001b; 2007 b & c; Baddeley & Hitch, 1974) and Logie's models (Logie, 2003; Logie & van der Meulen, 2009) have offered accounts for the majority of the results presented in this

research project. There are still some discrepancies to be settle in these models. However, the constructs of memory binding seem to offer a promising approach toward this aim. Furthermore, combined evidence coming from neuropsychological and experimental research would eventually make the greatest contributions.

8.3 Implications for the current knowledge on age-related memory changes

In Chapter 1 (Part II, Section 1.6) the available literature suggesting that ageing impairs memory for related information more than memory for individual elements was reviewed. A hypothesis was proposed by Naveh-Benjamin (2000) which posits that associative memory problems are typical hallmarks of cognitive ageing. Extensive literature showed a wide range of associative memory problems in the long-term domain in the elderly. More recently, the effects of age on short-term memory have been investigated. In this area however, the evidence does not seem as clear. While in some experiments short-term memory for bound or related information has been found to be impaired in ageing (Cowan et al., 2006; Mitchell et al., 2000; Mitchell et al., 2006) others, including those presented in this thesis, have found no effects of age on short-term memory binding (see also Brockmole et al., 2008).

Why do these studies produce different outcomes? The answers to this question can be found in the methodology devised for these experiments. In most of the short-term memory studies in which age was found to affect binding processes, participants were requested to study and remember either the association between objects and their spatial locations or the association between two distinct items which did not result in a new entity. However, in

those studies where short-term memory binding was insensitive to the effects of age, participants studied arrays of items defined by combinations of shapes and colours, or by combinations of colours into bicoloured objects, or the combination of a set of spatial locations into configural patterns (Olson et al., 2004). In all cases the combined information led to the representation in memory of objects with an identity. That is, a colour and a shape or different locations bound into a visual pattern result in integrated objects that can be differentiated from other objects based only on the combination of these features. However, combining objects and spatial locations does not result in a new object with a new identity, but in the association of two unrelated pieces of information that should be held in memory as such in order to successfully remember these complex events. That same object could appear in a different location and still be the same object. In sum, a shape and colour can define a new object but a shape or an object and a spatial location cannot.

As discussed in detail in Chapter 3, object processing and object identification are carried out by brain regions other than those responsible for processing the relation between objects and spatial locations. That detailed discussion will not be repeated here. However, it is important to reiterate some of that discussion in the light of the experimental data obtained and in order to stress the implications for the assessment of elderly people. If we consider the relational hypothesis of the hippocampal functions presented in the review paper by Moses and Ryan (2006) and also discussed by others (e.g., Mayes et al., 2007), it may be possible to argue that older people have problems remembering where objects were presented or what names belong to what faces because these types of relational information are processed by the hippocampus. There is now compelling evidence suggesting that hippocampal atrophy is present in some older adults who are still classified as healthy (Mitchell et al., 2000). Furthermore, experimental data has shown that while performing a short-term memory task involving

object-location associations, older people have had less activation of the hippocampal regions than younger adults (Mitchell et al., 2000). In her review of the literature, Grady (1998) suggested that prefrontal regions and the hippocampus seem to be the brain areas most affected by ageing.

However, and as it was acknowledged by the authors (Moses & Ryan, 2006), hippocampal functions account less for the type of binding in which features are integrated into single and unified representations (i.e., conjunctive binding). Moses and Ryan (2006) also addressed the conjunctive hypothesis of the hippocampal functions which, despite referring to long-term memory, resembles in its functional description those processes occurring in short-term memory, particularly, those involved in short-term memory binding. These types of short-term conjunctive binding processes seem to be less reliant on the functions of the hippocampus and more dependent on cortical mechanisms. From these perspectives, and considering the results presented throughout the series of experiments of this thesis, it is possible to conclude that for the purpose of assessing whether an individual is going through the process of normal ageing or is showing specific or more general rapid decline the use of relational long or short-term memory tasks would not be sufficient. However, the use of conjunctive memory tasks which do not tap hippocampal functions directly may be more promising tools for such purpose. In the next Section Alzheimer' Disease will be considered as an example of abnormal ageing which supports this claim.

8.4 Implications for the early detection of Alzheimer's Disease

In contrast to normal ageing, Alzheimer's Disease seems to impair all forms of association occurring in both short- and long-term memory. The results

presented in this thesis can be considered the first empirical evidence of short-term memory binding deficits in Alzheimer's Disease. In fact binding as a function of short-term memory had not been explicitly assessed in Alzheimer's Disease to date (see Chapter 5). With the tasks used in this project, memory for features and memory for objects have been separated and the associative memory problems shown by Alzheimer' Disease patients have been consequently refined. The memory binding tasks used in the assessment of Alzheimer's Disease patients led to the conclusion that Alzheimer's Disease affects short-term memory for features bound into objects rather more than for individual features. As this type of memory was found to be preserved in healthy older adults, this suggests that short-term memory binding is a process specifically impaired by Alzheimer's Disease as compared to normal ageing.

These results support the claim that short-term memory binding tasks may be seen as tasks that could reliably separate normal from abnormal ageing. I would like to reiterate the evidence discussed in previous Sections to understand why this may be the case. Whereas regions involved in object processing and object identification (e.g., ventral visual stream, perirhinal regions) are unaffected or reorganized in older people, they are damaged in the very early stages of Alzheimer's Disease. Alzheimer's Disease could be thought of as a disconnection syndrome whereby even in its early stages short connecting pathways are interrupted by the neurodegeneration (Bancher, Braak, Fischer, & Jellinger, 1993; Braak & Braak, 1996; Braak et al., 1993; Calderon et al., 1997; Calderon et al., 2004). Therefore, it is not difficult to understand why the integration of features that define objects' identities is also impaired in mild Alzheimer' Disease patients.

According to the results presented in Chapter 7, in a genetic variant of Alzheimer's Disease these memory binding deficits seem to start developing

years before the disease can be detected by more traditional tasks. Clearly our results were found in a genetic variant of Alzheimer's Disease and although we cannot generalise from this to sporadic forms, this finding certainly presents an exciting prospect for future research. These results may change the way we have of conceived the physiopathology of Alzheimer's Disease to date. We have been driven by the idea that episodic memory in general and the associative long-term memory in particular were the earliest memory systems affected by Alzheimer's Disease. We learned that this was due to the damage to the hippocampus and that the hippocampus is important for these types of memory. However, the fact that asymptomatic carriers of the gene defect E280A (Chapter 7, Experiment 17) showed short-term memory binding deficits more than 10 years before converting to Alzheimer's Disease (Lopera et al., 1997), and that these deficits are detected within an otherwise completely normal neuropsychological profile, suggests that the hippocampus may not be the only structure early targeted by the neurodegenerative process of Alzheimer's Disease. Of course, this diagnostic power might only apply to the E280A patients. Longitudinal follow up studies would be needed to assess whether short-term binding tasks can also be useful for predicting conversion to Alzheimer's Disease of apparently healthy older people who are not carriers of the E280A mutation, but who might have, for example, the APOE e4 Allele (e.g., Deary et al., 2002) or of people with Mild Cognitive Impairment.

As has been shown throughout this thesis, one reason behind the controversy between the lack of an age-effect found with the short-term memory binding tasks used here and the age-effect found using tasks assessing relational binding reported in the literature, is that the latter heavily depends on the integrity of the hippocampus, targeted by both normal ageing and Alzheimer's Disease. However, to perform well on the short-term memory tasks described in this thesis, structures other than the

hippocampus need be recruited, namely cortical areas involved in object processing.

Why relational episodic memory deficits have occupied the centre of attention of the scientific community working on Alzheimer's Disease? The reason may be that short-term memory binding tasks had not been used to assess Alzheimer's Disease patients. Nor had they been used with the purpose of differentiating healthy elderly from Alzheimer's Disease patients. From these perspectives, the results of this research project can be considered as novel evidence of the role of short-term memory binding in the early assessment and detection of Alzheimer's Disease.

8.5 Summarizing

1. The impact of ageing on associative memory is not uniform. Long-term memory for related events is considerably affected by ageing whereas short-term memory for this type of information is only affected when the to-be-associated information does not lead to define the identity of objects.

2. The effect of Alzheimer's Disease however, does not distinguish between subtypes of associative memory. This statement is supported by a large body of literature on associative learning and Alzheimer's Disease and by the series of experiments carried out in this project.

3. Therefore, short-term memory binding tasks that assess the integration of features into unified objects should be considered promising tools for both assessing normal ageing and detecting Alzheimer's Disease early among the elderly population.

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At first it was difficult for me to sort, in what might be a "fair order", the names of those who definitely had to be named in this Section. Then, I realized that all had had crucial roles in this work. Hence, I stopped worrying about this issue and decided to follow the order in which these names were involved in this story which began well before this project.

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Glossary

Perceptual Binding:	Also known as "perceptual grouping" refers to binding operations occurring in perception. These binding functions enable objects to become individual entities as early as in perception from where they will be directed to other higher cognitive functions. The role of attention (the Feature Integration Theory) and neuronal synchrony as mechanisms underlying perceptual binding are discussed in depth in Chapter 1 (Section 1.3).
Memory Binding:	Function subserving the integration of information in memory either via relational or conjunctive operations. It is unclear whether memory directly represents objects that were once bound in perception (i.e., memory binding as an automatic process) or whether this as a more creative and resource demanding process.
Associative Memory:	Memory function envisaged as the responsible for representing different pieces of information (i.e., colours, shapes, temporal order, names, faces, etc.) together either into unitary items (i.e., objects) or into multi-item events (i.e., episodes). This form of memory is subserved by binding operations.

Associative Learning: Mechanism(s) responsible for forming long lasting representations of these multi-feature objects or complex events (i.e., Long-term memory).

Short-term memory binding: The function responsible for holding in short-term memory multi-feature objects or complex events. This function enables the representation of complex items using different formats (i.e., object- or feature-based) depending on the nature of the bound information. Furthermore, the level of creativity available to this memory function (i.e., possibility of forming new representations) also depends on the nature of the information represented which in turn determines whether or not there will be access to long-term memory traces. This was the memory binding function investigated in this project.

Relational Binding: This function is responsible for representing the association of independent pieces of information into new relational units. This form of representation is flexible in that either the constituent parts or the whole unit can be accessed or can link to other units. This memory operation underpins the representation in memory of complex events such as objects and their spatial locations, faces and names, or pairs of semantically unrelated words. The association of these items does not lead to the formation of new

conceptual or functional units. That is, it does not modify the identity of the combined items.

Conjunctive Binding: This function underpins the formation of integrated units with new identity. That is, the integration process leads to the formation of items which identity differs from the identity of the constituent parts which in turn change as the result of the integration. This form of representation is inflexible as the unit parts cannot be accessed individually, that is either the whole or none unit can be retrieved from memory. This memory operation may be thought of as that underpinning memory binding of objects and colours, shapes and colours, semantically related words (i.e., lexical units). This form of representation in the domain of short-term memory is the one investigated in this research project.

Inter-item binding: This memory function enables different items to be represented within associated units. This form of representation is subserved by relational binding processes and is though to be mediated by hippocampal functions either when is occurs in the short- or long-term domain. From the retrieval perspective, successful memory of these complex events seems to depend on recall processes.

Intra-item binding: This memory function enables different features to be represented within integrated units. This form of representation is subserved by conjunctive binding processes and is though to be mediated by functions outwith the hippocampal territory (i.e., perirhinal and entorhinal cortices or other neocortical regions outside the medial temporal lobes). From the retrieval perspective successful memory of these complex events seems to depend on recognition processes in which the familiarity component plays a crucial role. This form of binding in the domain of short-term memory was the one investigated in this research project.

Object-based memory: Refers to the format used to represent integrated information in memory. The object-based hypothesis posits that different pieces of information (e.g., features) can be represented in memory as unified objects as long as these different features belong to the same objects (i.e., share a common spatial location). This hypothesis suggests that this is the form in which these different parts are stored in memory. In this thesis it was shown that this hypothesis holds true as long as objects comprise different features types.

Feature-based memory: The feature-based hypothesis disregards the proposition of the object-based hypothesis and states that the different pieces of information (i.e.,

features) are not represented as single-unified entities but as single features which are integrated into these units. Two new issues arise from this hypothesis. First, the binding is therefore a piece of information which has to be stored in memory in addition to each feature. Second, the binding process has a memory cost. In this thesis it was shown that this hypothesis holds true if objects comprise the same type of feature.

Cost-free binding: The idea that binding features into single units (i.e., objects) does not add extra cost to memory comes from the object-based hypothesis. This idea arises from the series of experiment carried out by Luck and Vogel (1997) and Vogel et al. (2001) which were replicated by other authors with different results. A thorough review of this series of study is presented in Chapter 1. In this thesis was shown that whether objects are represented in an object- or feature-based format, the binding process does add extra cost to memory.

Multiple Resources Theory: This theory was born from the observation that binding features into single units was not always a cost-free process but that interference arises when features processed within the same or neighbour dimensions were to-be-bound. The theory proposes that the integrative process utilises resources provided by different and separate dimensions. The overall capacity

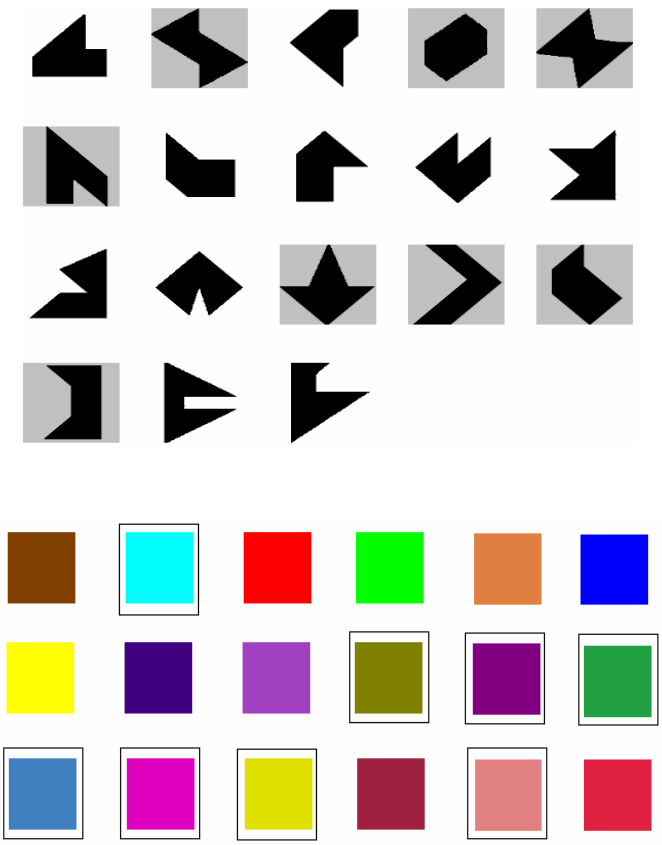
available to this binding function depends on the capacity of each dimension. If objects to-be-held in memory comprise features processed within the same dimension, more interfere will arise and less efficient will be the integrative process as resources within this single dimension would be depleted faster. In the case for objects comprising different feature types the integration will dispose of more resources as different dimensions would be supporting (i.e., feeding) this binding function.

Feature dimension: There seems to be ambiguity in the way this term is used in the literature. In reports on memory binding it is often found terms such as "domains" or "dimensions" referring to those networks processing different features of sensory inputs. In this thesis the term "dimension" was used to refer to these networks and "domain" to more complex networks subserving the function of memory systems (i.e., verbal or visual) rather than individual memory operations.

Appendix 1

Pilot study devised to select abstract shapes and colours

Shapes (18) and colours (18) given to participants in a confusion matrix study (pairs of items were classified as same or different using speeded decisions) designed to investigate the discriminability of visual materials to be used for constructing the visual arrays of Experiments 1-4, 7, 8, 15, and 17. Over a gray background (shapes) or within a square (colours) are those items who met criteria of highly distinguishable (i.e., response times were faster than the lower bound of the confidence interval 95% when they were presented in pairs with any other highlighted item).

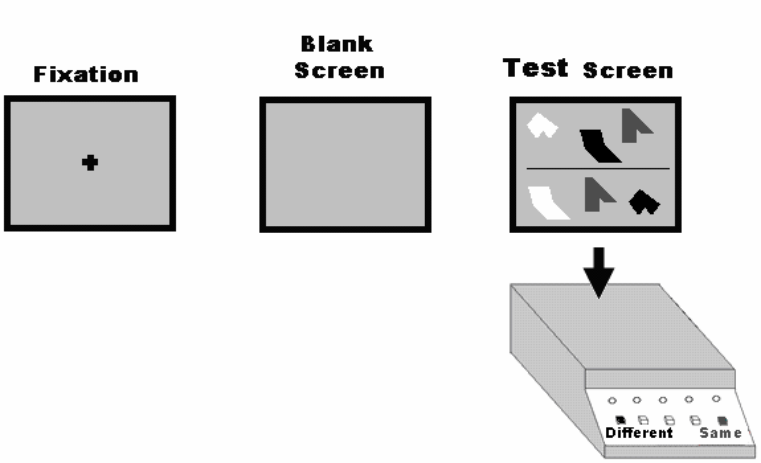


Appendix 2

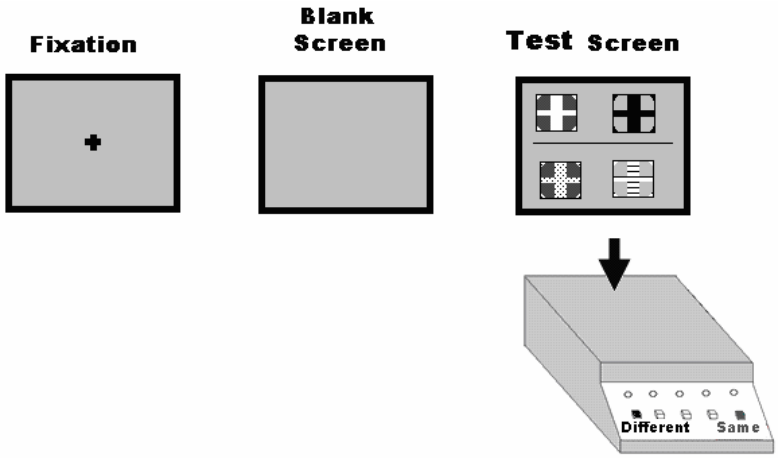
(I) Perceptual binding tasks

(A) Perceptual task given to participants entering Experiments 3, 4, 8, 15, and 17. (B) Perceptual task given to participants entering Experiments 5, 6, 16, and 17. Successful performance on versions of tasks A and B was set as inclusion criterion for all participants entering experiments assessing short-term memory for shape-colour or colour-colour binding.

(A)



(B)



(II) - Experimental instructions

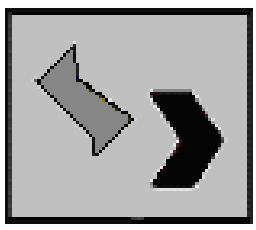
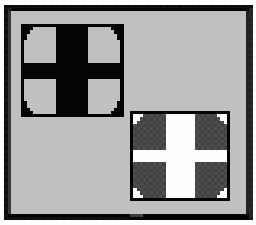
Script presented to participants entering Experiments 4-6, 7, 15-17 to explain the task.

In this task memory for shapes, colours and combinations of colours and shapes will be tested. During the task you will see different numbers of colours, shapes or patterns of colours and shapes and your task is to remember as many of these objects as you can.

You will be told what to do at each step. You will be given plenty of opportunity to take breaks.

During the task you will see a black cross on the centre of the screen for a short period of time, please focus on this cross.

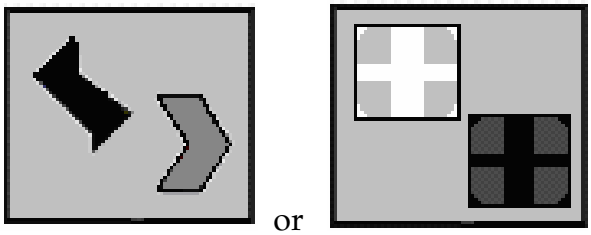
Immediately after the cross disappears, you will see a screen with 2 or 3 objects (coloured squares, shapes or patterns).
Your task is to try and remember as many of these objects as you can.

 or 

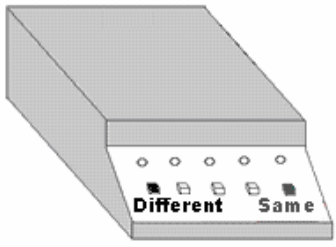
This screen will be followed by a blank screen for a short period of time.

The blank screen will be followed by a new screen with 2 or 3 objects which are in different positions on the screen.

At this point, you will have to decide whether these objects are the same or different to those you saw in the first screen. The positions of the objects are not important, you must just say whether the objects are the same or different.



If you think these objects are the same as before, you will press the button **(*)** "SAME" of the button box. If you think these objects are different, you will press the button "DIFFERENT". Please, take your time to make your decision.



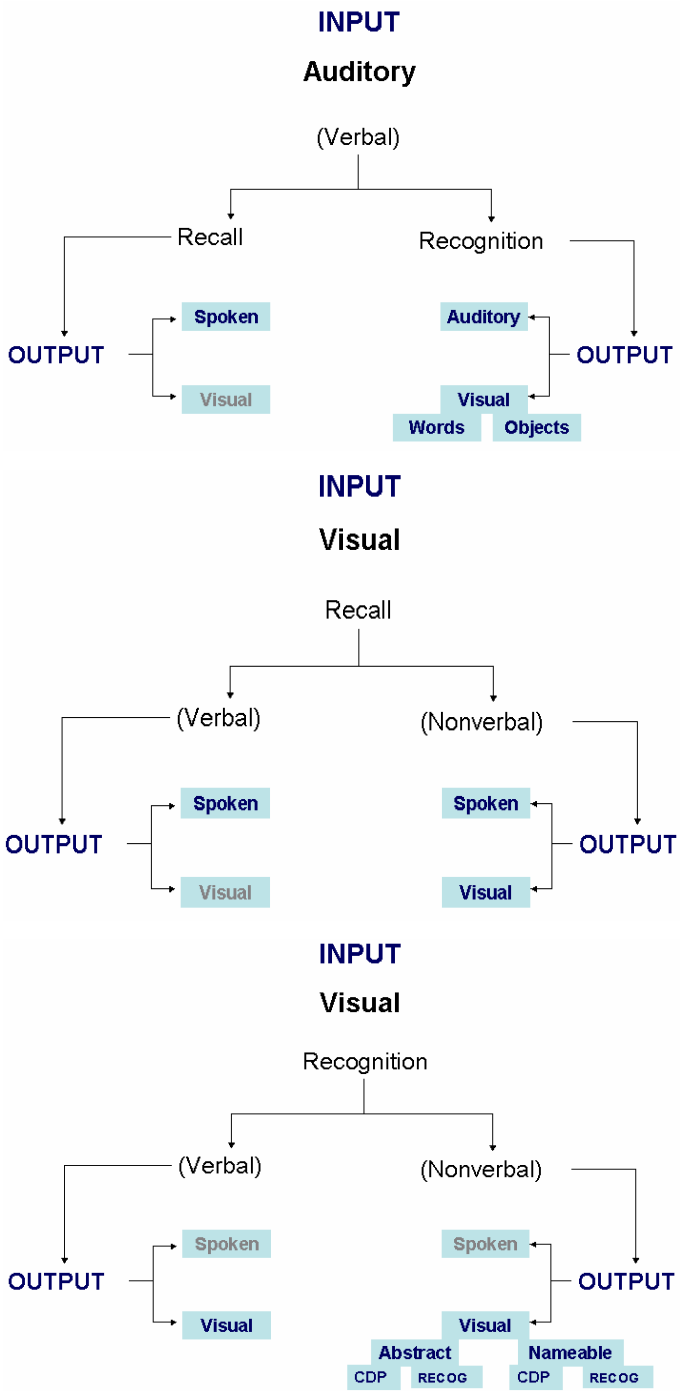
If you have any question about this General Information ask me now.

(*) In studies involving patients (Experiments 15-17), participants responded verbally and the experimenter inputted their responses using the button box.

Appendix 3

Short-term memory tasks devised to assess ES

Diagram of tasks devised to assess ES across sensory modalities (i.e., visual and auditory), memory domains (i.e., verbal and visual) and retrieval processes (i.e., recall and recognition).



INPUT: the modality of presentation used (study phase).

OUTPUT: The way the retrieval phase was delivered (probe phase)

CDP: Change detection paradigm.

RECOG: recognition based on selection from set of items.

Abstract and Nameable: refer to the nature of the stimuli used.

Verbal and Nonverbal: refer to memory domains explored regardless the nature of the stimuli used (verbal or visual).

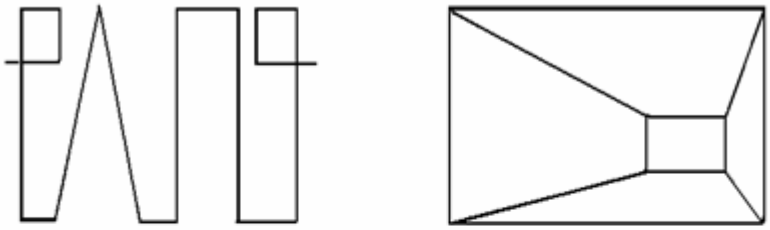
(Boxes with text in gray represent areas not explored)

Appendix 4

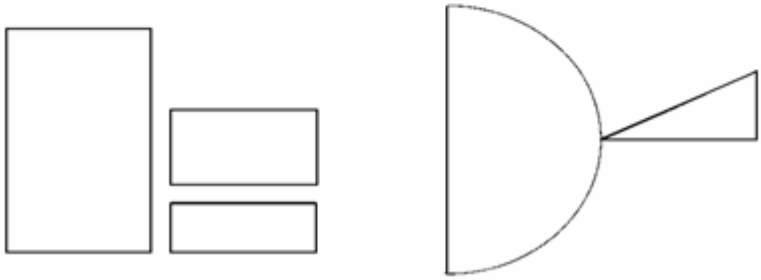
Designs D and E of the Visual Reproduction Test

In this test, five different designs are used to assess visual memory. In designs A to C, each card presents one item. In designs E and D (shown below as (A) and (B) respectively) each card presents two items. Cards are presented one at a time for 10 seconds and participants are requested to remember as many details as they can. The card is then covered and participants are requested to draw the item(s) from memory in a booklet provided. Memory is assessed immediately after the presentation and 25 to 30 minutes latter.

(A)



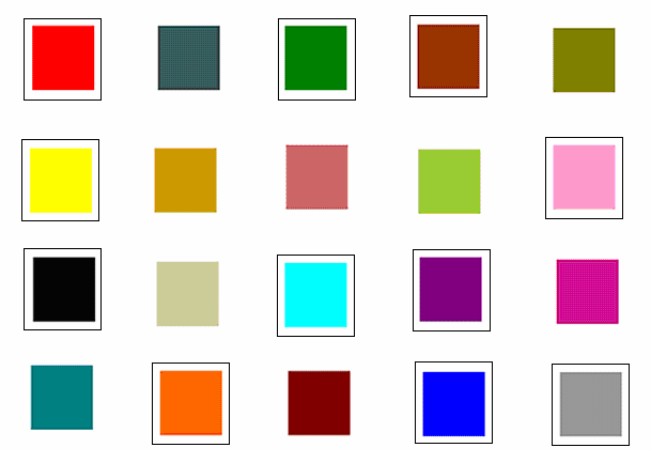
(B)

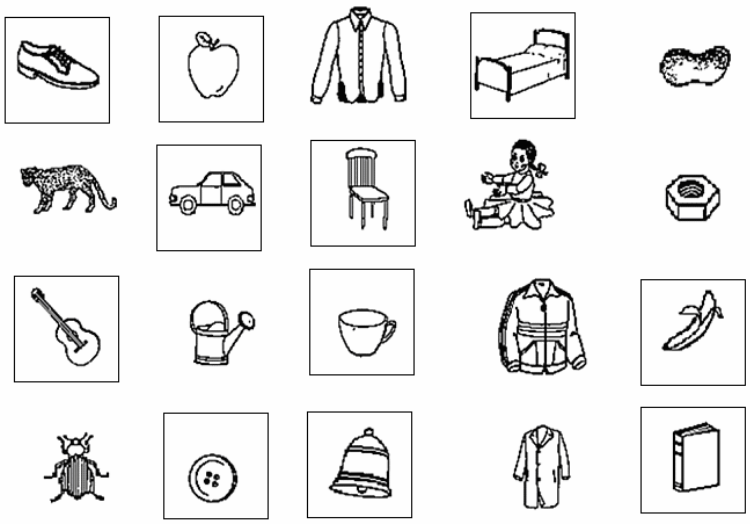


Appendix 5

Tasks devised for screening object or colour naming problems

Arrays presented to participants entering Experiments 9, 10, 13 and 14 to assess their object and colour naming functions. In boxes are highlighted the actual stimuli used in the task (these boxes were not shown to participants).





Appendix 6

Examples of the stimuli used in Experiment 11

Nouns	Adjective	Noun-Adjective Binding
Accordion	Bent	Inflated Balloon
Anchor	Burnt	Wooden Broom
Ashtray	Carved	Burnt Cigarette
Balloon	Closed	Knitted Basket
Basket	Colour	Folded Accordion
Bicycle	Colouring	Flaming Candle
Bottle	Electronic	Locked Bicycle
Broom	Flaming	Round Doorknob
Button	Flashing	Hanging Anchor
Candle	Folded	Glassy Ashtray
Cannon	Full	Sunken Bottle
Cigarette	Glassy	Shooting Cannon
Doorknob	Greasy	Stamped Envelope
Envelope	Hanging	Flashing Button
Football	Inflated	Spinning Football
Guitar	Knitted	
Hammer	Locked	
Hanger	Round	
Helicopter	Spinning	
Paintbrush	Sunken	
Pencil	Shooting	
Pliers	Toasted	
Pumpkin	White	
Sailboat	Wooden	

Appendix 7

Instructions for Experiments 13 and 14

This experiment explores memory for colours, objects and the combination of colours and objects. During the experiment you will be presented with screens consisting of different colours, objects, or combinations of colours and objects. Your task is to try and remember as many of these items as you can.

Before moving on to the specific instructions, you will be presented with one set of objects and one set of colours. Please name these objects and colours as you know them (here the arrays shown in the Appendix 5 are presented).

During the experiment you will be presented with an initial display consisting of a varied number of items (e.g., 3 or 4, 6 or 8). Your task is to try to remember as many of these items as you can. These items will look like this:

 or  or 

After the items disappear, you will see a second test screen like this one:

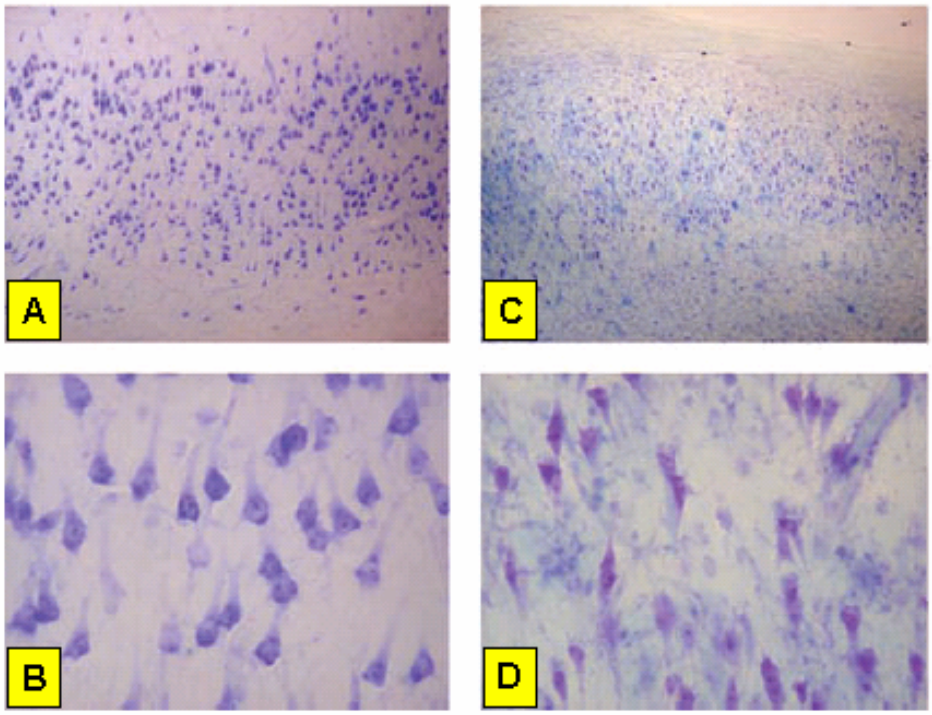
When you see this screen, you will start recalling loudly and slowly the items you saw before. For example, you will report the objects, the colours, or the coloured objects as you saw then in the initial screen.

If you have any question, please ask me now.

Appendix 8

Neuropathological changes in Alzheimer's Disease E280A

Slides from the hippocampal CA1 region showing the neuronal lost in a patient with Familial Alzheimer's disease due to the mutation E280A (C and D) as compared to a healthy control (A and B). The slides C and D belong to a female patient who was 53 years old by the time of the onset of the disease and lasted for 7 years after the diagnosis.



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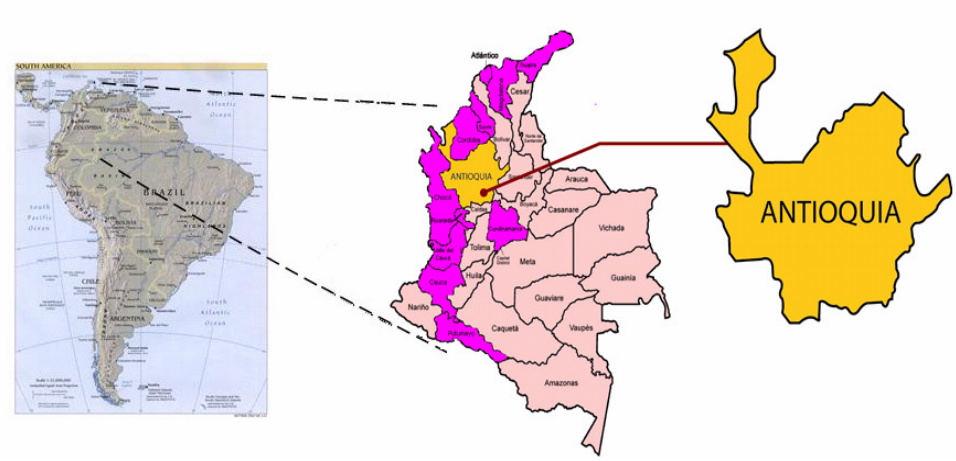
Appendix 9

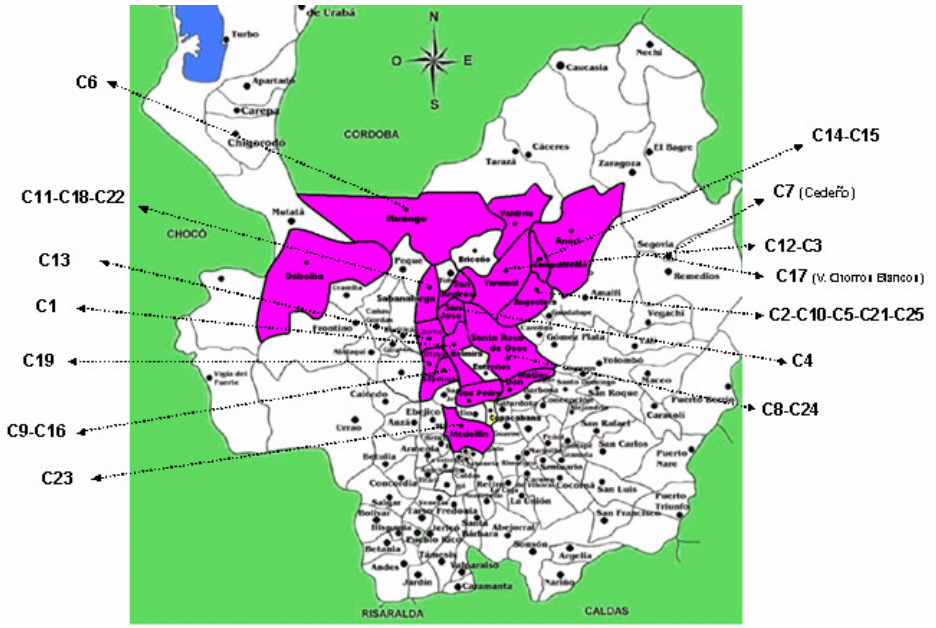
Geographic distribution of families with the mutation E280A

(A) Antioquia, Colombia, (B) Geographic distribution of families with the mutation E280A.

(A)



(B)



(C1 – C25 families identified to date)