

## COMMENTARY

Stress and the Engagement of Multiple Memory Systems:  
Integration of Animal and Human StudiesLars Schwabe<sup>1,2\*</sup>

**ABSTRACT:** Learning and memory can be controlled by distinct memory systems. How these systems are coordinated to optimize learning and behavior has long been unclear. Accumulating evidence indicates that stress may modulate the engagement of multiple memory systems. In particular, rodent and human studies demonstrate that stress facilitates dorsal striatum-dependent “habit” memory, at the expense of hippocampus-dependent “cognitive” memory. Based on these data, a model is proposed which states that the impact of stress on the relative use of multiple memory systems is due to (i) differential effects of hormones and neurotransmitters that are released during stressful events on hippocampal and dorsal striatal memory systems, thus changing the relative strength of and the interactions between these systems, and (ii) a modulatory influence of the amygdala which biases learning toward dorsal striatum-based memory after stress. This shift to habit memory after stress can be adaptive with respect to current performance but might contribute to psychopathology in vulnerable individuals. © 2013 Wiley Periodicals, Inc.

**KEY WORDS:** multiple memory systems; hippocampus; striatum; spatial learning; stimulus-response learning; stress; glucocorticoids; noradrenaline

## INTRODUCTION

Learning and memory can be supported by multiple memory systems. Over 100 years ago, William James (James, 1890) distinguished in his classic writings between memory and habit. Different ways of learning were also described by Tolman (1948) in his maze tasks for rodents in the first half of the 20th century. First direct evidence for distinct memory systems in the brain came from a few years later from the landmark studies with the patient H.M. After surgical removal of his medial temporal lobes, H.M. suffered from severe anterograde amnesia (Scoville and Milner, 1957). Although he could not form any new explicit memories, he could learn some procedural skills (Corkin,

1965, 1968) and his working memory was largely intact (Drachman and Arbit, 1966), suggesting that some forms of memory depend on the medial temporal lobe, whereas others do not. In the following decades, several other patients were introduced who also showed impairments in some forms of memory but not in others after circumscribed brain damage (Gabrieli et al., 1995; Knowlton et al., 1996; Vargha-Khadem et al., 1997; Bohbot et al., 2004). At the same time, elegant lesion studies in rodents provided compelling evidence for double or even triple dissociations between memory systems (Packard et al., 1989; Kesner et al., 1993; McDonald and White, 1993). Most recently, neuroimaging studies confirmed the existence of separate memory systems in the human brain (Poldrack et al., 2001; Iaria et al., 2003; Albouy et al., 2008).

Whereas it is widely accepted that there are multiple, anatomically and functionally distinct memory systems, it is less clear how these systems relate to one another. Are different memory systems independent of each other or do they interact? And if they interact, are these interactions cooperative or competitive? Although memory systems can process information in parallel and simultaneously (McDonald and White, 1994; White and McDonald, 2002), a strict independence appears rather unlikely as it has been repeatedly demonstrated that the manipulation of one memory system can affect the performance of another (Packard et al., 1989; Kim and Baxter, 2001; Schroeder et al., 2002). Some authors characterized the interactions between memory systems as competitive (Poldrack et al., 2001; Poldrack and Packard, 2003), others as cooperative (McIntyre et al., 2003; Voermans et al., 2004). However, no matter if the interactions between memory systems are seen as competitive or cooperative, there are situations in which different memory systems suggest distinct behavioral responses (Fig. 1) and a question arises as to which factors determine which system dominates behavior in such situations.

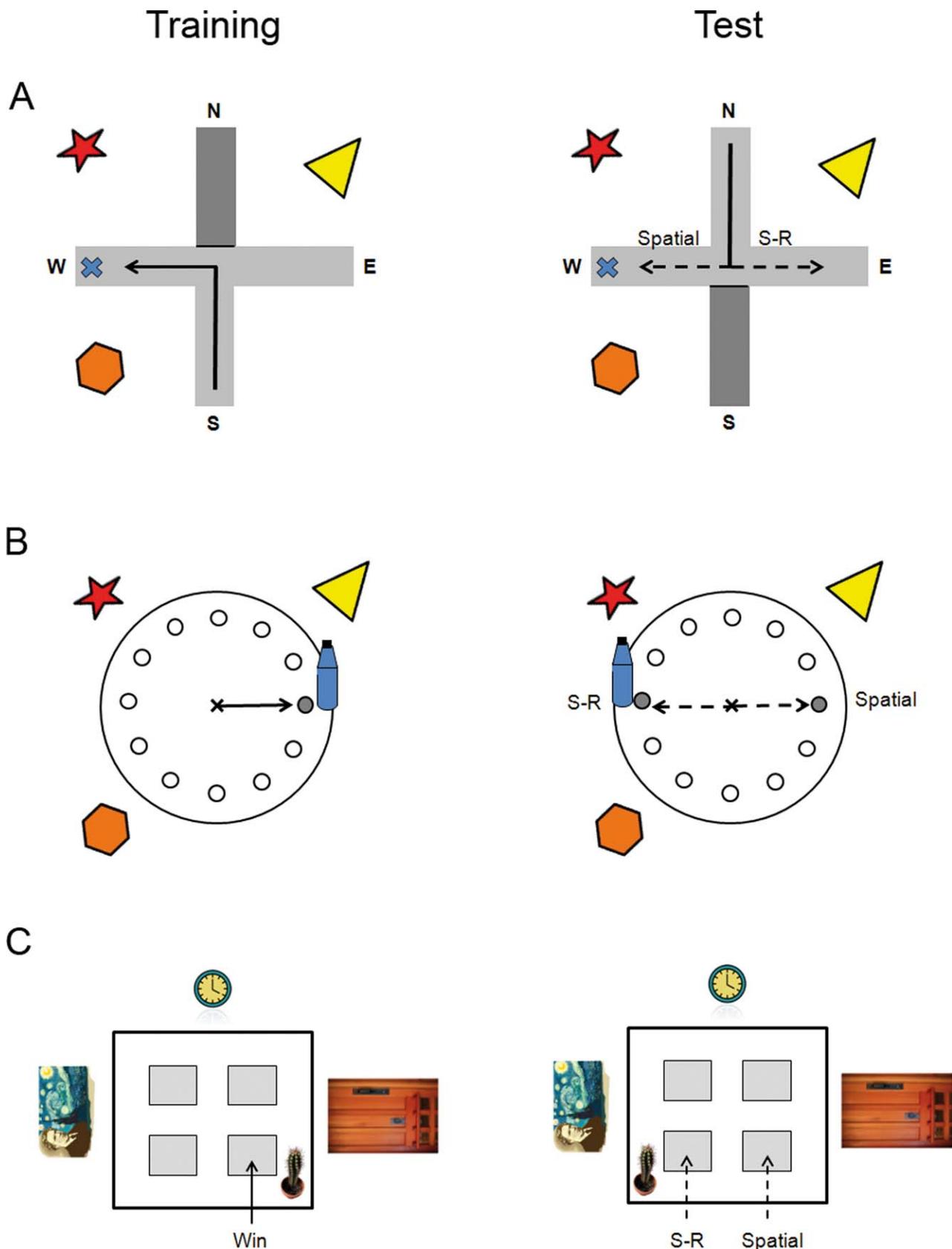
It is well established that practice is a critical factor for the relative engagement of multiple memory systems (Packard and McGaugh, 1996; Iaria et al., 2003). During early stages of learning, performance is thought to depend on “declarative,” explicit memory systems such as the hippocampus or prefrontal cortex.

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**FIGURE 1.** Tasks used to separate hippocampus-dependent and dorsal striatum-dependent memory systems. (A) Scheme of a plus-maze task in which rodents can learn the spatial location of the target in relation to several extra-maze cues or simply a motor response. In a test trial, the starting position is changed from the south arm to the north arm. Going into the west arm, in this test trial, indicates spatial memory, whereas going into the east arm is indicative for stimulus-response (S-R) memory. (B) Similarly, in a circular hole board task rodents can learn the location of an exit hole using the relationship between multiple extra-maze cues or by learning the association with a

single proximal cue. This cue is relocated in a test trial which reveals the engaged memory system: going to the hole in the position where the exit had been during training reflects a spatial strategy; going to hole next to the novel location of the proximal cue indicates an S-R learning strategy. (C) Scheme of a card task used in humans. Participants are trained to identify a win-card out of four identical cards and can learn the position of this win-card again using multiple room cues or using a single proximal cue. Relocating the proximal cue in a test trial shows the engaged learning strategy. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

As training proceeds, however, explicit memory systems are replaced by “procedural,” more implicit systems such as the dorsal striatum (Balleine and Dickinson, 1991; Packard and McGaugh, 1996; Poldrack et al., 2001; Chang and Gold, 2003; Iaria et al., 2003). This shift from explicit to implicit memory systems across the course of learning is referred to as proceduralization; behavior becomes autonomous and independent of explicit control (Anderson, 1987). In addition to practice, there is also first evidence that distraction may favor the engagement of procedural memory, at the expense of declarative memory (Foerde et al., 2006). Similarly, feedback timing during learning appears to be an important factor for the relative use of multiple memory systems, with immediate feedback promoting procedural learning and delayed feedback facilitating declarative learning (Foerde and Shohamy, 2011).

Here, I will focus on stress as another critical modulator of the engagement of multiple memory systems. During stressful experiences, numerous hormones, peptides, and neurotransmitters are released (Joëls and Baram, 2009), two of which play a key role in stress effects on memory: adrenaline and glucocorticoids (cortisol in humans, corticosterone in rodents). Adrenaline is released from the adrenal medulla and exerts indirect effects on the brain, mainly via the vagus nerve and noradrenergic brainstem centers (Williams and Clayton, 2001). Glucocorticoids, released from the adrenal cortex, can readily enter the brain and bind to glucocorticoid receptors (GR) and mineralocorticoid receptors (MR; Reul and de Kloet, 1985; de Kloet et al., 2005). Adrenaline, noradrenaline, and glucocorticoids can alter information processing in many memory systems, including the amygdala (Roozendaal et al., 2006a; van Marle et al., 2009), the prefrontal cortex (Roozendaal et al., 2004; Elzinga and Roelofs, 2005; Schwabe et al., 2012c), the dorsal striatum (Guenzel et al., 2013; Quirarte et al., 2009), and, most prominently, the hippocampus (de Quervain et al., 2003; Diamond et al., 2006; Wiegert et al., 2006; Schwabe et al., 2009a). In the first part of this article, I will review animal and human data demonstrating that stress and stress hormones may not only affect information processing within a single memory system, but that they can also orchestrate the engagement of multiple memory systems. Based on these findings, I will develop a model that aims to explain how stress may alter relative use of distinct memory systems in the brain.

## STRESS AND THE ENGAGEMENT OF MULTIPLE MEMORY SYSTEMS

Most multiple memory system views have been dualistic. Distinctions were, for instance, made between a taxon and a locale system (O’Keefe and Nadel, 1978), a declarative and a non-declarative system (Squire et al., 1993), a reference and a working memory system (Olton et al., 1979), or a simple and a configural association system (Sutherland and Rudy, 1989). These dualistic frameworks are very simplified because there are certainly more than two memory systems, each consisting of subsystems and sub-

functions (Eichenbaum and Cohen, 2001). However, because two of these systems have been in the spotlight of the memory systems literature, these will also be the focus of the following review: (i) a hippocampus-dependent “cognitive” system that processes relationships between multiple cues and allows spatial or declarative learning (O’Keefe and Nadel, 1978; Packard et al., 1989; Burgess et al., 2002; White and McDonald, 2002; Eichenbaum, 2004), and (ii) a dorsal striatum-dependent “habit” system that subserves stimulus-response (S-R) and procedural learning (White and McDonald, 2002; Yin and Knowlton, 2006; Graybiel, 2008).

## Stress and the Modulation of Hippocampal and Dorsal Striatal Memory: Rodent Studies

Hippocampal and striatal contributions to learning and memory in rodents have mainly been separated in navigation tasks. Typically, rodents are first trained to locate a certain target in an environment that allows both hippocampus-based spatial learning strategies and dorsal striatum-based S-R learning strategies. Changing the testing environment (i.e., the starting position or the location of a proximal cue) in a test trial reveals which memory system controls learning (Figs. 1A, B). Using such a dual-solution task, Kim et al. (2001) were the first to show that stress can modulate the engagement of multiple memory systems. In their study, rats had been exposed to foot shocks before they were trained in a cued-hidden platform version of the Morris water maze in which the location of the escape platform could be acquired in relation to multiple extra-maze cues (spatial strategy) or to a single proximal cue (S-R strategy). Relocating this proximal cue in a test trial 24 h later showed that rats that were stressed before learning used significantly more often an S-R learning strategy compared to control rats that were all using a spatial strategy. A similar shift from hippocampus-dependent spatial learning to dorsal striatum-dependent S-R learning was reported after fear reactivation (Hawley et al., 2013) or chronic stress (Schwabe et al., 2008). Interestingly, the relative use of hippocampal and dorsal striatal memory systems may even be “pre-programmed” by aversive experiences very early in life. For example, maternal ethanol consumption during pregnancy or maternal separation during the first weeks of life may bias learning toward the dorsal striatal habit system later in life (Sutherland et al., 2000; Grissom et al., 2012).

Acute stress and emotional arousal before learning changes the engaged learning strategy 24 h later (Kim et al., 2001) as well as immediately after learning (Schwabe et al., 2010a), suggesting that stress can affect how a task is acquired. In addition, however, stress may modulate the use of multiple memory systems also during retrieval, when task encoding is unaffected by stress or arousal. For instance, injecting an  $\alpha$ 2-adrenoceptor antagonist, an anxiogenic drug which leads to increased noradrenergic stimulation, after training in a dual-solution task and shortly before retention testing resulted in the same shift toward S-R memory that was seen when rats underwent a stressor before learning (Elliott and Packard, 2008), indicating that emotional arousal may not only affect the relative engagement of multiple memory systems during learning but also during memory retrieval.

The stress-induced shift from spatial to S-R learning appears to be due to a differential sensitivity of the hippocampus and dorsal striatum to stress and stress hormones. Several studies agree that stress, corticosterone, or increased noradrenergic activation impair the hippocampus-dependent system in spatial single-solution tasks (Wingard and Packard, 2008; Packard and Gabriele, 2009; Schwabe et al., 2010b). The effects of stress (hormones) on S-R learning are less clear. Noradrenergic arousal has been shown to enhance the consolidation of dorsal striatum-dependent S-R memories (Wingard and Packard, 2008; Packard and Gabriele, 2009). Stress or corticosterone, however, did not influence early S-R learning (Schwabe et al., 2010b). Thus, in contrast to the hippocampus-dependent system, the dorsal striatum-dependent system may be enhanced or at least remain unaffected by stress.

The effects of stress or emotional arousal on multiple memory systems seem to be mediated by the basolateral amygdala (McGaugh et al., 1996; McGaugh, 2002). Intra-basolateral amygdala injections of an  $\alpha$ 2-adrenoceptor antagonist were sufficient to enhance S-R learning and to impair spatial learning (Wingard and Packard, 2008). Conversely, inactivation of the basolateral amygdala blocked the effects of peripheral  $\alpha$ 2-adrenoceptor antagonist injections on hippocampus-dependent and dorsal striatum-dependent memory (Packard and Gabriele, 2009). Moreover, intra-amygdala injections of an  $\alpha$ 2-adrenoceptor antagonist before learning or recall in a dual-solution task was sufficient to bias memory toward the dorsal striatum-dependent S-R system (Packard and Wingard, 2004; Elliott and Packard, 2008).

Recent evidence suggests that this shift from spatial toward S-R memory after stress may be beneficial for memory performance. Pharmacological blockade of the MR prevented the stress-induced modulation of hippocampal and dorsal striatal memory systems in mice (Schwabe et al., 2010a). This finding demonstrates the critical role of glucocorticoids, and MR activation in particular, for the shift from hippocampal to dorsal striatal learning. However, the blockade of the shift toward dorsal striatum-based learning after stress was paralleled by significantly impaired performance. In addition, it was shown that stressed mice that used an S-R strategy performed comparable to non-stressed control mice, whereas stressed mice that kept using a spatial strategy were impaired both relative to controls and to stressed mice that shifted toward an S-R strategy.

Taken together, there is strong evidence that stress and emotional arousal favor dorsal striatum-dependent S-R memory over hippocampus-dependent spatial memory in rodents and this shift in the relative use of multiple memory systems may rescue performance after stress.

### **Stress and the Modulation of Hippocampal and Dorsal Striatal Memory: Human Studies**

Accumulating evidence indicates that stress may promote a shift from hippocampus-dependent to dorsal striatum-dependent memory in humans as well (Schwabe et al., 2010d; Schwabe and Wolf, 2013). The first study showing this modulatory influence of stress in humans used a dual-solution task

that was designed to parallel the key features of the cued-hidden platform water maze that was employed by Kim et al. (2001) in rats (Schwabe et al., 2007). Participants were trained to locate a “win-card” out of four cards in a three-dimensional model of a room. Same as in the cued water maze, multiple room cues and a single proximal cue allowed both spatial and S-R learning and a test trial, in which the proximal cue was relocated, revealed the used learning strategy (Fig. 1C). Choosing the card in the location where the win-card had been during training indicated spatial learning, whereas the choice of the card next to the novel location of the proximal cue reflected the use of an S-R strategy. Results showed that, compared to non-stressed control subjects, participants who underwent a psychosocial stressor before learning used significantly more often an S-R strategy. As in rodents, chronic stress or stressful experiences during critical periods of brain development in humans also led to a bias toward dorsal striatum-based learning (Schwabe et al., 2008, 2012a).

Glucocorticoids seem to play an important part in this hippocampus-to-dorsal-striatum shift in the control of learning. S-R learning was more likely in the face of high stress-induced cortisol responses (Schwabe et al., 2007). However, spatial learners were reported to have higher basal cortisol concentrations than S-R learners (Bohbot et al., 2011). Moreover, pharmacological elevations of cortisol concentrations shifted learning strategies also dose-dependently toward more spatial learning (Schwabe et al., 2009b). Although these studies used different approaches (e.g., behavioral stressor vs. pharmacological elevation of glucocorticoid concentrations), these findings appear contradictory and could suggest that there is no linear relationship between glucocorticoid levels and the relative use of multiple memory systems but perhaps rather a u-shaped glucocorticoid effect. It is assumed that the hippocampus dominates learning when glucocorticoid levels are low, at least during early stages of training (Packard and McGaugh, 1996; Kim et al., 2001). Moderate glucocorticoid levels may impair hippocampal functioning (Cousijn et al., 2012; Schwabe and Wolf, 2012) but leave the dorsal striatum intact (Schwabe and Wolf, 2012), thus allowing the latter to control learning. High glucocorticoid levels, however, might affect the functionality of both systems and hence restore the balance between the two systems, which allows the hippocampus to take over control again (Schwabe et al., 2009b). Alternative explanations for the reported effects of glucocorticoids on the engagement of multiple memory systems take the well-established role of noradrenergic arousal in glucocorticoid effects on memory (Roosendaal et al., 2006b) and the context-dependency of glucocorticoid actions on learning and memory (Joëls et al., 2006, 2011) into account.

Although most rodent and human studies examined the engagement of hippocampal and dorsal striatal memory systems in spatial navigation tasks, these two systems may also interact beyond spatial navigation. For example, converging evidence from neuropsychological and neuroimaging studies indicates that both the hippocampus and the dorsal striatum can contribute to probabilistic classification learning (Knowlton et al., 1994, 1996; Poldrack et al., 1999, 2001; Foerde et al.,

2006). Performance in such classification tasks has been shown to be sensitive to emotional manipulations (Steidl et al., 2006, 2011). Direct evidence for a modulatory effect of stress on the systems involved in classification learning was presented by a recent fMRI study (Schwabe and Wolf, 2012). Here, participants were exposed to a stressor before they performed the “weather prediction task” during which they learned how to classify stimuli into two categories (“sun” and “rain”) based on trial-by-trial feedback (Knowlton et al., 1994, 1996). Stress before learning did not alter classification performance. However, stressed participants had reduced explicit task knowledge and used more often procedural learning strategies compared to non-stressed control subjects, suggesting that stress promoted a shift from hippocampus-dependent declarative to dorsal striatum-dependent procedural learning. This conclusion was confirmed by the neuroimaging data. In control participants, classification performance correlated significantly with hippocampal activation. In stressed participants, however, activation of dorsal striatal regions was associated with performance. Hippocampal activation was reduced and even negatively correlated with performance after stress. This study demonstrated for the first time the stress-induced shift from hippocampus-based to dorsal striatum-based memory systems in the human brain. Furthermore, these data suggested that attempts to recruit the impaired hippocampal memory system after stress result in reduced performance.

Another recent study has not only replicated these findings but extended them significantly by providing some first insights into the neuroendocrine mechanisms underlying the influence of stress on the relative engagement of multiple memory systems in humans (Schwabe et al., in press). In order to assess the involvement of glucocorticoids, and the MR in particular, in stress effects on the use of hippocampal and dorsal striatal memory systems, participants were administered the MR antagonist spironolactone before stressor exposure and classification learning in the scanner. In line with the previous rodent data (Schwabe et al., 2010a), MR blockade prevented the stress-induced shift toward dorsal striatum-dependent learning and resulted in impaired classification performance. These findings provide further striking evidence for a role of glucocorticoids in the modulation of multiple memory systems after stress. Moreover, functional connectivity analyses revealed that stress increased amygdala connectivity with the dorsal striatum but decreased amygdala connectivity with the hippocampus, indicating that the amygdala may orchestrate the engagement of multiple memory systems after stress in humans.

## A MODEL

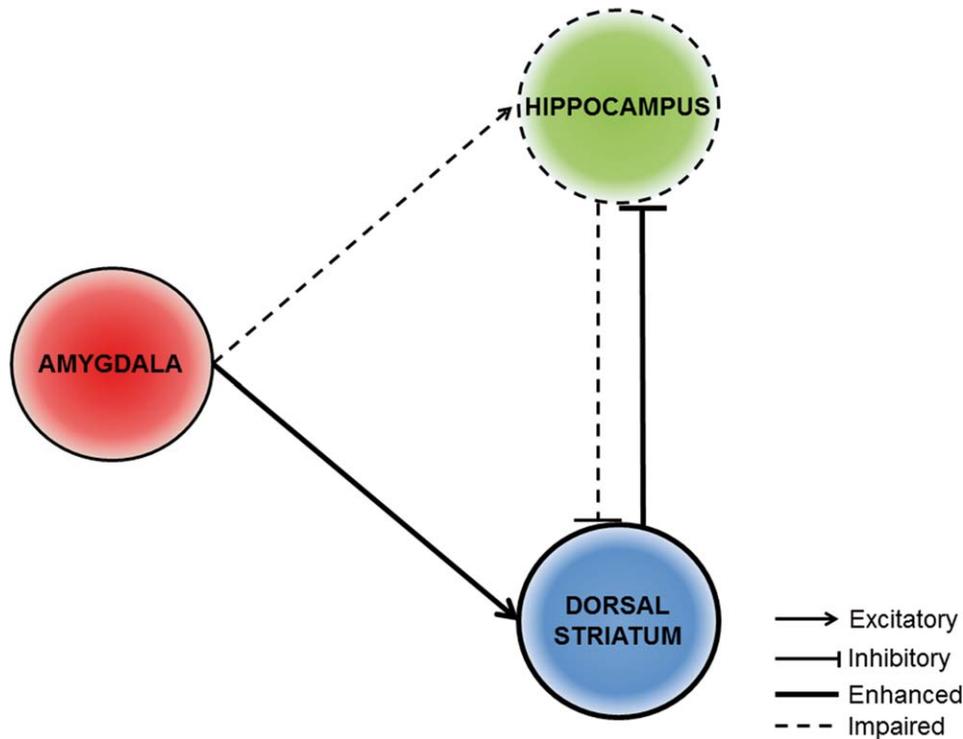
The hippocampus is one of the relatively few brain regions in which MRs and GRs are co-localized at high densities (Reul and de Kloet, 1985; Joëls and Baram, 2009), suggesting that this area is particularly sensitive to stress and glucocorticoids.

Indeed, there is good evidence from neurophysiological, neuroimaging, and behavioral studies that hippocampal activity and functionality are affected by stress. Although stress is thought to enhance hippocampus-dependent memory processes when stress is part of the learning experience or occurs around the time of learning (Sandi et al., 1997; Joëls et al., 2006; Diamond et al., 2007), stress or glucocorticoids out of the learning context impair hippocampal neuroplasticity (Kim et al., 2001; Wiegert et al., 2006; Diamond et al., 2007), hippocampal activation (de Quervain et al., 2003; Schwabe and Wolf, 2012), and hippocampus-dependent learning and memory processes (Kim et al., 2001; Diamond et al., 2006; Schwabe et al., 2009a). In contrast to the hippocampus, the dorsal striatum has long been assumed to be more or less unaffected by stress. In the last few years, however, it was repeatedly reported that the dorsal striatum may be influenced by stress and stress hormones as well. For instance, injections of glucocorticoids or  $\alpha$ 2-adrenoceptor antagonists before or shortly after learning have been shown to facilitate dorsal striatum-dependent memory processes (Wingard and Packard, 2008; Packard and Gabriele, 2009; Quirarte et al., 2009).

Stress-induced alterations in the functionality of hippocampus and dorsal striatum will most likely affect the interplay of these memory systems. It has been shown that hippocampal inactivation enhances dorsal striatum-dependent learning (Packard et al., 1989; Schroeder et al., 2002) and, conversely, that disruption of the dorsal striatum strengthens hippocampus-dependent learning (Mitchell and Hall, 1988). These findings point to inhibitory connections between hippocampus and dorsal striatum. Moreover, injections of glutamate into the hippocampus prevented the practice-related shift toward S-R memory, whereas intra-caudate glutamate injections accelerated this shift (Packard, 1999), indicating that strengthening of one system may hamper the other. Thus, stress-induced impairments of the hippocampal system should reduce its inhibitory influence on the dorsal striatum. At the same time, stress-induced enhancements of the dorsal striatum should increase its inhibitory effect on the hippocampus.

Both rodent and human data suggest that stress effects on multiple memory systems are mediated by the amygdala. Amygdala lesion or inactivation abolished stress (hormone) effects on hippocampus and dorsal striatum in rats (Roosendaal et al., 2006b; Wingard and Packard, 2008; Packard and Gabriele, 2009). Moreover, intra-amygdala injections of an  $\alpha$ 2-adrenoceptor antagonist were sufficient to prompt the stress-induced shift toward dorsal striatum-based learning (Packard and Wingard, 2004). In humans, stress increased amygdala-dorsal striatum coupling but decreased amygdala-hippocampus coupling (Schwabe et al., in press). MR blockade prevented both these stress-induced alterations in amygdala connectivity with hippocampus and dorsal striatum and the shift from hippocampal to dorsal striatal memory, which suggests that the modulatory influence of the amygdala may even be necessary for the shift in the engagement of multiple memory systems.

Based on these considerations, it is proposed that the stress-induced modulation of the engagement of hippocampal and



**FIGURE 2.** Proposed model of how stress changes the engagement of hippocampal and dorsal striatal memory systems. Hormones and neurotransmitters that are released during stressful experiences impair the hippocampus-dependent system and reduce its inhibition of the dorsal striatum. At the same time, stress may enhance the dorsal striatum-dependent system and its inhibitory

control of the hippocampal system. The amygdala mediates stress effects on both memory systems and orchestrates the engagement of these two through altered coupling with the hippocampus and dorsal striatum, respectively. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

dorsal striatal memory systems involves, at least, two mechanisms (Fig. 2):

1. Stress hormones exert differential, perhaps even opposite effects on the hippocampus and dorsal striatum which leads to a relative strengthening of the dorsal striatal system and to a relative impairment of the hippocampal system. These changes in the relative strength of the two memory systems reduce the inhibitory influence of the hippocampus on the dorsal striatum and, at the same time, increase the inhibition of the hippocampus by the dorsal striatum.
2. Stress modulates the connectivity of the amygdala with the hippocampus and dorsal striatum. The amygdala acts as a conductor that orchestrates the engagement of multiple memory systems and favors the dorsal striatum-dependent system after stress.

The endocrine and cellular mechanisms involved in the impact of stress on the relative use of multiple memory systems are not entirely clear yet. Converging evidence from human and rodent studies indicates that glucocorticoids play a part and that their effects are mediated by the MR (Schwabe et al., 2010a, in press). Because stress effects on the engagement of multiple memory systems occur relatively quickly after the stressor and intracellular MRs are already saturated by basal glucocorticoid levels (Reul and de Kloet, 1985; Ariza et al.,

1988), it appears reasonable to assume an involvement of low-affinity, membrane-bound MRs, which allow rapid, non-genomic glucocorticoid actions (Joëls et al., 2008) and are present in the amygdala (Karst et al., 2010). In addition to glucocorticoids, findings from rodent studies point also to an important role of noradrenergic activity in the modulation of multiple memory systems (Packard and Wingard, 2004; Elliott and Packard, 2008). For stress effects on single memory systems, it is well documented that glucocorticoids interact with noradrenaline in the basolateral amygdala which then modulates memory processes in other brain regions such as the hippocampus or prefrontal cortex (Roosendaal et al., 2006b, 2009). However, whether such glucocorticoid-noradrenaline interactions are also critical for changes in the relative use of multiple memory systems remains to be tested.

## CONCLUSIONS

Stress may affect a broad range of cognitive functions, including learning and memory (Lupien et al., 2009; Joëls et al., 2011; Schwabe et al., 2012b). The findings reviewed in this article indicate that stress can not only modulate the

performance of single memory systems, but that stress may also orchestrate the engagement of multiple memory systems. In particular, it has been shown that stress and stress hormones promote a shift from hippocampus-dependent to dorsal striatum-dependent memory. It is argued that this shift is owing to (i) differential effects of stress hormones on hippocampus and dorsal striatum and (ii) a modulatory influence of the amygdala which becomes more strongly connected to the dorsal striatum and less connected to the hippocampus after stress.

The modulatory effect of stress on the relative use of multiple memory systems is not limited to the hippocampus and the dorsal striatum. For example, instrumental action can be controlled by a “goal-directed” system that is based on the prefrontal cortex and dorsomedial striatum and a habit system that is primarily supported by the dorsolateral striatum (Balleine and Dickinson, 1998; Yin et al., 2005, 2006; Valentin et al., 2007; Tricomi et al., 2009). Recent studies in rodents and humans demonstrate that stress before instrumental learning favors the habit system, at the expense of the goal-directed system (Dias-Ferreira et al., 2009; Schwabe and Wolf, 2009; Gourley et al., 2012), and that this shift toward the habit system requires concurrent glucocorticoid and noradrenergic activity (Schwabe et al., 2010c, 2011). Together with the evidence reviewed here, these findings suggest that stress favors rather simple but more rigid habit learning over flexible but cognitively demanding cognitive learning. The aberrant engagement of habit processes has been related to psychiatric disorders such as addiction or posttraumatic stress disorder (Everitt and Robbins, 2005; Goodman et al., 2012), and many of these are characterized by dysfunctional stress responses (McFarlane et al., 1997; Bremner et al., 2003; Koob and Le Moal, 2008). Understanding how the stress-induced bias toward habit memory may contribute to such disorders and, more generally, how exactly stress biases the engagement of distinct memory systems are challenges for future research on multiple memory systems.

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