Handbook of binding and memory: perspectives from cognitive neuroscience

Edited by

Hubert D. Zimmer,
Department of Psychology, Brain and Cognition Unit,
Saarland University, Germany

Axel Mecklinger,
Department of Psychology, Experimental Psychology Unit,
Saarland University, Germany
and

Ulman Lindenberger,
Director, Center for Lifespan Psychology,
Max Planck Institute for Human Development, Germany

OXFORD
UNIVERSITY PRESS

OXFORD
UNIVERSITY PRESS
Great Clarendon Street, Oxford OX2 6DP
Oxford University Press is a department of the University of Oxford.
It furthers the University's objective of excellence in research, scholarship,
and education by publishing worldwide in
Oxford New York
Auckland Cape Town Dar es Salaam Hong Kong Karachi
Kuala Lumpur Madrid Melbourne Mexico City Nairobi
New Delhi Shanghai Taipei Toronto
With offices in
Argentina Austria Brazil Chile Czech Republic France Greece
Guatemala Hungary Italy Japan Poland Portugal Singapore
South Korea Switzerland Thailand Turkey Ukraine Vietnam
Oxford is a registered trade mark of Oxford University Press
in the UK and in certain other countries
Published in the United States
by Oxford University Press Inc., New York

First published 2006

British Library Cataloguing in Publication Data
Data available
Library of Congress Cataloging in Publication Data
Data available
Typeset by Newgen Imaging Systems (P) Ltd., Chennai, India
Printed in Great Britain
on acid-free paper by
Biddles Ltd., King's Lynn, UK
ISBN 0–19–852967–8 978–0–19–852967–5
10 9 8 7 6 5 4 3 2 1

Chapter 11

Ageing deficit in neuromodulation of representational distinctiveness and conjunctive binding: computational explorations of possible links

Shu-Chen Li and Ulman Lindenberger

Introduction

> The mind is a kind of theatre, where several perceptions successively make their appearance; pass, repass, glide away, and mingle in an infinite variety of postures and situations.
>
> What we call a mind is nothing but a heap or collection of different perceptions, united together by certain relations and suppos'd, tho' falsely, to be endow'd with a perfect simplicity and identity.
>
> To me, there appear to be only three principles of connexion among ideas, namely, resemblance, contiguity in time or place, and cause or effect.
>
> (David Hume, *A Treatise of Human Nature*, Book I, Part 4, Section 6, and Part 1, Section 7; *An Enquiry Concerning Human Understanding*, Section 3.)

Although David Hume, the eighteenth-century Scottish empiricist philosopher, was sceptical about the veracity with which human perceptual and memory processes capture and store the manifold world and our experiences in it, he was certain that the mind works by combining assorted aspects of experienced reality and that such combinatory processes pose a task for the mind to solve. What modern students of mind and brain are still uncertain about are, indeed, the details of so-called 'binding mechanisms'. How—or, in Hume's term, by what relations—are multiple features of the experiential world and the stored memory episodes bound together to produce coherent neurocognitive representations? Hume himself proposed three relational principles: resemblance, spatial and temporal contiguity, and causality. Parallel to, although not necessarily motivated by, Hume's contention, much of current cognitive and

neuroscience research on the issues of binding focuses on mechanisms for flexible coding of conjunctive relations between multiple attributes of objects and complex memory events, or both. Put more generally, the research on perceptual and memory binding aims at understanding the neurocognitive mechanisms that afford dynamic versatile implementations of representations, so that the mind can fluently integrate information across time, space, attributes, or ideas (reviewed by Treisman 1999).

Apart from investigating mechanisms supporting flexible combinatorial information processing in young adults, ontogenetic changes in the brain (Sowell *et al.* 2003) and cognitive functions (Li *et al.* 2004) across the lifespan can be expected to affect the efficacy of binding mechanisms. Understanding ontogenetic factors operating during either child development or ageing that strengthen or weaken, respectively, our capacity to handle perceptual and cognitive combinatorial complexity may shed light on basic mechanisms of binding. The question of how ageing may affect the mechanisms subserving conjunctive integration of information has gained increasing research attention (Spencer and Raz 1995; Chalfonte and Johnson 1996; Mitchell *et al.* 2000; Naveh-Benjamin 2000; Naveh-Benjamin *et al.* 2003). In this chapter, and based on earlier work (Li and Lindenberger 1999; Li 2002), we present a neurocomputational model that formalizes the disproportionate deficits in conjunctive feature binding in older adults. First, we provide a brief and selective review of the empirical literature on adult age differences in conjunctive feature binding. Secondly, we present the general neurocomputational framework adopted in the present and earlier simulations of adult age changes in information processing efficiency. Thirdly, we present a series of simulations that are specifically aimed at relating age-associated conjunctive binding differences to a triad consisting of deficient neuromodulation, less efficient distributed conjunctive coding, and reduced representational distinctiveness. Finally, we relate our findings to other models of binding, and discuss their generality.

Ageing and conjunctive memory binding

Ageing affects different aspects of memory function to varying degrees (reviewed by Zacks *et al.* 2000). Overall, memory for explicitly encoded event information (i.e. episodic memory) and online memory processing capacity (i.e. working memory) show greater ageing deficits than memory for general facts (i.e. semantic memory), personal history (i.e. autobiographic memory), or incidentally encoded events (i.e. implicit memory). With respect to episodic memory,

complex memory events often involve various kinds of information, such as the persons involved in the events, the time or place at which the events took place, and other general background contextual information. Various researchers have suggested that mechanisms for binding together multiple details of a memory episode may be compromised by ageing (MacKay and Burke 1990; Light 1991; Chalfonte and Johnson 1996; Naveh-Benjamin 2000).

Thus far, three aspects of ageing-related memory binding deficits have been identified: memory for contextual information, memory for feature combinations of a given event, and memory for associations between events. Regarding context and source memory (Johnson *et al.* 1993; McIntyre and Craik 1987), older adults experience greater difficulty than younger adults in remembering contextual details of memory episodes, such as whether the remembered actions were imagined or performed, whether the information was presented visually or aurally, whether the remembered event happened before or after other events, and whether the memory episode happened in one or other possible locations (reviewed by Spencer and Raz 1995). Concerning feature combinations, older adults show poorer memory performance than younger adults when different features of the studied items (e.g. objects and locations, objects and colours, or words and font types) need to be combined (Chalfonte and Johnson 1996; Naveh-Benjamin 2000). As for associations between items or events, negative age differences in cued recall for paired associates, revealing a deficit in retrieving associative information, have been found in many studies (Kliegl and Lindenberger 1993; reviewed by Kausler 1994). More recent studies have also shown that older adults have disproportional difficulties relative to young adults in encoding and storing associations between memory items (Naveh-Benjamin 2000; Naveh-Benjamin *et al.* 2003).

In summary, cognitive ageing appears to adversely affect some, if not most, aspects of conjunctive binding in the domain of episodic memory. Older adults exhibit disproportional performance deficits relative to younger adults under task conditions that require conjunctive associations between multiple features (e.g. the contexts and contents of the memory events, stimulus attributes, or the associations between events). Ageing-related memory encoding and binding deficits have been attributed to frontal hippocampal circuitry (Mitchell *et al.* 2000; Grady *et al.* 2003) but have not been linked formally to impaired neuromodulation involving this circuitry. We now review a theory that relates cognitive ageing to deficient neuromodulation of representational distinctiveness and then demonstrate through simulations that less efficient distributed conjunctive coding may underlie ageing-related deficits in conjunctive memory binding.

Deficient neuromodulation and cognitive ageing

The factors contributing to cognitive ageing deficits cut across behavioural, cognitive, and neurobiological levels. Therefore integrative theories facilitating cross-level data synthesis and hypothesis testing (Churchland and Sejnowski 1988) are necessary for a comprehensive understanding of neurocognitive ageing. Building on various approaches for modelling neuromodulation from computational neuroscience, few recent computational theories have explored computational principles that relate ageing-related decline of neuromodulation to behavioural manifestations of cognitive ageing. For instance, with respect to the ability of monitoring the valence of behavioural consequences, a recent model relates weakened phasic activity of the mesencephalic dopamine system to ageing-related deficits in error processing (Nieuwenhuis *et al.* 2002). Another theory has focused on functional interactions between dopaminergic modulation and the dorsal lateral prefrontal cortex (PFC) to capture the effect of ageing on context representation and maintenance (Braver *et al.* 2001). Below, we briefly summarize ageing-related decline in neuromodulatory systems, and then focus on a cross-level theory that elucidates a potential sequence of functional relations from deficient dopaminergic modulation to reduced neural information processing fidelity, with ensuing consequences for cortical representational distinctiveness that may underlie various behavioural manifestations of cognitive ageing (Li *et al.* 2000). As will be demonstrated in later sections, this approach can also be used to model the effects of deficits in conjunctive feature binding on episodic memory for associated events.

Ageing and neuromodulation

Brain ageing involves structural losses in neurons and the connections between them (reviewed by Schneider *et al.* 1996). Severe progressive neuroanatomical degeneration resulting from cell death and reduced synaptic density is typical of pathological ageing (e.g. Alzheimer's disease). In normal ageing, the volumes of various cortical regions also show slightly declining trends. The most substantial shrinkage is observed in the PFC (Raz 2000; Head *et al.* 2002). Parallel to the less severe neuroanatomical changes, the milder cognitive declines that occur during normal ageing are likely to be due to neurochemical shifts in still relatively intact neural circuitry (Morrison and Hof 1997). Such neurochemical shifts affect the efficacy of signal transmission, which, in turn, regulates neural activity within and across cell assemblies. Various transmitter systems are affected by ageing and have implications for cognitive declines associated with pathological and normal ageing. For instance, the transmitter acetycholine (Ach) is important for

long-term memory consolidation. It plays a specific role in the memory deficit for retaining new information seen in Alzheimer's patients (Hasselmo 1995). Furthermore, for an understanding of the neurochemical circuits of the ageing brain, it is important to consider both the effects of various transmitters independently and the interactions between multiple transmitters, such as the recently discovered interaction of glutamate with other transmitters (e.g. dopamine, GABA, and acetylcholine) (Segovia *et al.* 2001).

Among various neuromodulatory systems, the monoamines (e.g. serotonin and the catecholamines, particularly dopamine) are promising neurochemical correlates of normal cognitive ageing. There is evidence of a reduction in dopamine D_2 receptors of about 7–11 per cent per decade during normal ageing, starting at about age 20 years in the nigrostriatal region (Wong *et al.* 1997). There is now also evidence of D_2 receptor loss in various other extrastriatal regions (Kaasinen *et al.* 2000; reviewed by Bäckman and Farde 2005), such as the anterior cingulate cortex (13 per cent), the frontal cortex (11 per cent), the hippocampus (10 per cent), and the amydgala (7 per cent). In addition, D_1 receptor loss has been observed in the striatum (Giorgi *et al.* 1987) and the frontal cortex (de Keyser 1990, Zahrt *et al.* 1997).

In addition to the trends of ageing-related declines of dopamine receptors in different brain regions across the adult lifespan, there is also more direct experimental evidence for functional relationships between deficient dopaminergic modulation and cognitive deficits. For instance, deficient dopaminergic modulation was found to be associated with increased fluctuation in response speed and reaction time in old rats (MacRae *et al.*1988). Drugs that facilitated dopaminergic modulation were found to alleviate working memory deficits in old monkeys (Arnsten and Goldman-Rakic 1985; Arnsten *et al.* 1994). In humans, ageing-related attenuation of the striatal D_2 receptor binding mechanism was found to be statistically associated with age differences in processing speed and episodic memory (Bäckman *et al.* 2000).

From deficient neuromodulation to increased neuronal noise and less distinctive representation

Although ample evidence indicates that deficient dopaminergic modulation has implications for cognitive ageing, many details of this neuromodulation–cognition link await further explication. At the cellular level, empirical and theoretical work on how dopaminergic modulation affects the memory field and signal integration of PFC neurons has only recently begun (Camperi and Wang 1998; Durstewitz *et al.* 1999; Goldman-Rakic *et al.* 2000). At a higher level of abstraction, a general feature of the net effect of dopamine in decreasing

background firing rate and enhancing the excitability of target neurons has been modelled as the regulation of the signal-to-noise ratio of neural information processing by altering the gain parameter *G* of the neural network's activation function (Servan-Schreiber *et al.* 1990). It has also been demonstrated recently that simulating ageing-related decline of dopaminergic neuromodulation by attenuating the parameter *G* in neural networks suggests a possible chain of mechanisms that relate deficient neuromodulation to increased neuronal noise and less distinctive cortical representations both within and across processing pathways (Li *et al.* 2001; Li and Sikström 2002).

Reduced responsivity and increased neuronal noise

Reducing the parameter *G* simulates ageing-related attenuation of dopaminergic modulation by decreasing the slope and flattening the non-linearity of the S-shaped logistic activation function (i.e. making it more linear), such that a unit's average response to excitatory and inhibitory input signals is reduced (Figure 11.1(a)). When the values of a unit's G are randomly chosen (i.e. stochastic G manipulation; Li *et al.* 2000) from a set of values with a lower average (i.e. mean G reduction, but keeping the range of the distribution constant), the unit's response to a given external signal fluctuates more across discrete time steps. This implies decreased signal transmission fidelity (Figure 1B). In other words, a given amount of random variations in G—simulating random fluctuations in dopamine transmitter substance due to probabilistic transmitter release or stochasticity in receptor binding efficacy (Hessler *et al.* 1993)—generates more haphazard activation during signal processing if the average of the processing units' Gs is reduced. This functional interaction between fluctuation and level depicts a potential neurochemical mechanism for a common hypothesis of an ageing-related increase in neural noise introduced by Welford (1965): As ageing attenuates neuromodulation, the impact of transmitter fluctuations due to probabilistic transmitter release and other sources of neuronal noise (e.g. background spiking activity) on the overall level of haphazard neuronal activity is being amplified.

Reduced representational distinctiveness

With respect to the efficiency of conjunctive coding, of particular interest here is that the simulations also show that, as reduced responsivity leads to increased intra-network random activation variability, another subsequent effect is a decrease in the **distinctiveness** of the network's internal representations. Low representational distinctiveness means that the activation profiles formed across the network's hidden units for different stimuli are less readily

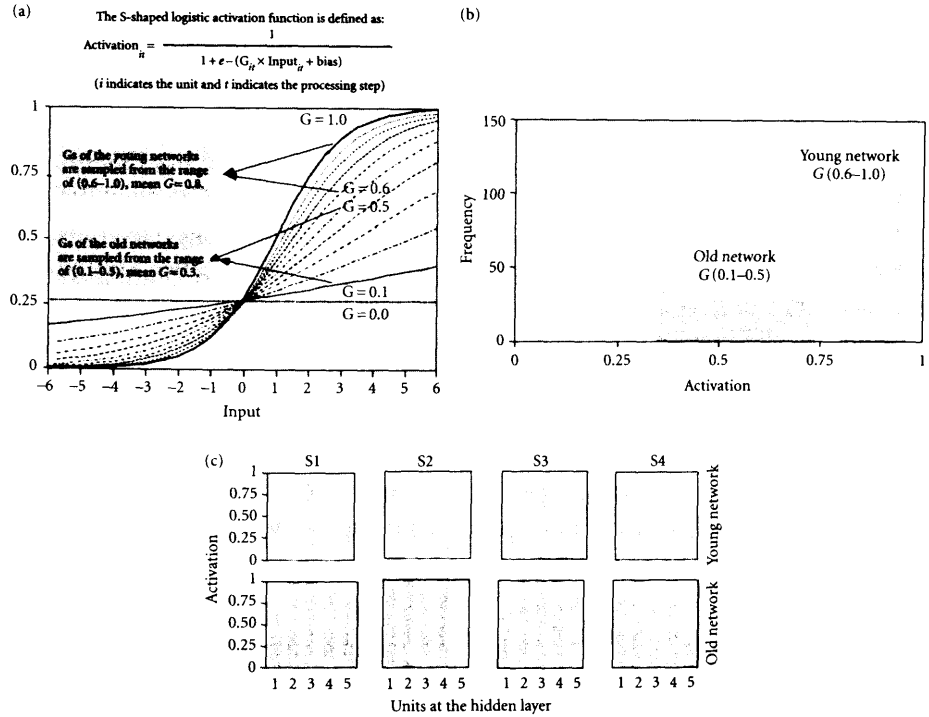

Figure 11.1 Simulations of gain modulation, neuromodulation, and ageing. (a) The S-shaped logistic activation function at different values of *G*. Physiological evidence suggests that the logistic function with a negative bias captures the function relating the strength of an input signal to a neuron's firing rate, with its steepest slope around the baseline firing rate. Reducing mean *G* flattens the activation function such that a unit becomes less responsive. Ageing-related decline of dopaminergic modulation can be simulated by sampling values of *G* from a distribution with a lower mean. (b) *G* and the variability of activation across processing steps. Reducing mean *G* (0.8 and 0.3 for the 'young' and 'old' networks, respectively) increases the temporal variability of a unit's response to an identical input signal (set to 4.0) across 1000 trials. (c) Internal activation patterns across five hidden units of one 'young' and one 'old' network in response to four different stimuli (S1–S4). The internal representations of the four stimuli are much less differentiable in the 'old' network than in the 'young' network. (Adapted with permission from S.-C. Li *et al. Neurocomputing*, **32–33**, 879–890, 2000.)

differentiable from each other. Figure 11.1(c) shows the internal activation patterns across units at the hidden layer of a 'young' (higher mean *G* in the top row) and an 'old' (lower mean *G* in the bottom row) network in response to four input stimuli. Because more units are required to distributively code the feature combinations of the different stimuli, the internal stimulus representations are less distinctive (patterns representing different memory

events are less differentiable from each other) in the 'old' than in the 'young' network.

Taken together, a potential biological implication of these theoretical effects could be that, as people age, declining dopaminergic modulation reduces cortical neuron responsivity and increases neural noise in the ageing brain. Consequently, the efficiency of distributed coding of neuronal activity is reduced, such that the internal representations elicited by different stimuli and contexts become less differentiated. This theoretical sequence of potential effects has been tested in a series of simulations that captured a range of cognitive ageing phenomena, such as adult age differences in learning rate, asymptotic performance, interference susceptibility, working memory, complexity cost, intra- and inter-individual variability, ability dedifferentiation, and the coactivation of different neurocognitive processes (Li *et al.* 2001; Li and Sikström 2002).

Neurocognitive representations of concurrent exogenous and endogenous events (e.g. perception and sensation) and later reinstatements of these events (e.g. memory and action) are the primitives of subsequent information processing carried out by various neural circuits. It has been argued that perceptual, motor, and memory processes all involve the binding together of multiple representations of stimulus features, task goals, and contexts (Johnson 1992; Treisman 1998; Wolpert *et al.* 2001; Nadel *et al.* 2000). Thus deficient neuromodulation resulting in less efficient distributed conjunctive coding may have implications for ageing-related deficits in memory binding.

Relating reduced representational distinctiveness with deficits in conjunctive binding

Neurocomputational models aid the search for mechanisms that bind diverse features into coherent representations through formal analysis and hypothesis testing. Thus far, associative network theories emphasize distributed dynamical processes that tune each processing unit to subsets rather than to all relevant features (O'Reilly and Busby 2002; cf. Singer 1998). As reviewed above, earlier simulation work has shown that deficits in neuromodulation can result in less distinctive stimulus representations and, by implication, less efficient distributed conjunctive coding. Less distinctive representation can lead to erroneous conjunctions, which is deleterious in distributed and context dependent coding (Singer 1998) and thus may affect the efficacy of memory binding. We extend this principle to model ageing-related deficits in two aspects of memory binding.

A feature–association conjunctive binding model of ageing-related associative deficits

Deficits in associative conjunction binding in older adults has been systematically investigated in a series of recent experiments that examined both inter-item associations and intra-item feature conjunctions (Naveh-Benjamin 2000; Naveh-Benjamin *et al.* 2003). Of particular interest, one of the experiments clearly demonstrated that ageing differentially affects the encoding and storage of associative memory more than item memory (Naveh-Benjamin 2000, Experiment 2). Participants in this experiment were presented with word pairs during the study phase, but were instructed to study the word pairs either as two single words (the study words instruction) or as pairs (the study pairs instruction). During the testing phase, the participants were tested with both an associative test and an item test. The associative test required correct recognition of studied word pairs (targets) from rearranged word pairs (lures), whereas the item test required correct recognition of studied words (targets) from non-studied words (lures). The results showed that, when the associations between word pairs were learned intentionally (i.e. under the study pair instruction), older adults exhibited differentially poorer performance in the associative test than younger adults.

A feature–association conjunctive binding model (Li *et al.* 2005) was constructed to simulate the ageing-related deficit of associative binding observed in Naveh-Benjamin's (2000) experiment. The model (Fig. 11.2) involves parallel processing paths for feature conjunctive binding of item information and for

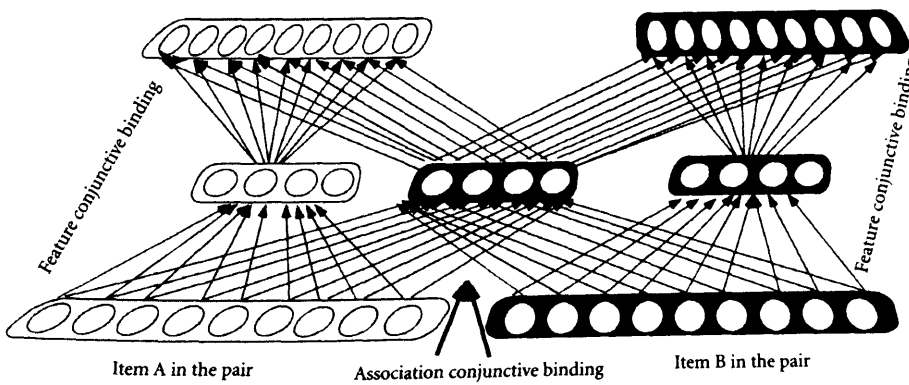

Figure 11.2 Schematic diagram of the network structure for the feature–association conjunctive binding model. (Adapted with permission from S.-C. Li *et al. Psychological Science*, **16**, 445–450, 2005.)

association conjunctive binding of inter-item associations. The multiple features of the two items in a given study pair are distributedly processed within each of the corresponding feature conjunctive binding paths, with converging connections from the input item-feature layer to the internal item-representation layer and divergent connections from the internal layer to the output item-response layer. The association conjunctive binding path in the middle processes inter-item association. The features of both items are distributedly processed through the input connections that converge on the internal association-representation layer and the divergent connections to the output item-response layer.

Network architecture

The networks had 18 inputs, 12 hidden units, and 18 output units that were separately connected by feedforward connections between layers within the feature conjunctive binding and the association conjunctive binding path. The first half of nine input and output units are dedicated to feature information for the study item on the left side of a given study pair (e.g. item A from the A–B pair). The second half of the remaining nine input and output units are dedicated to feature information for the item on the right side of the pair (e.g. item B from the A–B pair). The first four hidden units code distributed representation of feature conjunction of item A in the pair. The middle four hidden units are dedicated to the distributed representation of the association between the two items. Finally, the last four hidden units code the distributed representation of feature conjunction of item B. The specific network architecture of presenting item–item associations as intra-layer associations is designed specifically to stimulate Naveh-Benjamin's (2000) experimental paradigm closely. The effect of reducing the gain parameter in simulating the ageing deficit of paired associate memory using the more traditional way of representing item–item associations as input–output associations has been demonstrated elsewhere (Li *et al.* 2000). Although the model is currently set up to account for associative binding at the inter-item level, conceivably a similar architecture could also be used to simulate specific feature binding effects if within-item feature specificities are systematically present in the stimulus patterns.

Parameter values

Learning rate, momentum, and bias were fixed parameters and were set to 0.1, 0.8, and –4.0, respectively. The networks were initialized with random weights in the range $[-1,1]$. The stochastic gain manipulation (Li *et al.* 2000) affected all hidden and output units of the networks. Two groups of 10 networks were identical in all respects except for the mean values of their gain (G) parameters.

The two network groups can be considered as the yoked control for each other, as identical sets of 10 random seeds were used to define the initial weight configurations for both groups. The mean G of each of the 10 old networks was 0.9, whereas the mean G of each of the 10 young networks was 1.2. The range of the uniform distribution from which the values of G were sampled was fixed at 0.4 for both groups of networks.

Study and test phases

Before providing the networks with the study pairs for learning, both groups of networks were trained to reach the same performance level with a sample of single-item patterns to establish initial item knowledge. During the study phase, the networks were trained to learn item pairs for 10 trials. Connection weights were trained with back-propagation learning. Analogous to Naveh-Benjamin's (2000) experimental manipulation of study instructions, the emphasis on studying the presented pairs as either single items or intact pairs was implemented by either presenting only the item pairs (the study pair instruction) or presenting the item pairs as well as individual items of the pair to the network during the study phase (the study item instruction). At the test phase, both groups of networks were tested under two conditions. In the associative test condition, the networks were presented with intact target pairs and rearranged lure pairs. In the item test condition, the networks were presented with single target items and single lures. A standard indicator of the match between the expected outputs and the actual network outputs (the cosine between target and actual outputs (Goebel and Lewandowsky 1991)) was computed. If a test pair (or item) was a target test pair (or target item) and the cosine was greater than a fixed threshold, a hit was scored. If a test pair (or item) was a lure pair (or lure item) and the cosine was greater than the threshold, a false alarm was scored. The response threshold was fixed at a cosine of 0.99 for the study pair introduction and a cosine of 0.975 for the study word introduction.

Results

With only two assumptions—ageing-related deficit in dopaminergic modulation can be simulated by reducing the mean G of the network activation function and the response criterion is slightly lower in the incidental learning condition (the study word instruction)—the model was able to capture the age effects observed in Naveh-Benjamin's (2000) four experimental conditions (Fig. 11.3). The simulation accounts for differential ageing effects on item and associative memory. The performance of old networks was relatively spared in the item test and more impaired in the associative test. In particular, details of the three-way age $\times$ instruction $\times$ test type interaction, indicating that older adults had

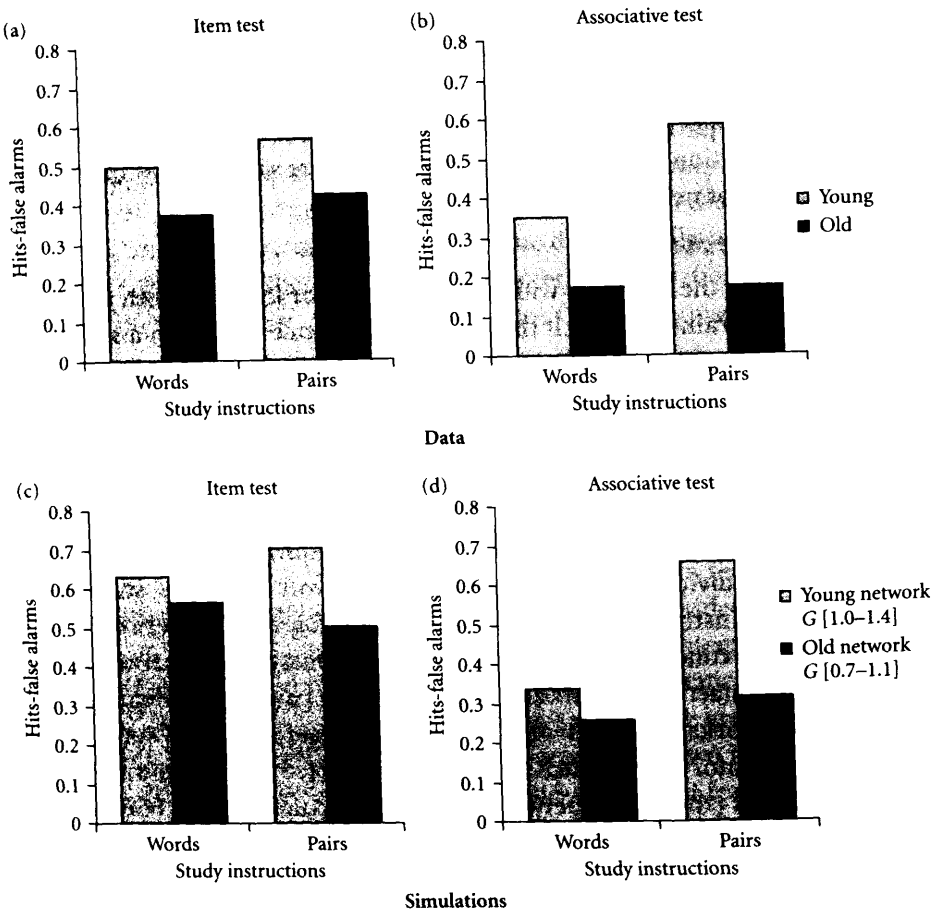

Figure 11.3 Empirical data (replotted from Naveh-Benjamin 2000, Experiment 2) and simulation results of adult age differences in associative binding. (Adapted with permission from S.-C. Li *et al. Psychological Science*, **16**, 445–450, 2005.)

disproportionately greater difficulty in encoding and storing associative information when the associations were learned intentionally, (i.e. comparing young and old associate test performance across study instructions Figs 11.3(b) and 11.3(d)), were captured well by the simulation results (Li *et al.* 2005).

Internal activation patterns

Examining the internal feature conjunctive representations of the items and the internal association conjunctive representations at the hidden layer revealed that the disproportionately poor associative memory of the old networks was indeed caused by less efficient coding of associative information owing to inferior *G*

modulation. Figure 11.4 shows summary activation maps of individual networks with a range of mean G values from 1.6 to 0.6. On the vertical axis, the first 18 patterns correspond to activations in response to the associative test, whereas the remaining 12 patterns correspond to activations in response to the item test. On the horizontal axis, the first four units correspond to the distributed representation of feature conjunction of item A in the pair, the middle four units correspond to the distributed representation of association conjunction of the

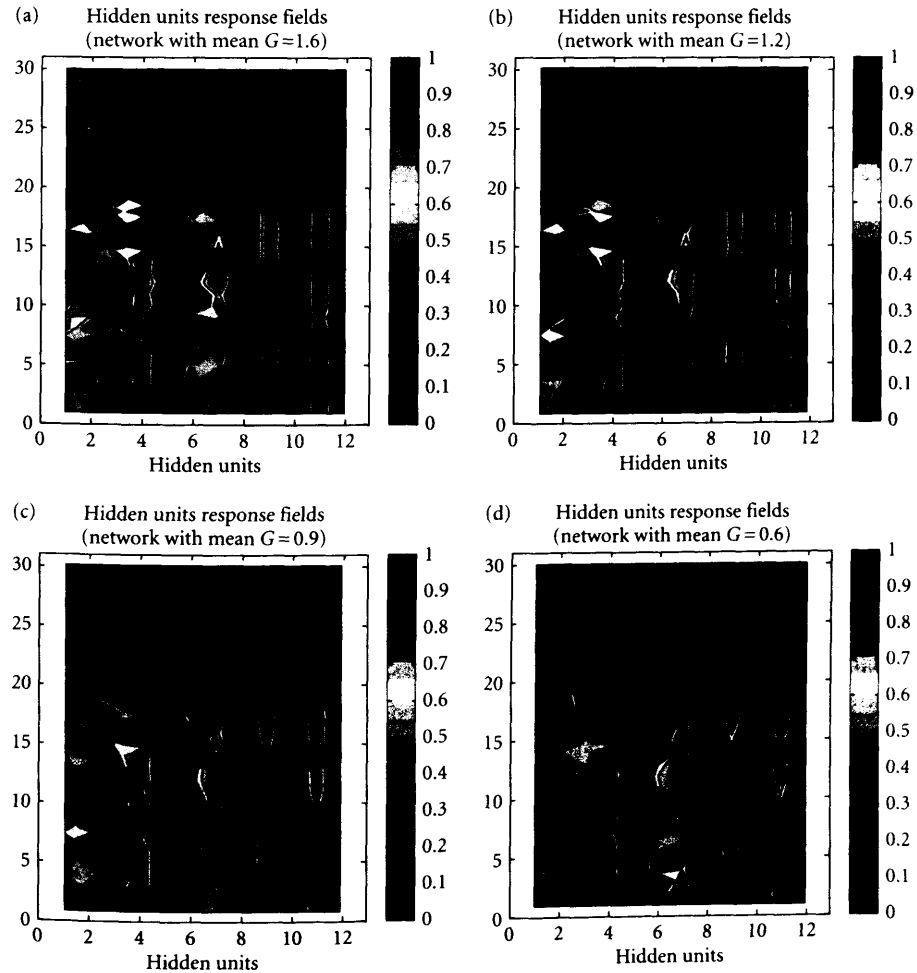

Figure 11.4 Summary hidden-unit activation maps of four networks illustrating the effects of reducing mean G on the distinctiveness of distributed coding of associative information. Red coloration indicates that the units are highly activated, whereas blue coloration indicates low activation (see text for explanation). See also colour plate section.

pair, and the last four units correspond to the representation of the feature conjunction of item B in the pair. Overall, far fewer units were involved in coding item than associative information (comparing the top and bottom portions of the activation maps). Most relevantly, the effect of the *G* manipulation is clearest in the activation patterns represented by the middle four units when responding to the associative test (i.e. activation patterns corresponding to the first 18 stimulus patterns across hidden units 5–8). Going from high mean *G* (Fig. 11.4(a)) to low mean *G* (Fig. 11.4(d)), the distributed coding of associative conjunction goes from highly distinctive with only a few highly activated units to less distinctive with the majority of units being highly active. These internal activation patterns show that reducing mean *G* to simulate ageing-related deficit in neuromodulation leads to less efficient distributed coding of associations between items, which, in turn, contributes to the poor associative memory of the old networks.

Contextual support and representational distinctiveness

As reviewed above, in addition to the deficit of associative binding between items, old adults also have difficulty in remembering contextual details of memory events. Comparing across a wide range of studies, Spencer and Raz (1995) showed that context memory is more sensitive to ageing than content memory. In line with more recent conceptions of situated cognition that stress the dynamic interaction between neurocognitive processes and the contexts (reviewed by Clark 1999), Craik (1983) suggested that the overall behaviour reflects compensation of some interactive mix of self-initiated processing by enhanced environmental contextual support. On the one hand, older adults show deficits in context memory; on the other hand, cognitive ageing researchers have suggested that, in comparison with themselves, the memory performance of older adults can be enhanced by providing contextual support (Craik and Anderson 1999).

In an earlier study (Li 2005), we explored the trade-offs between ageing-related decline in the neuromodulation of representational distinctiveness and the influence of contextual support in enhancing representational distinctiveness to counteract the effect of deficient neuromodulation in a different network architecture. The earlier model examined the effects of contextual support in a fully connected network without separated feature and associative conjunctive binding pathways. Simulation results from that study showed that reducing mean *G* (simulating ageing-related deficiency in dopaminergic modulation) gave rise to less distinctive representations of study items, which led to the poor memory performance. However, providing external contextual cues improved the memory performance of the old networks, relative to

themselves, through context-dependent enhancement of efficiency in distributed conjunctive coding.

Discussion

Thus far, results from the neurocomputional simulations reviewed and presented in this chapter show that deficient neuromodulation may play a role in ageing-related deficits of memory binding. Specifically, the simulations explicate a sequence of effects from reduced responsivity of a single unit due to non-optimal *G* modulation, through less efficient distributed conjunctive coding of stimulus patterns across assemblies of units, to behavioural manifestations of an associative binding deficit. Clearly, this cross-level theoretical link is a conjecture awaiting further vigorous empirical testing. At the same time, our proposal can serve as a vantage point for discussing relations between various binding mechanisms that have been proposed so far.

Relations to other theories of binding

Among the various views on perceptual and memory binding, it has been suggested that the brain may use two general coding principles to represent relations between currently perceived object features or the regenerated representations of stored experiences. One principle involves coarse population codes of percepts or stored representations that are bound together through conjunction units (Barlow 1972), and the other involves dynamic context-dependent temporal binding of cell assembly codes (von der Malsburg 1985; Singer and Gray 1995). Obviously, these two principles differ: The first achieves binding by convergence (conjunction binding) and the second through temporal synchrony. However, both principles operate on distributed coding. Moreover, the two principles may complement each other. It has been suggested that stereotyped, frequently occurring, and particularly relevant conjunctions should be represented by specific binding units, because this strategy is faster and less susceptible to binding errors; whereas unanticipated conjunctions should be recruited by dynamically configured population codes that represent meta-conjunctions for which there are no pre-existing binding units (Singer 1999). Therefore mechanisms that may affect the representational distinctiveness of the distributed coding of neuronal activities related to stimulus and response, such as neuromodulation simulated in our model, would have implications for both binding principles.

Thus far, the effect of neuromodulation on temporal binding has rarely been investigated. However, two computational models suggest that neuromodulation may affect synchronization (e.g. the stability of synchronization and degrees of

synchrony) by either influencing the intrinsic complexity of single-cell dynamics or the effective structure of whole networks (Harris-Warrick and Marder 1991; Wennekers and Pasemann 2001; Breakspear *et al.* 2003). For instance, increasing a parameter that corresponds to increasing the population of transmitter receptors decreases the coupling strength required to achieve stable synchronization (Breakspear *et al.* 2003). In other words, with deficient neuromodulation the ageing brain may require greater coupling strength between cortical columns to achieve synchronization-based binding. The details of how neurochemically modulated representation distinctiveness may affect the coupling strength between local networks and the overall stability of synchronization are open questions for future investigation.

It has also been proposed recently that the neocortex and the hippocampus may engage in two types of conjunctive learning (O'Reilly and Rudy 2001). The neocortex uses distributed overlapping representations for intentional effortful conjunctive learning, whereas the hippocampus uses relatively sparse coding for relatively more automatic incidental conjunction. Although our simulations did not explicitly model both anatomical regions and focused only on the neocortex, our results did show a clear effect of neuromodulation of representational distinctiveness on internally learned conjunctive binding (i.e. with the study pair instruction). There is recent evidence showing ageing-related differences in the functional connectivity between the PFC and hippocampus. In old adults, a stronger connectivity between dorsal lateral PFC and regions involved in attention regulation and the hippocampus is related to better memory performance (Grady *et al.* 2003). Considering our simulation results together with the empirical finding, we conjecture that dopaminergic modulation of representational distinctiveness in regions of the neocortex, such as the PFC, may affect the functional connectivity of the frontal-hippocampal circuitry (Grady *et al.* 2003). If the representations of neural activities elicited by different stimuli are less distinct in the neocortex because of suboptimal neuromodulation, processes requiring dynamic interactions between these representations and neural activities in other brain regions, such as the hippocampus, are likely to be affected. Other researchers (Mitchell *et al.* 2000) have suggested that the dynamics of the frontal-hippocampal circuitry may be implicated in ageing-related deficit of memory binding.

Finally, feature integration theory (Treisman and Gelade 1980) suggests that attention plays an important role in solving the binding problem, but at the same time attention limits may be set by the number of distinctly firing neuronal assemblies to code separate objects (Treisman 1996). Our simulations suggest that neuromodulation affects the distinctiveness of distributed conjunctive

coding and may have implications for the relation between attention and basic binding mechanisms. With respect to ageing research, these theoretical observations imply that ageing-related conjunctive binding deficits should not be restricted to mechanisms of episodic memory binding, but should generalize to other binding mechanisms, such as the relations between attention, working memory, and perceptual binding.

Relation to other memory models

Regarding comparisons with other memory models, the feature–association conjunctive binding model (Li *et al.* 2005) is conceptually similar to global memory models which assume combination of multiple memory cues, distributed storage, and separate representations of item and associative information, such as the TODAM model (Murdock 1993). Not all classical memory models can account for the distinctions between item and associative memory (reviewed by Clark and Gronlund 1996). As shown, our model accounts for the finding that item memory is less sensitive to instruction manipulation (intentional versus incidental) than associative memory (Hockley and Cristi 1996).

In addition, the feature–association conjunctive binding model accounts for the differential ageing of item and associative memory. However, a limitation of the model is that it does not directly address the issue of retrieval time course. One possibility of extending the model is by augmenting it with an attractor network involving recurrent connections between the representation and output layers. Nevertheless, assuming that processing times are monotonically related to lack of match between target and actual outputs (Seidenberger and McClelland 1989), the performance advantage of item over associative test in our current implementation suggests that the retrieval time course is faster for item than for associative information, and that this effect is stronger in old networks. However, the model's ability to account simultaneously for the effects of stimulus repetition and response deadline on memory ageing (Jacoby 1999; Light *et al.* 2004) needs to be investigated in future modifications of the model that directly incorporate temporal dynamics.

Conclusion

The neurocognitive system may require multiple mechanisms across different levels to store and dynamically represent relations between multiple objects and complex memory events. Research on adult lifespan differences in associative and context memory is helpful for identifying basic factors contributing to binding mechanisms. Neurocomputational simulations of ageing-related decline

in representational distinctiveness suggest that neuromodulatory processes may play a basic role in binding by affecting the efficiency of distributed conjunctive coding across cells within an assembly. The neurocognitive system's task to bind together multiple less distinctive assembly codes is harder for individuals, such as older adults, whose neuromodulatory processes function suboptimally.

References

Arnsten, A.F.T. and Goldman-Rakic, P.S. (1985). Alpha 2-adrenergic mechanisms in prefrontal cortex associated with cognitive declines in aged non-human primates. *Science*, **230**, 1273–1276.

Arnsten, A.F.T., Cai, J.X., Murphy, B.L., and Goldman-Rakic, P.S. (1994). Dopamine D_1 receptor mechanisms in the cognitive performance of young adult and aged monkeys. *Psychopharmacology*, **116**, 143–151.

Bäckman. L. and Farde, L. (2005) The role of dopamine functions in cognitive ageing. In *Cognitive Neuroscience of Aging: Linking Cognitive and Cerebral Aging* (ed R.Cabeza, L.Nyberg, and D.C. Park). New York: Oxford University Press, pp. 58–84.

Bäckman, L., Ginovart, N., Dixon, R.A., *et al.* (2000). Age-related cognitive deficits mediated by changes in the striatal dopamine system. *American Journal of Psychiatry*, **157**, 635–637.

Barlow, H.B. (1972). Single units and cognition: a neurone doctrine for perceptual psychology. *Perception*, **1**, 371–394.

Braver, T.S., Barch, D.M., Keys, D.A., *et al.* (2001). Context processing in older adults: evidence for a theory relating cognitive control to neurobiology in healthy ageing. *Journal of Experimental Psychology: General*, **130**, 746–763.

Breakspear, M., Terry, J.R., and Friston, K.J. (2003). Modulation of excitatory synaptic coupling facilitates synchronization and complex dynamics in a nonlinear model of neuronal dynamics. *Neurocomputing*, **52–54**, 151–158.

Camperi, M. and Wang, X.J. (1998). A model of visuospatial working memory in prefrontal cortex: recurrent network and cellular bistability. *Journal of Computational Neuroscience*, **5**, 383–405.

Chalfonte, B.L. and Johnson, M.K. (1996). Feature memory and binding in young and older adults. *Memory and Cognition*, **24**, 403–416.

Churchland, P.S. and Sejnowski, T.J. (1988). Perspectives on cognitive neuroscience. *Science*, **242**, 741–745.

Clark, A. (1999). An embedded cognitive science? *Trends in Cognitive Sciences*, **3**, 345–351.

Clark, S.E. and Gronlund, S.D. (1996). Global matching models of recognition memory: how the models match the data. *Psychological Bulletin and Review*, **3**, 37–60.

Craik, F.I.M. (1983). On the transfer of information from temporary to permanent memory. *Philosophical Transactions of the Royal Society London, Series B, Biological Sciences*, **302**, 341–359.

Craik, F.I.M. and Anderson, N.D (1999). Applying cognitive approach to problems of ageing. In *Attention and Performance XVII* (ed D. Gopher and A. Koriat). Cambridge, MA: MIT Press, pp. 583–615.

de Keyser, J., De Backer, J.P., Vauquelin, G., and Ebinger G. (1990). The effect of ageing on the D1 dopamine receptors in human cortex. *Brain Research*, **528**, 308–310.

Durstewitz, D., Kelc, M., and Güntürkün, O. (1999). A neurocomputational theory of the dopaminergic modulation of working memory functions, *Journal of Neuroscience*, **19**, 2807–2822.

Giorgi, O., Calderini, G., Toffano, G., and Biggio, G. (1987). D_1 dopamine receptors labeled with ^{3}H-SCH 23390:decrease in the striatum of aged rats. *Neurobiology of Aging*, **8**, 51–54.

Goebel, R.P. and Lewandowsky, S. (1991). Retrieval measures in distributed memory models. In *Relating Theory and Data: Essay on Human Memory in Honor of Bennet B. Murdock* (ed W.E. Hockley and S. Lewandowsky). Hillsdale, NJ: Erlbaum.

Goldman-Rakic, P.S., Muly, E.C., 3rd, and Williams, G.V. (2000). D1 recoptors in prefrontal cells and circuits. *Brain Research Reviews*, **31**, 295–301.

Grady, C.L., McIntosh, A.R., and Craik, F.I.M. (2003). Age-related differences in the functional connectivity of the hippocampus during memory encoding. *Hippocampus*, **13**, 572–586.

Harris-Warrick, R.M. and Marder, E. (1991). Modulation of neural networks for behavior. *Annual Review of Neuroscience*, **14**, 39–57.

Hasselmo, M.E. (1995). Neuromodulation and cortical function: modeling the physiological basis of behavior. *Behavioural Brain Research*, **67**, 1–27.

Head, D., Raz, N., Gunnin-Dixon, F., Williamson, A., and Acker, J. D. (2002). Age-related differences in the course of cognitive skill acquisition: the role of regional cortical shrinkage and cognitive resources. *Psychology and Aging*, **17**, 72–84.

Hessler, N.A., Shirke, A.M., and Malinow, R. (1993). The probability of transmitter release at a mammalian central synapse. *Nature*, **366**, 569–572.

Hockley, W.E. and Cristi, C. (1996). Tests of separate retrieval of item and associative information using a frequency-judgment task. *Memory and Cognition*, **24**, 796–811.

Johnson, M.K. (1992). MEM: mechanisms of recollection. *Journal of Cognitive Neuroscience*, **4**, 268–280.

Johnson, M.K., Hashtroudi, S., and Lindsay, D.S. (1993). Source monitoring. *Psychological Bulletin*, **114**, 3–28.

Kaasinen V., Vilkman, H., Hietala, J., *et al.* (2000). Age-related dopamine D_2/D_3 receptor loss in extrastriatal regions of the human brain. *Neurobiology of Aging*, **21**, 683–688.

Kausler, D. H. (1994). *Learning and Memory in Normal Aging*. New York: Academic Press.

Kliegl, R. and Lindenberger, U. (1993). Modeling intrusions and correct recall in episodic memory: adult age differences in encoding of list context. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, **19**, 617–637.

Köning, P., Engel, A.K., Roelfsema, P.R., and Singer, W. (1995). How precise is neuronal synchronization? *Neural Computation*, **7**, 469–485.

Li, S.-C. (2002). Connecting the many levels and facets of cognitive ageing. *Current Directions in Psychological Science*, **11**, 38–43.

Li, S.-C. (2005). Neurocomputational perspectives linking neuromodulation, processing noise, representational distinctiveness, and cognitive ageing. In *Cognitive Neuroscience of*

Aging: Linking Cognitive and Cerebral Aging (ed R. Cabeza, L. Nyberg, and D.C. Park). New York: Oxford University Press, pp. 354–380.

Li, S.-C. and Sikström, S. (2002). Integrative neurocomputational perspectives on cognitive ageing, neuromodulation, and representation. *Neuroscience and Biobehavioral Reviews*, **26**, 795–808.

Li, S.-C., Lindenberger, U., and Frensch, P. A. (2000). Unifying cognitive ageing: from neuromodulation to representation to cognition. *Neurocomputing*, **32–33**, 879–890.

Li, S.-C., Lindenberger, U., and Sikström, S. (2001). Aging cognition: from neuromodulation to representation. *Trends in Cognitive Sciences*, **5**, 479–486.

Li, S.-C., Lindenberger, U., Hommel, B., Aschersleben, G., Prinz, W., and Baltes, P.B. (2004). Lifespan transformations in the couplings among intellectual abilities and constituent cognitive processes. *Psychological Science*, **15**, 155–163.

Li, S.-C., Naveh-Benjamin, M., and Lindenberger, U. (2005). Aging neuromodulation impairs associative binding. *Psychological Science*, **16**, 445–450.

Light, L.L. (1991). Memory and aging: four hypotheses in search of data. *Annual Review of Psychology*, **42**, 333–376.

Light, L.L., Patterson, M.M., Chung, C., and Healy, M.R. (2004). Effects of repetition and response deadline on associative recognition in young and older adults. *Memory and Cognition*, **32**, 1182–1193.

McIntyre, J.S. and Craik, F.I.M. (1987). Age differences in memory for item and source information. *Canadian Journal of Psychology*, **41**, 175–192.

MacKay, D.G. and Burke, D.M. (1990). Cognition and aging: a theory of new learning and the use of old connections. In *Aging and Cognition: New Knowledge Organization and Utilization* (ed T.M. Hess). Amsterdam: Elsevier, pp. 213–263.

MacRae, P.G., Spirduso, W.W., and Wilcox, R.E. (1988). Reaction time and nigrostriatal dopamine function: the effect of age and practice. *Brain Research*, **451**, 139–146.

Mitchell, K.J., Johnson, M.K., Raye, C.L., and D'Esposito, M. (2000). FMRI evidence of age-related hippocampal dysfunction in feature biding in working memory. *Cognitive Brain Research*, **10**, 197–206.

Morrison, J.H. and Hof, P.R. (1997). Life and death of neurons in the ageing brain. *Science*, **278**, 412–429.

Murdock, B.B., Jr (1993). TODAM 2: a model for the storage and retrieval of item, associative, and serial-order information. *Psychological Review*, **100**, 183–203.

Nadel, L., Samsonovich, A., Ryan, L., and Moscovitch, M. (2000). Multiple trace theory of human memory: Computational, neuroimaging, and neuropsychological results. *Hippocampus*, **10**, 352–368.

Naveh-Benjamin, M. (2000). Adult age differences in memory performance: tests of an associative deficit hypothesis. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, **26**, 1170–1187.

Naveh-Benjamin, M., Hussain, Z., Guez, J., and Bar-On, M. (2003). Adult age differences in episodic memory: further support for an associative-deficit hypothesis. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, **29**, 826–837.

Nieuwenhuis, S., Ridderinkhof, K.R., Talsma, D., *et al.* (2002). A computational account of altered error processing in older age: dopamine and error-related processing. *Cognitive, Affective, and Behavioral Neuroscience*, **2**, 19–36.

O'Reilly, R.C. and Busby, R.S. (2002). Generalizable relational binding from coarse-coded distributed representations. In *Advances in Neural Information Processing Systems (NIPS) 14* (ed T.G. Dietterich, S. Becker, and Z. Gahramani). Cambridge, MA: MIT Press.

O'Reilly, R.C. and Rudy, J.W. (2001). Conjunctive representations in learning and memory: Principles of cortical and hippocampal function. *Psychological Review*, **108**, 311–345.

Raz, N. (2000). Aging of the brain and its impact on cognitive performance: integration of structural and functional findings. In *The Handbook of Aging and Cognition* (2nd edn) (ed F.I.M. Craik and T.A. Salthouse). Mahwah, NJ: Erlbaum, pp. 1–90.

Rizzuto, D.S. and Kahana, M.J. (2001). An auto-associative neural network model f paired-associate learning. *Neural Computation*, **13**, 2075–2092.

Schillen, T.B. and König, P. (1994). Binding by temporal structure in multiple feature domains of an oscillatory neuronal network. *Biological Cybernetics*, **70**, 397–405.

Schneider, E.L., Rowe, J.W., Johnson, T.E., Holbrook, N., and Morrison, J. (ed) (1996). *Handbook of the Biology of Aging*. New York: Academic Press.

Segovia G., Porras, A., Del Arco, A., and Mora, F. (2001). Glutamatergic neurotransmission in ageing: A critical perspective. *Mechanisms of Ageing and Development*, **122**, 1–29.

Seidenberger, M.S. and McClelland, J.L. (1989). A distributed, developmental model of word recognition and naming. *Psychological Review*, **96**, 523–568.

Servan-Schreiber, D., Printz, H., and Cohen, J.D. (1990). A network model of catecholamine effects: gain, signal-to-noise ratio, and behavior. *Science*, **249**, 892–895.

Singer, W. (1998). Consciousness and the structure of neuronal representations. *Philosophical Transactions of the Royal Society London, Series B, Biological Sciences*, **353**, 1829–1840.

Singer, W. (1999). Neuronal synchrony: a versatile code for the definition of relations? *Neuron*, **24**, 49–65.

Singer, W. and Gray, C.M. (1995). Visual feature integration and the temporal correlation hypothesis. *Annual Review of Neuroscience*, **18**, 555–586.

Sowell, E.R., Peterson, B.S., Thompson, P.M., Welcome, S.E., Henkenius, A.C., and Toga, A.W. (2003). Mapping cortical change across the human life span. *Nature Neuroscience*, **6**, 308–315.

Spencer, W.D. and Raz, N. (1995). Differential effects of ageing on memory for content and context: a meta-analysis. *Psychology and Aging*, **10**, 527–539.

Treisman, A. (1996). The binding problem. *Current Opinion in Neurobiology*, **6**, 171–178.

Treisman, A. (1998). Feature binding, attention and object perception. *Philosophical Transactions of Royal Society London, Series B, Biological Sciences*, **353**, 1295–1306.

Treisman, A. (1999). Solutions to the binding problem: progress through controversy and convergence. *Neuron*, **24**, 105–110.

Treisman, A. and Gelade, G. (1980). A feature integration theory of attention. *Cognitive Psychology*, **12**, 97–136.

von der Malsburg, C. (1985). Nervous structures with dynamical links. *Berichte der Bunsen-gesellschaft physikalische Chemie*, **89**, 703–710.

Welford, A.T. (1965). Performance, biological mechanisms and age: a theoretical sketch. In *Behavior, Aging, and the Nervous System* (ed A.T. Welford and J.E. Birren). Springfield, IL: Thomas, pp. 3–20.

Wennekers, T. and Pasemann, F. (2001). Generalized types of synchronization in networks of spiking neurons. *Neurocomputing*, **38–40**, 1037–1042.

Wolpert, D.M., Ghahramani, Z., and Flanagan, J. R. (2001). Perspectives and problems in motor learning. *Trends in Cognitive Sciences*, **5**, 487–494.

Wong, D.F., Young, D., Wilson, P.D., Meltzer, C.C., and Gjedde, A. (1997). Quantification of neuroreceptors in the living brain. III: D2-like dopamine receptors: theory, validation and changes during normal ageing. *Journal of Cerebral Blood Flow and Metabolism*, **17**, 316–330.

Zacks, R.T., Hasher, L., and Li, K.Z.H. (2000). Human memory. In *The Handbook of Aging and Cognition* (2nd edn) (ed F.I.M. Craik and T.A. Salthouse). Mahwah, NJ: Erlbaum, pp. 293–357.

Zahrt, J., Taylor, J.R., Mathew, R.G., and Arnsten, A.F. (1997). Supranormal stimulation of dopamine D1 receptors in the rodent prefrontal cortex impairs spatial working memory performance. *Journal of Neuroscience*, **17**, 8528–8535.