Review

Sex influences on the neurobiology of learning and memory

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In essentially every domain of neuroscience, the generally implicit assumption that few, if any, meaningful differences exist between male and female brain function is being challenged. Here we address how this development is influencing studies of the neurobiology of learning and memory. While it has been commonly held that males show an advantage on spatial tasks, and females on verbal tasks, there is increasing evidence that sex differences are more widespread than previously supposed. Differing performance between the sexes have been observed on a number of common learning tasks in both the human and animal literature, many neither purely spatial nor verbal. We review sex differences reported in various areas to date, while attempting to identify common features of sexually dimorphic tasks, and to place these differences in a neurobiological context. This discussion focuses on studies of four classes of memory tasks for which sex differences have been frequently reported: spatial, verbal, autobiographical, and emotional memory. We conclude that the female verbal advantage extends into numerous tasks, including tests of spatial and autobiographical abilities, but that a small but significant advantage may exist for general episodic memory. We further suggest that for some tasks, stress evokes sex differences, which are not normally observed, and that these differences are mediated largely by interactions between stress and sex hormones.

Sex influences on brain function are ubiquitous. Differences between the sexes have been documented at every level of neuroscience, from single neurons in cell culture to systems level processes as measured by neuroimaging. In some cases, consideration of sex may significantly alter, even reverse, conclusions about brain function drawn from the study of one sex alone (Cahill 2006). In some fields, such as the study of drug addiction, the evidence for sex differences is so strong that consideration of sex as a factor is becoming the norm, rather than the exception (Wetherington 2007).

The claim that these neurobiological sex differences extend to the behavioral level has typically been more controversial. A recent review of the literature on this topic warns against the "costs of overinflated claims of gender differences." The review holds that overall "males and females are alike on most—but not all—psychological variables" (Hyde 2005), but notes exceptions where sex does have an effect, including sexual and aggressive behaviors. Still, given how broadly sex differences are distributed on the neural level, it seems unlikely that their behavioral effects would be restricted solely to these domains.

One area of behavior not considered in Hyde's review is the influence of sex on learning and memory. It is becoming increasingly clear, however, that an understanding of the neurobiological and cognitive consequences of sex is relevant across this field. In the review that follows, behavioral evidence indicating differences between men and women from numerous memory tasks will be considered. We will argue that the effects of sex on memory depend critically on the kinds of memory being studied, with some tasks favoring males, while others favor females. We will further argue that the traditionally accepted view that males show an advantage in spatial processing while females excel at verbal tasks presents an incomplete picture (Maccoby and Jacklin 1974). In particular, evidence will be presented that the male spatial advantage does not apply to some spatial tasks, and that the female advantage in verbal processing extends into many memory tasks which are not explicitly verbal. Furthermore, evidence will be presented for significant sex differences in the way that stress and arousal modulate memory formation.

As many studies of the neurobiology of memory have yielded differing, even opposing, effects between the sexes, experimental designs that do not consider potential sex differences risk producing incomplete, or incorrect, conclusions. Sex can even be an important factor in situations for which no behavioral sex difference is evident. As will be discussed, substantial evidence suggests that for some tasks males and females may use differing neural paths to reach the same behavioral end point.

Although reports of sex differences in learning and memory are not a new phenomenon, with some evidence dating to the beginnings of experimental psychology, recent neurobiological findings have renewed interest in the issue. This fact, combined with increasing sophistication in examining sex influences on the psychological level, means the field is now much better positioned to move from simply documenting observed sex differences in learning and memory, to understanding the ways in which psychological level differences arise from their neural underpinnings.

In discussing behavioral sex differences, we include effect sizes wherever the published studies provided enough information to compute them. We do so for two reasons. First, effect sizes may be useful in identifying commonalities across sex differences: Sex effects of similar size found across varying studies might suggest that a common, sexually dimorphic cognitive faculty is at work. Second, there remains a widespread misconception in neuroscience that sex differences are uniformly small (Cahill 2006). As we will show, sex effects range from the trivial to the very large, depending on the specific task being tested, as in the case for most domains of neuroscience.

A note regarding organization

It is not possible to cover all relevant studies/issues in this review. Hence, our goal will be to address the most prominent sex differences in multiple forms of learning and memory, highlighting the

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E-mail lfcahill@uci.edu; fax (949) 824-5244. Article is online at http://www.learnmem.org/cgi/doi/10.1101/lm.918309. differences in the way sex affects different aspects of memoryrelated cognition, and attempting to place these results in a neurobiological context. Although we will focus primarily on human studies, in large part because much of this discussion will involve verbal and episodic memory, we also discuss evidence from animal work, and note where commonalities across species are observed.

It will be rightly observed that the classifications of types of memory used in this review in several cases overlap, and that some may draw upon abilities not generally thought of as mnemonic. Spatial rotation, for example, is considered by many to be a working memory task (Zimmer 2008) in that it requires the representation of a figure viewed from multiple angles to be held in memory and manipulated, and employs many of the same brain regions involved in prototypical working memory tasks (Schendan and Stern 2007). However, some would argue that such spatial ability draws on specific neural systems devoted only to spatial processing, distinct from those employed in working memory tasks (Logie 2003). Thus, while rotation does seem to engage working memory, it also seems to require processes distinct to visual imagery, and determining the relative contributions of these forms of processing to the task is difficult.

Similarly, although autobiographical memory, as measured by long-term retrospective recollection of one's life, is presented separately in this review, autobiographical tasks certainly draw on episodic memory, along with semantic information. Likewise, both autobiographical memory and episodic memory, measured in the short term, likely involve substantial verbalization. Many of the tasks classified as verbal memory in this review, particularly word list recall, can also be understood as episodic, as these abilities are likely tightly intertwined.

The organization of this work, therefore, is not intended as taxonomy of memory processes. Indeed, no complete taxonomy of this sort is agreed upon in the field. Rather than organizing the sections of this paper by theoretical memory categories, we have divided it by specific memory tasks, in the hope that this will facilitate ease of reference. Each of the sections of this review represents a distinct literature, with characteristic methods and tasks used to measure performance. It is hoped that this approach will allow researchers in each of these fields to easily find what is known about sex differences for the particular measures of memory that they study.

We will attempt to some degree to separate the contributions of different categories of memory to different tasks, and to establish which tasks draw on common or distinct faculties. However, when we argue that two sex differences are distinct, we intend only to imply that these memory tasks should be treated as separate *insofar as they are influenced by sex*.

For example, given consistent evidence of female advantages on verbal tasks, we suggest that a common sex difference contributes to sex differences in performance on verbal recall tasks, episodic, and object memory tasks. We remain agnostic, however, as to what extent the processing underlying these tasks may be neurally or functionally separated.

Last, it is worth noting that for the purposes of this discussion, behavioral differences between men and women will be described as "sex differences." While the term "gender differences" is used in many of the papers we discuss, we believe the former description is more appropriate. The term "gender" is commonly used to describe a psychological variable, referring to some combination of an individual's conception of self and role within society. In most of the studies to be described, the researchers did not have access to information on gender, but instead assumed that this variable matched the more observable data that they did have, regarding biological sex. However, biological sex and gender are not always aligned. Thus, we restrict our discussion to the observable variable, and make no assumptions regarding gender.

Our discussion begins with a brief historical perspective, followed by a review of some relevant neurobiological sex differences in brain regions and processes known to be involved in learning and memory. We next consider sex differences in two domains in which they have been most commonly observedspatial and verbal memory-with particular attention to recent experiments showing telling exceptions to the commonly accepted pattern seen in studies on this topic. Next, we will review the evidence for sex differences in autobiographical memory, with a particular interest in the notion that these differences represent a more general sex difference in episodic memory. Next, we will consider the influence of sex on the modulation of memory by emotional arousal and stress. We will argue that sex differences may be particularly evident in the study of emotional memory, in part because of newly discovered interactions between stress and sex hormones in memory. Finally, we will briefly address some intriguing new directions that the field of sex differences is taking, driven by new methodologies.

Some historical perspective

The publication in 1885 of Hermann Ebbinghaus' famous investigation of his own memory is generally taken as the start of modern memory investigations. Recognition of sex differences in memory followed shortly thereafter, when the British psychologist Havelock Ellis (1894) published what is considered the first large-scale study of biological and psychological sex differences. He devoted an entire chapter to what he called "The Intellectual Impulse," in which he made several observations about memory. Surveying the available studies largely addressing verbal memory, he noted "the superiority of the feminine mind in the matter of memory" (Ellis 1894), a conclusion, as we will see supported by several modern studies. Considering memory in children, he concluded that "memory... is found to be decidedly superior, on the whole, in girls" (Ellis 1894), a view held by many modern researchers regarding certain forms of memory, although he noted further that "this superiority is not found in every kind of memory." Finally, he noted differences in the developmental trajectories of memory function in boys and girls, again predating many modern investigations.

Many investigations followed. And as might be expected from the study of any two presumably overlapping yet offset populations in which many variables, known and unknown, will influence experimental findings, the literature often appeared confusing, with some studies reporting sex differences in a particular condition, others reporting none. By the time of Maccoby and Jacklin's (1974) landmark summary of sex differences on the psychological level, interest in the topic appears to have been waning, in part because sex differences in brain and behavior were considered anathema by the political zeitgeist of the time (Eagly et al. 1995). Maccoby and Jacklin (1974) noted several instances in which sex differences in some aspect of memory were reported (for example, in incidental memory of films), and noted large sex differences in memory-dependent verbal and spatial behaviors (as discussed later), yet concluded overall that "the two sexes show a remarkable degree of similarity in the basic intellectual processes of perception, learning, and memory."

Despite this largely negative conclusion, and despite the political zeitgeist, reports of sex differences in various aspects of memory, or in cognitive processes dependent upon memory, persisted. Renewed interest today in the issue of sex influences in memory appears driven heavily by neurobiological investigations, which have identified numerous sex differences in brain related to memory. In particular, neuroimaging has revealed differing neural networks underlying task performance between the sexes, both for tasks where performance differs and where performance is equivalent (Grabowski et al. 2003; Piefke et al. 2005). Equally important to current interest are the growing numbers of neurobiological investigations using non-human animals, for which human cultural explanations cannot explain observed sex differences (Cahill 2006), and which in some cases appear to reveal "sex specific" memory mechanisms in the brain.

Interestingly, one can find sex effects in some early studies of the neurobiology of memory, although these seem by and large to have been forgotten. For example, McGaugh and Thomson (1962) investigated the effects of a stimulant (strychnine) on foot shockmotivated maze learning in male and female rats. They report the "unexpected finding" of far superior learning rates in females. The authors consider several possible explanations of these large sex effects, concluding that they "should be examined systematically in subsequent research using these strains." Unfortunately this conclusion roughly coincided with the widespread advent of a "male only" strategy in animal studies of the neurobiology of memory, a strategy adopted, ironically, to avoid likely sex effects. Indeed, it is only much more recently that studies of memory in both male and female animals appear to be gradually returning.

Some neurobiological sex differences relevant to learning and memory

Neurobiological sex differences in brain regions implicated in learning and memory exist at multiple levels of analysis, from gross neuroanatomy to circuit properties to the molecular mechanisms underlying them. Before focusing on sex differences explicitly tied to memory, we will first briefly describe some of these neurobiological sex differences through which these differences could potentially be mediated.

Neuroanatomy

Multiple studies report larger whole brain volumes in men than women (Peters 1998; Allen et al. 2002; Cosgrove et al. 2007), as well as a larger percentage of brain volume in CSF (Agartz et al. 1992) and a higher ratio of white to gray matter (Gur et al. 1999). The volume of numerous brain structures, including many well known to be involved in learning and memory have also been found to differ significantly between the sexes. Both post-mortem and imaging studies have found that relative to brain size, women have larger volumes in the hippocampus (Filipek et al. 1994), caudate nucleus (Filipek et al. 1994; Murphy et al. 1996), anterior cingulate gyrus (Paus et al. 1996) dorsolateral prefrontal cortex (Schlaepfer et al. 1995), and planum temporale (Witelson et al. 1995). In contrast, the relative volumes of the amygdala (Giedd et al. 1996) and paracingulate gyrus (Paus et al. 1996) are consistently larger in men. Interestingly, an analysis of numerous brain structures showing sexual dimorphism indicates that the magnitude of sex differences in the size of human brain structures correlates with the degree to which the regions express sex steroid receptors during development, as inferred from animal studies (Goldstein et al. 2001), suggesting that structural differences are at least partially mediated developmental sex steroid influences.

Neurochemistry

In addition to morphological differences, significant sex differences exist in the metabolism of multiple neurotransmitters known to play an important role in cognition. Several studies show that the availability of dopamine transporters, which regulate synaptic dopamine levels, is significantly greater in women than in men (Lavalaye et al. 2000; Mozley et al. 2001; Staley et al. 2001). Similarly, in the striatum, a structure well known to be involved in habit learning, female presynaptic dopamine levels exceed those of age-matched males (Laakso et al. 2002). Amphetamine-induced release of dopamine in the globus pallidus is also larger in women (Riccardi et al. 2006), a fact which may help explain the increased susceptibility to drug addiction in females relative to males (Becker and Hu 2008).

Plasma serotonin levels are also higher in women than in men (Ortiz et al. 1988), although imaging data suggest that men synthesize serotonin more quickly (Nishizawa et al. 1997), and express larger numbers of 5-HT2 receptors. These global differences reflect the aggregate effect of numerous local neurochemical sex differences. The male advantage in 5-HT2 receptors seems to derive particularly from frontal and cingulate cortices (Biver et al. 1996). Microdialysis in rodents indicates that extracellular levels of both serotonin and dopamine in the amygdala are elevated in males relative to females, although females show a significantly larger serotonin response to stress (Mitsushima et al. 2006). While sex differences in dopamine seem to be insensitive to menstrual position, serotonergic sex differences do seem to be influenced by ovarian hormones. Exogenous sex hormone replacement significantly enhances 5-HT2a binding throughout the cortex (Moses et al. 2000), as well as increasing the effectiveness of the SSRI sertraline (Rasgon et al. 2007).

MR spectroscopy indicates higher GABA levels in women than in men throughout the cortex (Sanacora et al. 1999), and GABA receptor expression in rodents appears to be regulated by the estrous cycle (Lovick 2007). PET studies indicate increased μ opioid binding in women (Zubieta et al. 1999), and receptor density seems to be similarly modulated by menstrual cycle position (Smith et al. 1998). Increased expression of both muscarinic (Yoshida et al. 2000) and nicotinic (Koylu et al. 1997) acetylcholine receptors in females has also been reported.

Perhaps the largest sex difference in neurochemistry, however, can be found in circulating sex hormone levels. This point may at first seem so glaringly obvious as to be trivial. However, some studies have indicated that in addition to their role in regulating reproductive behavior, sex hormones can act as potent modulators of cognition. In rodents, exogenous estradiol can enhance the consolidation of object recognition (Luine et al. 2003), water maze navigation (Packard and Teather 1997), and inhibitory avoidance (Rhodes and Frye 2004). Similarly, the pharmacological suppression of ovarian hormone release can affect verbal memory (Sherwin and Tulandi 1996), working memory (Grigorova et al. 2006), and neural processing (Berman et al. 1997) in women, and these deficits can be reversed with hormone replacement. In older men, testosterone replacement has been shown to modulate spatial, verbal, and working memory, suggesting that the hormone plays a role in maintaining these abilities (Cherrier et al. 2007; Martin et al. 2008).

Physiology

Differences between the sexes also exist on the level of circuits, and the physiological properties of at least one key "learning and memory" structure, the hippocampus, exhibit significant sexual dimorphism. Whereas males show hippocampal LTP in response to both spaced and continuous tetanic stimulation, female hippocampi respond only to continuous stimulation (Yang et al. 2004). Using the same stimulation, both presynaptic LTP and EPSP slope LTP are enhanced in males. In females, however, only presynaptic changes are evident (Maren et al. 1994). These differences seem to be mediated by estrogen. In ovariectomized rats receiving perforant path stimulation, estrogen replacement significantly reduces both population spike LTP and EPSP spike potentiation (Gupta et al. 2001).

Sex influences in learning and memory

We now turn to a discussion of learning and memory tasks known to exhibit differences between the sexes, and of neurobiological differences that may relate to these behavioral differences.

Spatial memory

Sex-related differences in spatial memory are likely the most widely reported and studied of cognitive sex differences. Since Maccoby and Jacklin (1974) first concluded that males generally outperform females in measures of spatial ability, this finding has been consistently replicated in an abundance of studies spanning multiple developmental phases (McGivern et al. 1997; Lewin et al. 2001) and spatial tasks (Dabbs Jr. et al. 1998; Epting and Overman 1998; Driscoll et al. 2005).

While a male advantage in spatial processing is well established (for meta analyses, see Linn and Petersen 1985; Voyer et al. 1995), this observation is of somewhat limited explanatory value. This is because it is increasingly clear that spatial memory is not a unitary function, but a multidimensional concept including discrete components (Kessels et al. 2000), which can in some cases be neuropsychologically dissociated (Schacter and Nadel 1991). Furthermore, measures of spatial memory frequently involve performance factors such as spatial perception not directly related to any memory difference. Thus, to understand the specific nature of the male spatial advantage, one must compare tasks, which challenge differing components of spatial memory.

Linn and Petersen's (1985) meta-analysis suggested a classification of spatial tests into three categories: spatial perception, mental rotation, and spatial visualization. As this review is focused on memory, tests of spatial perception will not be considered here. We will consider spatial rotation, however, because it is generally conceptualized as a form of spatial working memory (Suchan et al. 2006) Furthermore, two types of studies that might be considered measures of spatial visualization—navigation and object location memory—will be considered separately, due to the distinctly different pattern of sex differences these two tasks exhibit. Therefore, three types of studies, which together comprise the majority of research on sex differences in spatial memory, will be considered: studies of mental rotation, spatial navigation, and object location memory.

Spatial rotation

In a spatial rotation task, participants are asked to judge between complex geometric figures to determine whether a figure is structurally different or an identical figure rotated three dimensionally (Shepard and Metzler 1971). The task therefore relies on the ability to envision an object viewed from multiple angles in space. Large and reliable sex differences favoring men have been found for this task (Vandenberg and Kuse 1978), and have been frequently replicated (Linn and Petersen 1985). While effect sizes for the male advantage vary somewhat from study to study (Voyer et al. 1995), they are on the whole consistently high (see Table 1;

Table 1. Effect sizes of cited studies in mental rotation

Paper	Advantage	Р	d	N
Sharps et al. (1993) (spatial instructions)	Male	<0.001	3.039	60
Moffat et al. (1998)	Male	<0.001	1.498	74
Beatty and Duncan (1990)	Male	<0.001	1.26	120
Peters (2005)	Male	<0.0001	0.96	212
Collins and Kimura (1997)	Male	<0.001	0.86	55
Vandenberg and Kuse (1978)	Male	<0.001	0.78	312
Silverman et al. (2000)	Male	<0.001	0.78	111
Epting and Overman (1998)	Male	<0.01	0.76	47
Galea and Kimura (1993)	Male	<0.01	0.57	85
Silverman et al. (2007)	Male	<0.05	0.48	95,742
Sharps et al. (1993) (nonspatial instructions)	Male	>0.1	0.042	60
Levine et al. (1999)	Male	<0.005	0.25	288

Beatty and Duncan 1990; Epting and Overman 1998; Peters 2005). The male advantage is observed cross-culturally, and as such is likely not the result of environmental factors (Silverman et al. 2007).

The point in development at which these sex differences emerge remains contested. While many studies report no differences before puberty (Waber et al. 1982; Grimshaw et al. 1995; Roberts and Bell 2000), others have argued that these differences can be detected when the task is modified for children (Kerns and Berenbaum 1991; Karadi et al. 1999; Levine et al. 1999). In these cases the task was altered either by exchanging geometric figures for human hands, which may promote a more egocentric strategy, or by measuring success without respect to reaction time, which would de-emphasize the working memory components of the task.

Similarly, studies of the relationship between testosterone and rotation ability have also yielded inconclusive results. Variation in fetal testosterone levels has been shown to affect male spatial ability later in life (Hier and Crowley Jr. 1982; Hampson et al. 1998). However, the evidence of effects of circulating T levels on rotation performance are unclear, with positive relationships (Christiansen and Knussmann 1987; Silverman et al. 1999) and negative relationships (Gouchie and Kimura 1991; Moffat and Hampson 1996) both having been reported, along with some studies showing no relationship at all (Alexander et al. 1998). One explanation for this variance may be the way in which performance was measured. In many studies, reaction time is used as a measure of success, but this may be misleading. Hooven et al. (2004) found that high testosterone predicted both low error rates and reaction times. However, the male advantage was evident only when test items were different, and was derived from the intercepts, rather than the slopes of their rotation functions. This finding does not support the view that mental rotation processes are correlated with T. Rather, the authors argue that T facilitates task performance through factors not directly related to rotation, specifically a decrease in response latency.

This discussion puts into focus the fact that even a relatively simple task like spatial rotation involves multiple distinct cognitive components, which may differ in the extent that they are influenced by sex (Caplan et al. 1985). In the context of sex differences in memory, spatial rotation has generally been conceptualized as a spatial working memory task (Suchan et al. 2006). However, performance on spatial rotation tasks appears to be considerably more sexually dimorphic than performance on other tests of visuospatial working memory. While sex differences in spatial span on the Corsi Block-Tapping Task have been previously reported (Orsini et al. 1987; Capitani et al. 1991), these have been relatively small effects found in samples in excess of 400, as opposed to the robust effect sizes seen for mental rotation. Other studies have failed to detect any sex-related difference on this task (Kessels et al. 2000; Nichelli et al. 2001; Postma et al. 2004), and other measures of spatial working memory have shown differences favoring women (Duff and Hampson 2001). The blocktapping test is perhaps not an ideal comparison, as it involves the integration of both spatial and temporal information. Nonetheless, it seems possible that the sex difference observed in mental rotation may be at least partially mediated by factors unrelated to working memory. One possibility is a difference in cognitive strategy, by which men normally employ a more explicitly spatial approach to solving mental rotation problems. Sharps and colleagues (1993) have shown that when instructions on a mental rotation test are altered to de-emphasize spatial elements of the task, women and men perform equivalently, despite superior male performance using traditional instructions.

Neuroimaging studies may help resolve the question of which specific cognitive processes vary by sex in a task found to exhibit a sex difference, when regions found to differ in their activity during such a task are known to be associated with processing of a particular kind. A number of neuroimaging studies have examined sex differences in mental rotation (Thomsen et al. 2000; Jordan et al. 2002; E. Weiss et al. 2003; Seurinck et al. 2004; Gizewski et al. 2006; Hugdahl et al. 2006). While the specific networks identified for each task vary somewhat across studies, nearly all have indicated regions of significantly different activity between the sexes.

Several studies of mental rotation have found significantly more activation in parietal areas, in particular the superior and inferior parietal lobule, in men (Thomsen et al. 2000; Jordan et al. 2002; E. Weiss et al. 2003; Hugdahl et al. 2006). In women, these studies indicate significant activity in right frontal regions, particularly the inferior frontal gyrus, not seen in men (Thomsen et al. 2000; E. Weiss et al. 2003; Gizewski et al. 2006; Hugdahl et al. 2006). The unique frontal activity in women has been interpreted as evidence of a different cognitive strategy to solving mental rotation problems. It has been suggested that these superior frontal regions may indicate conscious recall (Gizewski et al. 2006) or internal verbalization, suggesting a more effortful, "serial" approach compared to the "gestalt" approach employed by men (Thomsen et al. 2000; Hugdahl et al. 2006).

These studies are not without their limitations, however. Studies in which men and women are matched for their overall spatial performance have produced different results, showing no significant difference between men and women in frontal areas (Jordan et al. 2002), or few significant differences at all across the whole brain (Seurinck et al. 2004). Seurinck and colleagues, however, also used human hands instead of Shepard and Metzler (1971) three-dimensional (3D) figures, for the purpose of forcing a more egocentric strategy, which may minimize sex differences. In addition, only one of these studies controls for sex hormone variation across the menstrual cycle in women (Gizewski et al. 2006), comparing men to women in their mid-luteal phase. Under these conditions, increased parietal lobule activity in men is not detected; suggesting that activity in this region may be sensitive to ovarian hormones in women. As blood estrogen level has been shown to affect the overall size of hemodynamic responses (Dietrich et al. 2001), the inclusion of women in hormonally distinct phases may introduce substantial noise into analysis of BOLD-dependent signal.

Navigation

Large and consistent male advantages in both accuracy and completion time have also been observed on tests of spatial navigation, in which participants are asked to reconstruct a path through a map (Galea and Kimura 1993; Dabbs Jr. et al. 1998; Postma et al. 2004), a virtual environment (Astur et al 1998; Moffat et al. 1998; Sandstrom et al. 1998; Iaria et al. 2003), or real world space (Silverman et al. 2000; Malinowski and Gillespie 2001; Saucier et al. 2002). These effects are generally large and reliable, in a similar range to those seen for mental rotation effects (see Table 2).

Converging evidence suggests that the sex difference on tasks of this sort may be closely related to that seen in studies of mental rotation. Numerous studies of navigation ability have included mental rotation tasks as a measure of general spatial ability, and have found significant positive correlations between performances on the two tasks (Galea and Kimura 1993; Moffat et al. 1998; Silverman et al. 2000; Saucier et al. 2002). The relationship of navigation to testosterone also appears similar to that found for rotation. As in studies of rotation, clear sex differences are not evident for navigation in prepubertal populations (Leplow et al. 2003), suggesting that activational effects of testosterone may play a role. However, the correlation of circulating testosterone with navigation ability is disputed (Driscoll et al. 2005; Burkitt et al. 2007).

In addition to clear differences in performance, many studies of navigation have suggested sex differences in cognitive strategy. The different potential approaches to a wayfinding task have been described as a contrast between egocentric and allocentric strategies. An egocentric strategy involves focusing on local landmarks as directional cues, and orienting oneself in terms of personal directions (left/right), which are relative to one's position within the environment. In contrast, in an allocentric strategy one uses the absolute position of more general landmarks, which may be distant, and orients oneself in terms of absolute directions (north/ south), using a mental spatial map (O'Keefe and Nadel 1978; Maguire et al. 1999).

Broadly speaking, the evidence has suggested that men tend to favor a more allocentric strategy, while women are more frequently egocentric navigators. When asked, men report using an orientation strategy in which position relative to several reference points is tracked, significantly more than women. Women report focusing on learning only the specific turn-by-turn features of the route (Lawton 1994). When asked to describe the correct path, men use measures of distance (miles) and absolute directional terms (north, south, east, west) significantly more frequently, whereas women refer to significantly more landmarks (Lawton et al. 1996; Dabbs Jr. et al. 1998). Men have also repeatedly demonstrated more accurate judgments of distance traveled along a route (Galea and Kimura 1993; Postma et al. 2004) and absolute direction (Galea and Kimura 1993), while women correctly recall substantially more street names and landmarks along the route (Galea and Kimura 1993). Recognition tests have indicated that

Table 2. Effect sizes for cited studies of sex differences in navigation, by task

Paper	Task	Advantage	Р	d	N
Moffat et al. (1998)	VWM	Male	<0.001	1.4	74
Astur et al. (1998)	VWM crossings	Male	< 0.05	1.04	48
Silverman et al. (2000)	3D navigation	Male	< 0.001	0.95	186
Beatty and Duncan (1990)	3D navigation	Male	< 0.001	0.81	120
Malinowski and Gillespie (2001)	3D navigation	Male	< 0.001	0.8	1042
Astur et al. (1998)	VWM, probe %	Male	< 0.05	0.78	48
Astur et al. (1998)	VWM heading error	Male	< 0.05	0.65	48
Galea and Kimura (1993)	2D navigation, completion time	Male	< 0.05	0.47	97
Postma et al. (2004)	3D navigation	Male	< 0.05	0.46	64
Galea and Kimura (1993)	2D navigation, # trials to criterion	Male	< 0.05	0.4	97
Galea and Kimura (1993)	2D navigation, # errors	Male	< 0.001	0.36	97
Postma et al. (2004)	2D navigation	None	>0.1	0.08	64

(d) Values are significantly larger for virtual and real world navigations, compared to overhead view map tasks (VWM = virtual water maze).

women identify landmarks from previously viewed scenes when isolated from their background significantly better than do men, further indicating that landmarks are more salient to women (Barkley and Gabriel 2007).

Thus, it seems that men and women exhibit cognitive differences that would favor a landmark-based approach in women. Studies that require participants to use a particular cognitive strategy have generally supported this view. When participants are given instructions in Euclidean terms to follow a path, a significant sex difference favoring men is seen in both time to completion and number of errors. However, when these instructions are phrased in terms of landmarks, this sex difference is no longer apparent (Saucier et al. 2002). Similarly, in studies where men and women were asked to navigate a virtual water maze, performance has been shown to depend on the relevance of the information provided by landmarks. When landmarks are not visible, or not in stable positions, men significantly outperform women. However, when landmarks are stable between training and testing and provide relevant information regarding the position of the platform, men and women perform at equivalent levels (Sandstrom et al. 1998; Rizk-Jackson et al. 2006).

If women are capable of performing, as well as men, when using landmarks, why are sex differences still apparent when participants are free to use any strategy they choose? It has been suggested that wayfinding tasks produce significantly more anxiety in women, perhaps due to self-perceived stereotypes, and that this anxiety is increased by versions of the task that tend to favor men (Lawton 1994). Increased anxiety might underlie some memory differences, considering increasing evidence that the mnemonic effects of stress differ between men and women (Wolf et al. 2001; Zorawski et al. 2005; Andreano and Cahill 2006), which will be discussed in more detail below.

It may also be the case that the female strategy is limited by scale. When navigating within a single room (Lewin et al. 2001), or within an indoor environment, where absolute directional cues would be unavailable (Lawton et al. 1996), women and men perform at equivalent levels. Similarly, when asked to reproduce the layout of an apartment after watching a first-person video walking through it, women perform equivalently to men when landmark cues are available (O'Laughlin and Brubaker 1998). In contrast, when navigating through a larger outdoor environment, men are significantly better at returning to the starting point, which by the end of the trip is well out of view (Silverman et al. 2000; Malinowski and Gillespie 2001).

In the virtual water maze or in a smaller environment, all landmarks are visible regardless of one's position. When performing a larger scale outdoor navigation task, because the participant herself is moving through space, and some landmarks may not be visible, some internal representation of landmarks relative to the navigator will be required, and an at least partially Euclidean strategy must be used. Navigation through a two-dimensional (2D) map, however, requires no actual movement, and the entire environment is visible. A landmark-based strategy would therefore be most efficient under 2D conditions. Indeed, in studies where participants performed both map-based and real world navigation, women performed either equivalently to men (Postma et al. 2004) or, using landmark instructions, significantly better (Saucier et al. 2002) when navigating on a map, while showing a marked impairment relative to men in 3D environments. Table 2 further illustrates this point, showing that on comparisons between men and women in virtual or real world navigation from a first-person perspective, effect sizes are consistently large; however, effects are smaller and sometimes nonsignificant on map-based comparisons. A similar pattern has been observed in the animal research. While male rats generally outperform females on acquisition of the water maze (Frye 1995; Beiko et al. 2004), this difference is eliminated when a moving platform is used, reducing the spatial component of the task (Perrot-Sinal et al. 1996).

Thus, while men generally outperform women on navigation tasks, the male advantage can be eliminated and even reversed when salient landmark information is available throughout the task, and the position of the navigator relative to landmarks remains stable. It seems, therefore, that the male advantage in spatial navigation consists in a greater ability to maintain a representation of the position of features of the environment that are not visible, and critically to accurately update these relative positions as the navigator moves through space. While both men and women seem capable of effectively navigating when the information to produce an allocentric representation of space (i.e., a map) is provided, men seem better able to navigate in an allocentric way when primarily egocentric information is provided (when in a large real world environment), presumably through the representation of mental maps.

Neuroimaging studies of activity during navigation have reported conflicting results. Gron and colleagues have found areas of significant sexually dimorphic activity during the navigation of a virtual water maze, in particular increased male activation in the left hippocampus relative to females, and increased right parietal and prefrontal activity in females relative to males (Gron et al. 2000). However, a more recent paper finds no interaction between task and sex, even in anticipated regions of interest shown to be sexually dimorphic in previous studies, using a lenient statistical threshold (Ohnishi et al. 2006).

While the question of sexually dimorphic activity patterns during navigation remains unsettled, other studies have shown significantly different patterns of activation between the use of different cognitive strategies believed to differ significantly by sex (Iaria et al. 2003; Jordan et al. 2004; Gramann et al. 2006). Individuals relying on egocentric strategies show decreased activity relative to allocentric navigators in medial temporal areas including the hippocampus and parahippocampal region (Jordan et al. 2004). Similarly, an EEG study indicates recruitment of a primarily posterior-premotor network in egocentric navigators, contrasted with more temporal structures employed in allocentric strategies (Gramann et al. 2006). Assuming women use a predominantly egocentric strategy, these results agree with the findings of Gron and colleagues (2000), who also found women to engage hippocampal structures significantly less than men during navigation. However, these studies of cognitive strategy used only male subjects, and thus it is not possible to separate the influences of strategy from those of sex. Further studies examining the neural activity of both men and women using both strategies are necessary to resolve this question.

Object location

While males typically outperform females in tests of spatial ability, comparisons of memory for the location of objects indicate a strikingly different pattern. Significant female advantages have been observed in several studies of object location memory (Choi and Silverman 1996; James and Kimura 1997; McBurney et al. 1997; McGivern et al. 1997; Levy et al. 2005; Silverman et al. 2007). Others have not found superior performance in women, but have nonetheless found women and men to perform at equivalent levels (Dabbs Jr. et al. 1998; Epting and Overman 1998; Lewin et al. 2001; Postma et al. 2004). The female advantage on object location is seen cross-culturally (Silverman et al. 2007), although some evidence exists for a cultural influence, as genderstereotyped materials affect performance on the task differently between the sexes (McGivern et al. 1997).

These results are clearly opposed to those obtained from studies of other forms of spatial memory, and as such it is useful to consider how object location differs from other spatial tasks in terms of its cognitive demands. In the traditional object location task designed by Eals and Silverman (1994), participants are presented with an array of common objects during the training phase, and at test are presented with another array, in which half the objects have been moved to different locations. Participants must identify which objects have moved. As the task is administered on paper, the position of the test-taker relative to the objects, critical in many path-finding tasks, is not relevant. Similarly, while most mental rotation tasks are presented in such a way that the observer's position is unimportant, success on the task requires mentally changing one's angle of view. Furthermore, all spatial information on the object location task is 2D, as there is no apparent depth in Eals and Silverman's figures (Eals and Silverman 1994). In contrast, while the geometric figures of Vandenberg and Kuse (1978) used in mental rotation are 2D, they also include depth cues.

Additionally, as the object location task uses images of common items, a strategy of internal verbalization is possible as a solution to object location problems. The directional information used in wayfinding or information on the conformation of geometric figures in mental rotation is not nearly as easily labeled. Thus, it has been suggested that success on object location tests may represent a kind of verbal (Lewin et al. 2001), or item memory (James and Kimura 1997), for both of which sex differences favoring women have been previously reported.

To the extent that women's superior performance on object location tasks derives from spatial intelligence, one might expect it to correlate with performance on other measures of spatial ability. Findings on this question have been conflicting. One study, which reports large object location advantages for women, also reports a positive correlation between object location and mental rotation performance for women, but not men (McBurney et al. 1997). However, a similar study, which found no sex difference in object location memory, reports the opposite pattern, with a positive correlation in men, while finding no correlation in women (Dabbs Jr. et al. 1998).

In order to isolate factors explaining a female object location advantage, some studies have attempted to control for sex differences in verbal ability by using object location arrays of more uncommon objects, intended not to be nameable. Using such an uncommon array, Eals and Silverman (1994) report that sex differences persist; however, Epting and Overman (1998) found no sex difference with the same material. Similarly, when the array is composed of nonrepresentational inkblot figures, for which verbal labeling would be nearly impossible, no sex difference is found (Lewin et al. 2001).

Sex differences are also mitigated when the spatial requirements of the task are increased. James and Kimura (1997) attempted to separate location memory from item memory by examining performance by men and women on both the Eals and Silverman (1994) task and a modified version in which the repositioned objects at testing occupied locations that had not previously been occupied by any other item. (In the traditional object location task, the locations where items appear are held constant at the test, but the objects in those locations may have changed.) While the standard object location measure showed the expected female advantage, men and women performed at equivalent levels on the modified task. The authors concluded that women were better only at identifying object exchanges, and not at displacements of objects to new locations. Postma and colleagues (2004) have reported a similar result when positions in which objects may appear vary. They have further shown that when all objects are identical (thus significantly reducing the effectiveness of a labeling strategy), and participants have only to identify the specific locations in which objects appear, men actually show a significant advantage. It seems, then, that when

all nonspatial components are removed from the object location task, the familiar male spatial advantage re-emerges.

Only one study of which we are aware has used neuroimaging to compare activity during object location tasks. The findings of that study point strongly toward a sex difference in cognitive strategy. Women reported using a verbal strategy significantly more often than did men to solve the task; fMRI further indicated a significant difference in lateralization of hippocampal activity, with women showing left-lateralized activity, consistent with verbal activity, and men showing right-lateralized activity (Frings et al. 2006).

Taken together, the evidence is clear that women fare significantly better, relative to men, on tests of object location memory than when compared on other spatial tasks (see Table 3). This does not, however, necessarily indicate that the female advantage is explained by a form of spatial memory distinct from that measured by mental rotation tests, or even by spatial memory at all. While reports of female performance correlating with mental rotation ability suggest that women do use spatial information in solving object location problems, this appears to be only one component of the cognitive process involved. Indeed, studies that have attempted to deconstruct the processes involved in object location seem to indicate that as the task becomes more purely spatial, the female advantage becomes increasingly difficult to detect. Thus, these findings do not seem to be incompatible with the view that a male advantage exists for spatial processing. They may, however, provide further evidence for a female advantage in verbal or episodic memory, a possibility that will be further discussed later in this review.

Summary and conclusions

Substantial evidence indicates a large sex difference favoring men in performance on tasks of mental rotation. This may not, however, be indicative of a sex difference in spatial working memory, as some have argued, as sex differences are less consistent and of smaller size on other working memory measures. More studies comparing correlations of mental rotation performance with spatial working memory measures directly are required to address this question. Imaging studies have identified distinctly different networks activated during mental rotation tasks for men and women, with increased activation in the parietal lobules in men, and increased activity in frontal areas in women. Furthermore, varying the instructions to de-emphasize spatial components of mental rotation problems leads to equivalent performance between men and women. This seems to indicate the use of divergent cognitive strategies between the sexes in solving rotation problems.

Studies of spatial navigation also show consistent sex differences, which seem to be correlated with mental rotation ability, suggesting that similar spatial abilities are being employed in both tasks, at least in men. Strong evidence from both self-report and specifically designed behavioral tests indicate the use of differing cognitive strategies between men and women, with men relying on Euclidean directions, whereas women focus on the use of landmarks. Sex differences are increased when landmark information is sparse and navigation must be performed using a Euclidean strategy, and decreased when such information is available from the navigator's perspective. In map-based navigation tasks, where the entire field is visible at all times, women perform equivalently to men, suggesting that the male advantage consists in the ability to represent spatial relations from a map perspective mentally. Imaging studies are inconsistent in identifying sexually dimorphic patterns of activation during wayfinding tasks; however, such studies reveal significantly different patterns of activation between wayfinding using allocentric and egocentric strategies. Imaging studies controlling for both cognitive strategy and sex are needed to disentangle these two factors.

Women outperform men in several studies of object location memory, while other studies have shown no significant difference between the sexes. Where these differences have been observed, they are not consistently correlated with mental rotation performance, and thus do not seem to derive from the same spatial faculty which drives differences in rotation and wayfinding. Sex differences favoring women are attenuated by the use of stimuli, which are not easily verbally labeled, as well as when spatial demands are increased by varying the locations in which objects may appear, rather than simply shifting objects between previously known locations. These findings suggest that the female advantage on tasks of this type is not related to spatial ability, and thus is not inconsistent with findings of male superiority on other spatial tasks.

Verbal memory

The second of Maccoby and Jacklin's (1974) observations was a tendency in studies of verbal ability/memory for women to outperform men. While later reviewers have noted that the studies originally surveyed in the original review reported relatively small and inconsistent effects (Hyde and Linn 1988), numerous subsequent studies have robustly confirmed Maccoby and Jacklin's view (Kimura 1996). Furthermore, these analyses have considered a broad selection of measures of verbal abilities, only a subset of which are seen as measuring verbal memory.

Two general measures of verbal memory have been used in most studies to identify sex differences. In tests of verbal fluency, such as the Controlled Oral Word Association Test (COWAT) participants are asked to produce as many words as they can starting with a given letter or belonging to a particular semantic category (i.e., animals, fruits, and vegetables) within a certain period of time. In contrast, other methods such as the Rey Auditory Verbal Learning Test (RAVLT), and the California Verbal Learning Test (CVLT), present participants with a list of words, which they are then asked to recall at a later time. Studies of verbal fluency can be thought of as measuring vocabulary and semantic verbal memory, whereas studies of word lists may be seen as a more direct measure of episodic recall.

Both of these measures have shown consistent sex differences (see Table 4). Multiple studies have indicated better female performance on word generation tasks based on both phonological (Mann et al. 1990; Capitani et al. 1998; Thilers et al. 2007) and semantic categories (Hyde and Linn 1988; Bolla et al. 1998; Capitani et al. 1999). Superior verbal memory, as measured by recall of word lists, has been shown in both controlled experimental tasks (Kail Jr. and Siegel 1978; Kimura and Seal 2003) and larger surveys (Stumpf and Jackson 1994; Portin et al. 1995; Kramer et al. 1997). A female advantage has also been observed for other measures of episodic verbal memory including paired-associate learning (Youngjohn et al. 1991), story recall (Zelinski et al. 1993) and verbal recognition (Bolla-Wilson and Bleecker 1986; Bleecker et al. 1988; Temple and Cornish 1993; Weiss et al. 2003), as well as on standardized measures including the CVLT (Berenbaum et al. 1997; Kramer et al. 1997; Chipman and Kimura 1998), the RAVLT (Bolla-Wilson and Bleecker 1986; Bleecker et al. 1988), and the Weschler Adult Intelligence Scale (Portin et al. 1995).

In contrast to the male spatial advantage, superior female performance on verbal memory is consistently evident well before sexual maturity, with sex differences reported in groups as young as 5 yr (Kramer et al. 1997), as well as middle aged and older groups (Portin et al. 1995; Herlitz et al. 1997). It therefore seems unlikely that these differences are mediated by any activational effect of sex hormones. In fact, when groups of men and women matched for estradiol levels are compared, women nonetheless outperform men at verbal recall (Yonker et al. 2003). Although sex differences for verbal episodic tasks have been observed to be consistent across the life span (Herlitz et al. 1997; Gale et al. 2007), some have suggested that sex differences in verbal fluency are more age dependent. While most studies reporting sex differences in fluency have considered broad age ranges, several studies that examined only young adults have found no sex differences (Demakis and Harrison 1997; Tombaugh et al. 1999). Additionally, a recent meta-analysis has indicated a large effect of age, suggesting that consistent sex differences are not seen in participants younger than 60 (Rodriguez-Aranda and Martinussen 2006). This study, however, did not control for differences in education. Others that have considered this variable have shown sex differences in all age groups (Capitani et al. 1998). Nonetheless, there is evidence that age predicts a decline in verbal memory significantly earlier in men than women (Kramer et al. 2003).

Given the lack of clear evidence for activational effects of sex hormones on verbal memory, the possibility that sex differences are a result of more fundamental differences in brain organization should be considered. Evidence from numerous sources has suggested that language abilities are distributed across the brain differently in men and women, specifically indicating that language processing is more bilateral in women, but more leftlateralized in men (Kimura 1983). Following left temporal lobectomy, women's verbal memory is spared, whereas verbal memory in men declines significantly (McGlone 1978; Trenerry et al. 1995). Furthermore, while unilateral brain damage to the right or left consistently produces either spatial or verbal impairment, respectively, in men, no such consistent hemispheric pattern is evident in women (Inglis and Lawson 1982). These findings, however, could also be interpreted as indicating a sex difference in plasticity in response to injury (Trenerry et al. 1995).

Neuroimaging studies can avoid this potential confound, and numerous studies of this sort have investigated the question of sex differences in neural activation during verbal tasks. However, the majority of these studies have focused on activity during passive listening or grammatical, phonological, and semantic judgments about individual words. The findings of these studies have been somewhat inconsistent, and meta-analysis has indicated a small and nonsignificant effect size when comparing the sexes (Sommer et al. 2004). However, others have argued that this analysis collapses tasks with relevant cognitive differences (Kansaku and Kitazawa 2001). While studies measuring activity during semantic judgments of individual words show no sex differences (Frost et al. 1999; Gur et al. 2000), studies of phonological (identifying rhymes) and grammatical (generating past tense forms) judgments show a left-lateralized pattern of activation in men, and bilateral activation in women (Shaywitz et al. 1995; Pugh et al. 1996; Jaeger et al. 1998; Clements et al. 2006). In addition, studies of passive listening to verbal narratives have shown a similar sex difference in lateralization (Phillips et al. 2000; Kansaku and Kitazawa 2001).

None of the tasks imaged in the studies described above are designed to explicitly measure verbal memory, although studies of passive listening, where sex differences are evident, may indicate a difference during encoding. Perhaps the clearest evidence comes from the few studies that have compared neural activity between the sexes during the learning of foreign words. While learning words from a new language, women show bilateral activation of the fusiform cortex, while fusiform activity in men is focused in the left hemisphere (Chen et al. 2007).

To the extent that imaging and neuropsychological studies do indicate differing networks supporting language between the sexes, this would be consistent with claims of sex differences in cognitive strategy. Multiple studies have indicated that women show a higher degree of semantic clustering by semantic (Berenbaum et al. 1997) and phonological (Koren et al. 2005; Weiss et al. 2006) categories during verbal memory tasks. The amount of clustering used during recall has also been shown to be positively correlated with recall performance (Berenbaum et al. 1997). While women seem to outperform men at word list recall regardless of whether the words on the lists are concrete or abstract (Kimura and Clarke 2002), this advantage is not evident when meaningless nonsense words are used (Kimura and Seal 2003). This further suggests that women's advantage in verbal memory depends on encoding at the semantic level.

Summary and conclusions

Substantial evidence indicates a female advantage on tests of verbal memory, as measured by both word recall and fluency. This advantage has been observed throughout the life span, and does not appear linked to circulating sex hormone levels, although tests of fluency do seem to be more influenced by age then tests of recall. Multiple studies suggest that the sex difference in performance may be mediated by a cognitive strategy in women more focused on clustering of items to be remembered by semantic and phonological categories. Consistent with a difference in cognitive strategy, both neuropsychological and neuroimaging studies indicate sex differences in the networks subserving language function, with more bilateral participation in language in women relative to men. In neuroimaging, however, this sex difference is only evident for some language tasks, and few neuroimaging studies address verbal encoding directly. More studies designed to specifically address verbal memory in an imaging context may help to clarify this issue.

Episodic and autobiographical memory

Numerous studies of recall of life events reveal a female advantage in autobiographical memory. Compared to men, women's recall is more accurate (Pohl et al. 2005; Bloise and Johnson 2007) and more specifically detailed (Ross and Holmberg 1992; Seidlitz and Diener 1998; Pillemer et al. 2003). When not specifically prompted, women's narratives are longer than are men's (Friedman and Pines 1991). They recall their first event more quickly, recall more life events, and the first items recalled come significantly earlier in life (Cowan and Davidson 1983; Davis 1999). Women have also been shown to date events in their lives more accurately (Skowronski and Thompson 1990; Skowronski et al. 1991). The female advantage does not appear to be dependent on sexual maturity, being evident in childhood, as early as age 3 (Fivush et al. 1995; Buckner and Fivush 1998; Davis 1999).

The inherently subjective nature of autobiographical memory, as well as the fact that the encoding event can rarely be studied in the laboratory make it difficult to study the mechanisms of these differences experimentally. Furthermore, the complex and multimodal nature of autobiographical memories makes it likely that multiple factors mediate sex differences, possibly independently of each other. Some experimental support has been found for each of the possibilities discussed below.

The affective intensity hypothesis

It has been frequently suggested that women's autobiographical advantage is attributable to an enhancement of emotional recall. Women use significantly more emotional terms, and describe internal states significantly more, when producing autobiographical narratives (Friedman and Pines 1991; Bauer et al. 2003). Several studies have further shown that women outperform men on measures of emotional memory (Fujita et al. 1991; Bloise and Johnson 2007). In one study examining both neutral and emotional memory, a significant interaction between emotionality and gender was found, indicating that although women recalled significantly more emotional information than did men, they showed no advantage for neutral memory (Davis 1999). However, when men and women are queried about life events occurring in randomly selected time periods of the previous week (which were highly unlikely to be uniformly emotional), women's recall still significantly exceeds that of men (Seidlitz and Diener 1998).

The evidence therefore clearly suggests better recall of life events in women, as well as a focus, if not necessarily a selective one, on emotional events. Some have argued that this advantage may be mediated by a sex difference in the intensity of emotional experiences (Fujita et al. 1991). By this logic, since emotional memories tend to be more commonly included in autobiographical narratives, women's longer and more detailed narratives are due to the fact that more of their experiences are perceived as being more emotionally intense. Fujita and colleagues presented evidence from a combination of self and observer reports that women do have more intense affective experiences, irrespective of valence. Similarly, women show higher levels of emotional sensitivity on a standardized measures (e.g., Bloise and Johnson 2007), rate their memories as more emotional than men when recalling them (Seidlitz and Diener 1998), and use significantly more emotional terms than men in describing life experiences (Bauer et al. 2003).

However, sex differences during an emotional experience may not correspond with sex differences at retrieval. Seidlitz and Diener (1998) reported that women rated their memories as more emotional than did men after the recall test. In contrast, when rating experiences at the time they occurred (on a daily questionnaire over 6 wk), men rated their experiences as more emotional than did women. Thus, it was only during recall that women reported experiencing more emotion.

Imaging studies of neural activity during emotional experience have indicated significant sex differences during encoding, consistent with the affective intensity hypothesis. While there is some significant overlap, men and women show several distinct regions of activation correlated with arousal ratings while viewing emotional images, including the post-central gyrus and hippocampus in women, and the putamen in men (Canli et al. 2002). Similarly, during the processing of negatively valenced words, women show increased activity relative to men in the right putamen, right superior temporal gyrus, and left supramarginal gyrus (Hofer et al. 2007). ERP studies have also shown differing response patterns to emotional material between men and women (Orozco and Ehlers 1998; Gasbarri et al. 2007). Furthermore, sex differences have been identified in activity during encoding which predicts subsequent memory performance, particularly in the amygdala (Canli et al. 2002; Cahill et al. 2004). Taken together, these findings indicate not only a difference in the processing of emotional experience, but also that this difference is relevant to later recall.

The elaborative rehearsal hypothesis

The emotional intensity account of sex differences in autobiographical memory seems at minimum incomplete, however, in that it fails to account for reports of better female recall of nonemotional experiences. Another potential explanation which can address this latter factor is that men and women use differing cognitive strategies when encoding and consolidating their experiences. If women engage in more frequent and elaborative rehearsal than do men, this could explain memory differences irrespective of level of arousal. Women do report thinking of and discussing emotional events more frequently (Ross and Holmberg 1992), and tend to provide longer and more detailed accounts of life experiences when asked to reminisce on them (Friedman and Pines 1991; Seidlitz and Diener 1998) Studies of parent-child interactions also indicate that mothers discuss negative life events with their daughters in a more elaborative and interpersonally focused way than they do with their sons, which suggests that increased rehearsal in women may be a result of cultural influences (Fivush et al. 2003).

If women's superior autobiographical memory were mediated by more frequent or more effective rehearsal, one would predict that differences in recall would be small or nonexistent shortly after the event to be remembered, and increase over time. However, significant sex differences are evident as soon as 15 min after encoding (Bloise and Johnson 2007). In addition, when autobiographical recall after 6 wk is compared in the same subjects with recall 11 mo later, no sex difference in the change in recall was observed (Seidlitz and Diener 1998). Similarly, when participants are asked to estimate how frequently they thought of or discussed the events recalled at testing, and the frequency of reminiscence is included as a covariate in memory analyses, the gender effect on memory remains significant (Ross and Holmberg 1992). Thus, the evidence is strong that women do engage in more frequent autobiographical rehearsal than do men. It remains to be established, however, that this increased rehearsal mediates superior autobiographical memory in women.

Retrieval differences

It is also possible that women's superior autobiographical memory might derive from the fact that women are simply more efficient at retrieving memories of life events. Some support for this notion can be found in neuroimaging studies that indicate significantly different patterns of activation during autobiographical retrieval. When recalling both emotional and nonemotional life events, males show increased activity (as measured by fMRI) in the left parahippocampal gyrus relative to females, whereas females show increased activity in right dorsolateral prefrontal cortex, as well as the right insula (Piefke et al. 2005). PET studies have also indicated differing networks of activation between the sexes. Similar to fMRI findings, these studies show greater retrieval-associated activity in women in right inferior frontal cortex, as well as other novel areas including the anterior cingulate and right fusiform cortex (Nyberg et al. 2000). It is difficult to dissociate retrieval effects from those on encoding and consolidation in studies of autobiographical memory, however, as these studies necessarily measure memory by recall, which will be particularly sensitive to differences in retrieval ability. A study testing autobiographical memory by recognition or cued recall could resolve this question, but such a study would be difficult to design, and no such experiment of which we are aware has been reported to date.

Episodic memory

Another explanation for the female autobiographical advantage, not necessarily mutually exclusive with those previously discussed, is that enhanced female performance is evidence for a larger and more general sex difference in episodic memory. This view is based on the fact that a female advantage has been observed on several measures of memory which are neither explicitly verbal nor spatial (Herlitz and Rehnman 2008).

On the object identity task, a nonspatial variant of the object location task discussed above, which is believed to involve episodic memory, a recent meta-analysis has indicated a significant and homogenous advantage for women, although the average effect size, 0.229, is relatively small (Voyer et al. 2007). Women have also been reported to outperform men at the recognition of odors (Lehrner 1993; Oberg et al. 2002), faces (Bengner et al. 2006; Rehnman and Herlitz 2007), pictures (Galea and Kimura 1993), and objects (Herlitz et al. 1997). In addition, sex differences have been observed on multiple tasks which while including a verbal component seem to rely principally on episodic memory, such as recall of a list of directions (Herrmann et al. 1992), and narrative recall (Hultsch et al. 1991; Bloise and Johnson 2007). Thus, it has been argued that women have a general episodic advantage (Herlitz et al. 1997; Herlitz and Rehnman 2008).

It is difficult, however, to establish the independence of these effects from the well-established female advantage on verbal tasks.

As discussed earlier, verbalizing strategies are employed on tasks as distinctly spatial as pathfinding, so it is certainly possible that internal verbal labels might be applied to most of the stimuli used in episodic tests. Some studies have attempted to resolve this issue by comparing performance with purely verbal measures. Lehrner (1993) reports that although women significantly outperformed men at recognizing odors, the study did not report attaching verbal labels more frequently or more consistently than did men. In a study in which several tests of episodic memory were used, Herlitz and colleagues (1997) have also measured verbal fluency, a measure on which women consistently outperform men, to test its relative influence. Regression analyses indicate that both gender and verbal fluency significantly affect episodic memory performance, although their results show fluency accounting for a substantially larger portion of the variance than did gender. Nonetheless, when the influence of verbal fluency is accounted for, the effect of gender remains significant. No such sex difference was found for measures of semantic memory, verbal span, or priming.

Another method to separate episodic from verbal memory in these studies is to use material, which cannot be easily verbally labeled. While women outperform men at the recognition of familiar odors, no sex difference is found when unfamiliar chemical scents, which would not be easily labeled, are used (Oberg et al. 2002). Similarly, most studies of object memory use relatively common objects, for which a label would be readily accessible and a female advantage for object memory is frequently reported. However, when unfamiliar objects are used, the results are less clear. Eals and Silverman (1994) report that the female advantage persists on an object identity task where specialized and unfamiliar objects composed the array. However, when completely nonrepresentative inkblots are placed in the array, no sex difference is observed (Lewin et al. 2001).

Animal studies may be useful in separating out sex differences in episodic memory, as differences in verbal ability are not a concern. The only study of object location to assess sex differences in rodents of which we are aware indicates that females significantly outperform males on this task (Sutcliffe et al. 2007). Additionally, application of exogenous ovarian hormones, either alone or in concert, enhances performance on this task in females (Walf et al. 2006). This suggests that the sex difference may be dependent on activational effects of gonadal hormones.

Thus, while there is some statistical evidence for a sex difference in episodic memory, this difference is comparatively small when differences in verbal ability are accounted for. Relatively few studies have attempted to statistically separate the influence of verbal from episodic processing, and more such analyses are necessary to clarify the issue. While it may be impossible to design an episodic memory task for which no verbal labeling can be used, the few studies that have used stimuli which are difficult to label have not consistently shown a female advantage. Therefore, while a general female episodic advantage may exist, it is unlikely to fully explain women's advantage on tests of autobiographical recall.

Summary and conclusions

Robust and consistent evidence confirms that women have more accurate and detailed recall of life events than men. Several studies have indicated that this advantage is selective for emotional material, and self-report suggests that women describe significantly more of their experiences as emotionally arousing as do men. Neuroimaging of the encoding of emotional material also suggests sex differences in the way this material is processed, as well as sex differences during retrieval.

However, sex differences persist when men and women are queried about neutral material, suggesting that a difference in emotional memory cannot fully explain the female advantage. Women have also been shown to rehearse their experiences more and more elaboratively, but this has not been definitively connected to any memory difference. While sex differences have also been shown on a number of tasks, neither explicitly spatial nor verbal, suggesting a general difference in episodic memory, these effects are substantially reduced when differences in verbal memory are controlled for. Nonetheless, a small but significant episodic memory effect seems to exist independently of verbal differences.

Sex differences in stress effects on memory

Considering the evidence discussed above regarding sexual dimorphism in the circuitry of emotional memory, one might expect sex differences in the mnemonic effects of emotional arousal. In fact, a growing body of evidence from both human and animal models does indicate that the mnemonic effects of sex and stress hormones, both neurally and behaviorally, differ between the sexes. The effects of sex on performance seem to differ, however, depending on whether a stressor is acute or prolonged. In females, cyclic fluctuations in ovarian hormone levels also seem to modulate the effects of stress.

Acute stress

Overall, the cognitive outcomes of acute stress are significantly more positive in males than in females. This difference is particularly apparent in studies of aversive learning. In rodent studies, males consistently outperform females in studies of inhibitory avoidance, showing higher latencies to re-enter a chamber previously associated with shock (Drago et al. 1980; Heinsbroek et al. 1984; Kudo et al. 2004). Similarly, in studies of fear conditioning, males show more prolonged freezing, whether shock is signaled by context (Maren et al. 1994; Gupta et al. 2001; Wiltgen et al. 2001) or by a discrete CS (Pryce et al. 1999). Indeed, by nearly every behavioral measure, males show comparatively increased conditioned fear (Aguilar et al. 2003). These effects can also be seen in humans, as human males acquire fear conditioning significantly faster than do females (Milad et al. 2006).

The application of stressors either prior to, or post-training, has also revealed sexually dimorphic effects. Under low-stress conditions, female rats show superior acquisition of eye-blink conditioning. However, restraint stress prior to training enhances performance in males, yet impairs it in females (Hodes and Shors 2005). Similarly, acute restraint stress impairs working memory on a delayed alternation task in females, while males are unaffected (Shansky et al. 2006). Pretraining predator stress also affects memory differently between the sexes. While both males and females show impaired memory 24 h after training, stressed male mice make significantly more errors than do stressed females, despite the fact that females show more errors during acquisition (Park et al. 2008). In humans, social stress prior to conditioning enhances the acquisition of fear conditioning in men, while impairing acquisition in women (Jackson et al. 2006). Similarly, a post-training physiological stressor enhanced memory consolidation only in men, while having no effect on women (Andreano and Cahill 2006).

One notable exception to this pattern concerns post-traumatic stress disorder (PTSD), considered by many to be an extreme case of the enhancement of memory by an intensely stressful experience. While a pronounced sex difference has been observed in PTSD rates in those exposed to trauma, the data indicate that women are significantly more susceptible to PTSD than men (Gill et al. 2005; Olff et al. 2007). However, it is debatable whether the stressor in this case should be considered acute. While PTSD is generally triggered by a single traumatic event, the longer term consequences of PTSD, including traumatic flashbacks and disruption of ordinary HPA function might be more properly considered a form of chronic stress.

Sex differences have also been observed in the relationship between the stress hormone cortisol and memory, consistently indicating that cortisol is more tightly coupled with memory in males. Numerous studies have reported that in men, cortisol levels at encoding predict memory, while showing no relationship in women. This has been observed for studies of the acquisition and retention of fear conditioning in humans (Zorawski et al. 2005; Jackson et al. 2006) and rodents (Wood et al. 2001), as well as the consolidation (Andreano and Cahill 2006) and retrieval (Wolf et al. 2001) of verbal material. The effects of cortisol on working memory have also shown a sexually dimorphic pattern, such that a positive relationship is found in men, while the relationship in women is negative (McCormick et al. 2007). At least one other study, however, has noted relationships between cortisol and memory, which are sex independent (Park et al. 2008).

In addition to these behavioral sex differences, neural sex differences in the effects of stress have been observed. Exogenous cortisol applied prior to a fear conditioning task decreases activity in the anterior cingulate, as well as the orbitofrontal and prefrontal cortices of men. Women treated with the same dose of cortisol, however, show increased activity in these same regions (Stark et al. 2006). Some studies have further shown that in addition to different levels of activity in common networks, entirely different structures may be employed by men and women in the modulation of emotional memory. fMRI indicates that performance of a cortisol-inducing stress task produces sex-specific patterns of activation, with primarily frontal areas in men, and primarily limbic areas in women, showing increased activity (Wang et al. 2007). Similarly, recent rodent work indicates that the bed nucleus of the stria terminalis plays a sexually dimorphic role in emotional memory consolidation, such that inactivation of the region prevents memory enhancement in males, but not females (Bangasser and Shors 2008).

Chronic stress

Studies of the effects of chronic, rather than acute stress on memory have shown a markedly different pattern of results. While acute stress exerts a generally positive influence on male memory for numerous tasks, chronic stress has an impairing effect on male performance on the radial arm maze (Luine et al. 1994; Bowman 2005), object recognition and location (Beck and Luine 2002; Bowman et al. 2003), and water maze (Kitraki et al. 2004). In contrast, female performance on these measures is actually improved following chronic stress (Beck and Luine 2002; Kitraki et al. 2004; Bowman 2005). Females also show improved performance on the Y-maze after chronic stress, although on this task, a similar pattern is seen with acute stress (Conrad et al. 2003, 2004).

As all of these tasks depend on the hippocampus to some extent, the sex differences in behavior may reflect a sex difference in hippocampal function, particularly under stress. In fact, studies of the effects of stress on hippocampal morphology have also shown a sexually dimorphic pattern. In the CA1 region of the hippocampus, dendritic spine density is increased by acute stress in the male, but decreased in the female (Shors et al. 2001, 2004). In contrast, after 21 d of chronic restraint stress, male rats show significant dendritic atrophy in CA3, while females appear to be unaffected (Galea et al. 1997). Glucocorticoid receptor density in the hippocampus is also affected by stress in a sex-dependent fashion. Chronic stress significantly reduces GR immunoreactivity in male rats, while females show an increase in response to the same stressor (Kitraki et al. 2004).

Studies of hippocampal physiology also reveal numerous sex differences. While, as mentioned previously, males generally acquire larger magnitude LTP after tetanic stimulation, and show effects after fewer tetani (Maren et al. 1994; Yang et al. 2004), chronic isolation stress prior to tetanic stimulation produces a further enhancement of LTP in males, yet has no significant effect in females (Bronzino et al. 1996). Thus, it seems that the female hippocampus, compared to that of the male, is substantially more resistant to morphological and physiological changes induced by chronic stress. However, the evidence suggests that the female is also less affected by the transient effects of acute stress, which in the male generally improve cognition.

Sex hormone influences

One possible contributor to sex differences in emotional memory is the influence of ovarian hormones. In several of the studies previously discussed, female groups were further subdivided into hormonally distinct cycle positions, so that learning at different sex hormone levels could be compared. In each case, women trained during the early follicular phase, and rodents trained during behavioral estrus, when ovarian hormone levels are comparatively low, performed equivalently to males despite the finding of an overall sex difference (Wood et al. 2001; Milad et al. 2006; Shansky et al. 2006). In rodents, the impairment of eye-blink conditioning by pretraining stress in females is prevented by ovariectomy, or the estrogen antagonist tamoxifen, further suggesting that circulating estrogen may mediate this effect (Wood and Shors 1998). Similarly, ovariectomy eliminates the sex difference in fear conditioning, with ovariectomized females freezing at levels equivalent to males (Gupta et al. 2001).

The effects of sex hormone levels on cognition seem to be dependent upon the arousal level associated with the task being learned. While in the relatively nonarousing object recognition task, rats in the estrogen-rich proestrus phase or those receiving exogenous estradiol outperform estrus or vehicle-treated rats, the opposite pattern is seen in fear conditioning, where estradiol impairs learning (Gupta et al. 2001; Walf et al. 2006). Similarly, proestrus rats find the hidden platform in the water maze significantly faster than rats in estrus when the water is warm. However, when the temperature of the water is decreased, thus increasing the aversiveness of the task, this pattern reverses, with estrus rats outperforming those in proestrus (Rubinow et al. 2004). The substitution of cold water of the same temperature improved performance in males compared to warm water, similar to estrus females (Sandi et al. 1997).

In humans, only two studies of which we are aware have compared differing menstrual phases in terms of stress effects on memory (Kuhlmann and Wolf 2005; Andreano et al. 2008). When consolidation was studied, the results indicated a significant difference in the correlation between stress-induced cortisol and narrative recall between early follicular, late follicular, and midluteal phases, such that a positive relationship was seen in the midluteal phase, while a negative trend was seen in the early follicular phase (Andreano et al. 2008). Exogenous cortisol was found to impair retrieval during both mensis and the luteal phase, while cortisol did not impair memory in oral contraceptive users (Kuhlmann and Wolf 2005). Both studies indicate that sex hormone levels can affect cortisol's cognitive effects, although cortisol's effects differed on consolidation and retrieval. Further experiments are needed to examine possible interactions between sex and stress hormones across multiple phases of learning.

Thus, both human and rodent studies suggest that sex hormones can modulate the effects of stress on memory. The more developed animal literature seems to further indicate that sex differences in emotional memory peak when levels of ovarian hormones, particularly estrogen, are high, and are minimal or absent when sex hormone levels are low. Collectively these findings suggest that previously observed sex differences may be driven by the subset of females with relatively elevated sex hormone levels. Future studies would therefore benefit from careful consideration of sex hormone levels in females, as collapsing hormonally distinct groups may lead to overly generalized conclusions about females on the whole which could only properly apply to a particular menstrual group.

A specific hypothesis regarding the influence of sex on emotional memory

As discussed above, growing evidence identifies sex/stress hormone interactions in learning, highlighting the general importance of potential sex influences on stressful (emotional) learning situations. And as also noted above, evidence from a diverse array of studies indicates that females' memory is, on average, more detailed than that of males. A potential neurobiological mechanism underlying enhanced detail memory for emotional events in women comes from the discovery of a sex-related hemispheric lateralization of amygdala function in relation to long-term memory of emotional events. Several laboratories have reported that activity of the right, but not left, hemisphere amygdala in men viewing emotional material relates significantly to long-term retention of the material, yet in women viewing the same material, it is activity of the left, and not right, hemisphere amygdala that relates significantly to memory (Cahill et al. 2001, 2004; Canli et al. 2002; Mackiewicz et al. 2006). This lateralization effect is clearly robust. Cahill et al. (2004) reported a significant interaction between sex and hemisphere in the relationship between amygdala activity at encoding and subsequent memory of emotional material. Canli et al. (2002) note "both correlations were so robust that they were present even with multiple comparisons across the brain and without selecting the amygdala as a region of interest."

Cahill and van Stegeren (2003) combined the sex-related hemispheric laterality of amygdala function with evidence of hemispheric specialization in the processing of relatively global (gist) versus local (detail) aspects of a stimulus or scene. Substantial evidence indicates that the right hemisphere is biased toward the processing of more global, "gist" aspects of a stimulus or scene, while the left hemisphere is biased toward more local, finer detail processing of the same stimulus or scene (Fink et al. 1996, 1999; Ivry and Robertson 1998). Combining the evidence of a hemispheric lateralization of amygdala function in memory for emotional material ("males/right, females/left") with the evidence of hemispheric biases in processing global versus local information ("holistic/right, detail/left"), allowed the prediction that propranolol, a drug which should impair the amygdala's modulatory function in memory, should impair long-term memory for relatively global (gist) aspects of an emotionally arousing story in men, but impair memory for peripheral story details in women. Cahill and van Stegeren (2003) tested this prediction by reanalyzing published data from two studies demonstrating an impairing effect of propranolol on memory for an emotionally arousing story. The results revealed a double dissociation of sex and type of information (central versus peripheral) on propranolol's impairing effect on memory: Propranolol significantly impaired memory of central information in men but not women, yet impaired memory for peripheral details in women but not men. These results are consistent with the hypothesis that, under emotionally arousing conditions, activation of right amygdala/ hemisphere function produces a relative enhancement of memory for central information in males, and activation of left amygdala/ hemisphere function in females produces a relative enhancement of memory for peripheral details in women. This conclusion appears to merit testing in additional "emotional memory" paradigms to establish the generality of the effect.

Interestingly, a clear sex-by-hemisphere difference in amygdala function exists even during resting conditions. Kilpatrick et al. (2006) examined the patterns of covariance between the left and right hemisphere amygdalae and the rest of the brain in a large sample of men and women (36 of each) who received PET scans while simply resting with their eyes closed. The results revealed far wider patterns of covariance between the right hemisphere amygdala and the rest of the brain in men than in women, but far wider patterns of covariance between the left hemisphere and the rest of the brain in women than in men. This result has been robustly confirmed by Savic and Lindstrom (2008). A simple, but very important conclusion emerges from these studies: No matter what the sex-related lateralization of amygdala function ultimately proves to mean for memory of emotional events in men versus women, studies of the amygdala's role in memory (at least for humans) risk conclusions that are incomplete at best, and wrong at worst, if they fail to consider influences of sex and hemisphere.

Some promising new directions

The bulk of the evidence presented here has drawn from studies on the psychological or systems neuroscience level: behavior, pharmacology, and neuroimaging. However, intriguing new discoveries about sex influences on memory are coming from new technologies, in particular from powerful genetic manipulation methods, such as mouse knockout models. These findings suggest that sex differences persist on the level of molecules and genes. For example, Mizuno and colleagues (2007) have shown that the calcium/calmodulin kinase cascade, which activates gene transcription important in the formation of long term memory, appears to have a "sex specific" role in memory formation: Knocking out a particular kinase important to this pathway (CamKKbeta) impaired spatial memory performance exclusively in males. Female mice possessing the same genetic manipulation exhibited no deficit in performance. Furthermore male, but not female, knockout mice exhibited impaired LTP at hippocampal synapses. The authors further identified a gene, GAA, whose hippocampal expression was up-regulated by spatial training in wild-type males, but not in wild-type females. These findings suggest that the molecular and genetic pathways involved in the formation of spatial memories may differ between male and female mice. Subsequent experiments have indicated that when CaMKK genes are knocked out, expression of two splicing factors is altered in males only, and that one of these factors increases its expression after learning tasks in males only (Antunes-Martins et al. 2007). Thus, it appears that after learning, a process of what the authors call "male specific transcription" occurs, such that different molecular pathways are employed by males and females.

Wiltgen et al. (2005) provide another example of sex influences on learning in a transgenic mouse. These investigators examined the effects of a knockout of the delta subunit of the GABA(A) receptor on fear conditioning. They report that the delta knockout enhanced performance in both single cue and contextual fear conditioning tasks. However, this enhancing effect occurred only in females. No effect was seen in males with the same knockout. Again, the findings point toward potentially sexspecific molecular mechanisms related to memory. They also reinforce the conclusion that identical behavioral phenotypes in the two sexes cannot be assumed in molecular studies of memory.

As a final example of a new methodology enabling novel insight into sex influence on memory, consider a recent study by Quinn et al. (2007). These investigators took advantage of the "four core genotypes" (FCG) mouse model capable of dissociating genetic from hormonal contributions to behavior. Food-reinforced instrumental habit learning was found to be superior in animals that were genetically female, regardless of whether they expressed male or female hormones, a finding with clear implications for the well-established faster rate of habit learning in women becoming addicted. Clearly this approach is capable of disentangling genetic and hormonal contributions to the neurobiology of learning in a novel, extremely powerful fashion.

Conclusions and suggestions for future work

Overall, the evidence reviewed here confirms the common view that males outperform females at tasks involving spatial memory, while females show an advantage at verbal memory. However, we have also seen under closer scrutiny that the male advantage is absent for a subset of spatial tasks, including object location, small-scale navigation, and landmark-based navigation. Thus, the sex difference seems to be specific for tasks involving the mental representation of space, particularly of absolute direction: in other words, for tasks in which spatial information is the primary available cue.

In contrast, the verbal advantage shown by women applies more generally. Female advantages are present for verbal tasks of all sorts, tasks involving verbal components such as navigation by street names, and nonverbal tasks for which strategies of internal verbalization are easily applied, such as object location using common objects. Whereas the male spatial advantage seems to emerge when little other than spatial information is available, female verbal abilities are evident whenever a verbal strategy can be used.

It seems likely, therefore, that the comparatively promiscuous female advantage in verbal memory contributes to the sex differences observed in autobiographical and other forms of episodic memory. Where verbal ability has been considered as a factor in studies of episodic recall, it has been shown to have the largest effect driving the sex difference, although statistically significant episodic advantages in women that are independent of verbal ability also have been reported. Comparable analyses of the influence of verbal ability on autobiographical memory have not yet been performed to our knowledge, but should be. Furthermore other potentially influential factors, such as cognitive strategies in rehearsal, retrieval ability, and perceived arousal of life events have shown clear sex differences, although these differences have not been definitively connected to memory.

The evidence reviewed here suggests to us that particular attention to influences of sex should occur in studies of "emotional memory." Indeed, we suggest that, given rapidly emerging evidence for sex/stress hormone interactions in learning, emotional memory constitutes another set of memory tasks (along with verbal and spatial measures) for which sex influences are likely to be especially pronounced. Compared to sex differences in verbal and spatial behaviors, the memory for emotionally stressful events appears particularly sensitive to circulating sex hormone levels. While sex/stress hormone interactions are well established for the rodent estrus cycle, comparatively few studies have assessed these interactions in humans. The data clearly call for more widespread consideration of sex/stress hormone interactions in human memory.

Additionally, a neural sex difference has been identified which correlates specifically to the modulation of memory by emotion, further suggesting that sex differences in emotional memory are mediated by a neural mechanism distinct from those observed in other tasks. The established hemispheric lateralization of amygdala function both in relation to memory for emotional material, and even in resting conditions, also strongly supports the view that investigations of emotional memory must pay careful attention to sex influences. Indeed, the striking sex differences in amygdala function at rest imply that all studies of human amygdala function—not just those concerned with memory should consider potential sex influences. As regards memory, the

Paper	Task	Advantage	Р	d	N
McGivem et al. (1997)	Silverman, female stim	Female	<0.05	1.04	100
McBurney et al. (1997)	Silverman task	Female	< 0.005	0.89	103
McGivern et al. (1997)	Silverman task	Female	< 0.05	0.78	100
Postma et al. (2004)	Position memory	Male	< 0.05	0.49	64
James and Kimura (1997)	Object location (exchange)	Female	< 0.005	0.48	84
McGivern et al. (1997)	Silverman, male stim		NS	0.42	100
Silverman et al. (2007)	Silverman task	Female	< 0.05	0.34	95,742
Epting and Overman (1998)	Silverman task, object errors		NS	0.27	· 47
Epting and Overman (1998)	Silverman task, location errors		NS	0.04	47
Postma et al. (2004)	Silverman task		NS	0.03	64
Postma et al. (2004)	Object memory		NS	0.03	64
James and Kimura (1997)	Object location (shift)	Female	NS	0.03	90

Table 3. Effect sizes of cited studies in object location memory

data already allow the conclusion that, at minimum, men and women are not, on average, employing identical brain regions when storing the same emotional events into long-term memory.

Another pattern seen in the data reviewed here relates to neuroimaging studies of sex differences. Several such studies reviewed here, examining a number of different memory measures, both visuospatial and verbal, have reported significantly different networks of activation associated with task performance between the sexes, while reporting no behavioral sex difference in performance (Grabowski et al. 2003; Piefke et al. 2005; Clements et al. 2006; Hugdahl et al. 2006). Similarly, when task performance is explicitly matched between the sexes, neural sex differences persist for some tasks (Jordan et al. 2002). Thus, the fact that the sexes may perform equivalently on a given task does not necessarily imply that no sex differences exist in the neural mechanisms underlying the behavior. Researchers in the field of cognitive neuroimaging therefore should be particularly attentive to the possibility of sex differences, avoiding the use of mixed-sex samples where possible, and limiting the interpretation of single-sex samples to the sex studied.

Neuroimaging techniques properly applied, however, provide the potential for addressing many of the unanswered questions raised by this inquiry. In dimorphic tasks for which cognitive strategy may be an important factor, such as studies of navigation, neuroimaging allows for the identification of differing networks underlying task performance (Jordan et al. 2004). While studies have identified differing networks between ego- and allocentric navigators in men, no imaging study to date has considered both sex and cognitive strategy. This comparison is critical for understanding whether the male advantage occurs simply because a higher percentage of allocentric navigators are men, or whether the difference persists even when potential strategy differences are controlled.

Neuroimaging may also be an important tool for dissociating differing cognitive components of a task, and assessing to what extent each component exhibits a sex difference. Behavioral evidence clearly indicates both a female advantage in measures of verbal fluency and production, as well as verbal memory. It is not clear, however, to what extent the general advantage in verbal ability in women contributes to their relatively superior verbal memory performance. Imaging studies comparing the sexes during verbal learning could potentially distinguish activity related to verbal processing from that related to episodic encoding. As few, if any, sufficiently powered studies have focused on sex differences in verbal encoding, these important questions remain to be answered.

Table 4. Effect sizes of cited studies in verbal memory

Paper	Task	Advantage	Р	d	Ν
Chipman and Kimura (1998)	CVLT	Female	<0.01	0.97	49
Mann et al. (1990)	Story recall	Female	<0.001	0.92	175
Savage and Gouvier (1992)	RAVLT, delayed recall	Female	NS	0.88	20
Bolla-Wilson and Bleecker (1986)	RAVLT, recall	Female	< 0.005	0.85	45
Portin et al. (1995)	WAIS object memory	Female	<0.05	0.79	389
Yonker et al. (2003)	Verbal recall	Female	<0.05	0.77	36
Kimura and Seal (2003)	Verbal recall	Female	<0.05	0.66	53
Mann et al. (1990)	Verbal fluency	Female	<0.001	0.65	175
Portin et al. (1995)	WAIS verbal PA	Female	< 0.005	0.64	389
Bolla-Wilson and Bleecker (1986)	RAVLT, recognition	Female	<0.05	0.61	45
Bleecker et al. (1988)	RAVLT, recall	Female	<0.05	0.59	196
Berenbaum et al. (1997)	CVLT	Female	0.05	0.56	57
Chipman and Kimura (1998)	Incidental verbal memory	Female	<0.01	0.55	49
Youngjohn et al. (1991)	Verbal recall	Female	< 0.005	0.46	1492
Trahan and Quintana (1990)	Delayed verbal recall	Female	<0.05	0.39	140
Savage and Gouvier (1992)	RAVLT delayed recognition		NS	0.38	20
Yonker et al. (2003)	Verbal recognition		NS	0.36	36
Bleecker et al. (1988)	RAVLT, recognition		NS	0.35	196
Stumpf and Jackson (1994)	TMS learning facts	Female	< 0.05	0.34	96,968
Trahan and Quintana (1990)	Immediate verbal recall	Female	<0.01	0.31	140
Kramer et al. (1997)	CVLT	Female	<0.001	0.27	920
Youngjohn et al. (1991)	Verbal paired associates	Female	< 0.005	0.185	1534
Yonker et al. (2003)	Semantic memory		NS	0.12	36
Kimura and Seal (2003)	Verbal recall, nonsense		NS	0.07	53

RAVLT = Rey Auditory Verbal Learning Test and CVLT = California Verbal Learning Test.

A heightened attention to investigation of females in animal research could also begin to address many of the issues raised by human subject work. Obviously, sex differences in animals cannot be explained on the basis of differential use of verbal strategies between the sexes. Thus, the use of animal models can be particularly useful in areas where verbal labeling strategies may be mediating sex differences, such as object location and episodic memory. Similarly, sex differences in learning and memory in animals cannot be explained by human cultural considerations. Thus, a straightforward recommendation is that investigators of brain and memory should much more aggressively investigate memory function in females than they have to date (despite early indications of pronounced sex influences on learning, e.g., McGaugh and Thomson 1962). Fortunately, increased examination of female animals is occurring naturally in the field of genetically modified mice, in which both male and female mice are made, and thus studied.

Finally, we suggest that, in light of the accumulated evidence of sex differences in the neurobiology of learning and memory, the burden of proof regarding sex influences on brain and memory has shifted (Wetherington 2007). The data suggesting that sex can influence neurobiological memory functions, from the cellular to behavior levels, are now so abundant that it is no longer incumbent on those attending to the possibility of sex influences in their work to justify why they do so. It is incumbent on those not doing so to justify why not. We suggest that all investigators in the field should challenge the (generally implicit) assumption that sex matters little, if at all, in their work, and that doing so will advance our understanding of the basic mechanisms of learning and memory.

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