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Habits under stress: mechanistic insights across different types of learning

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Learning can be controlled by reflective, 'cognitive' or reflexive, 'habitual' systems. An essential question is what factors determine which system governs behavior. Here we review recent evidence from navigation, classification, and instrumental learning, demonstrating that stressful events induce a shift from cognitive to habitual control of learning. We propose that this shift, mediated by noradrenaline and glucocorticoids acting through mineralocorticoid receptors, is orchestrated by the amygdala. Although generally adaptive for coping with acute stress, the bias toward habits comes at the cost of reduced flexibility of learning and may ultimately contribute to stress-related psychopathologies.

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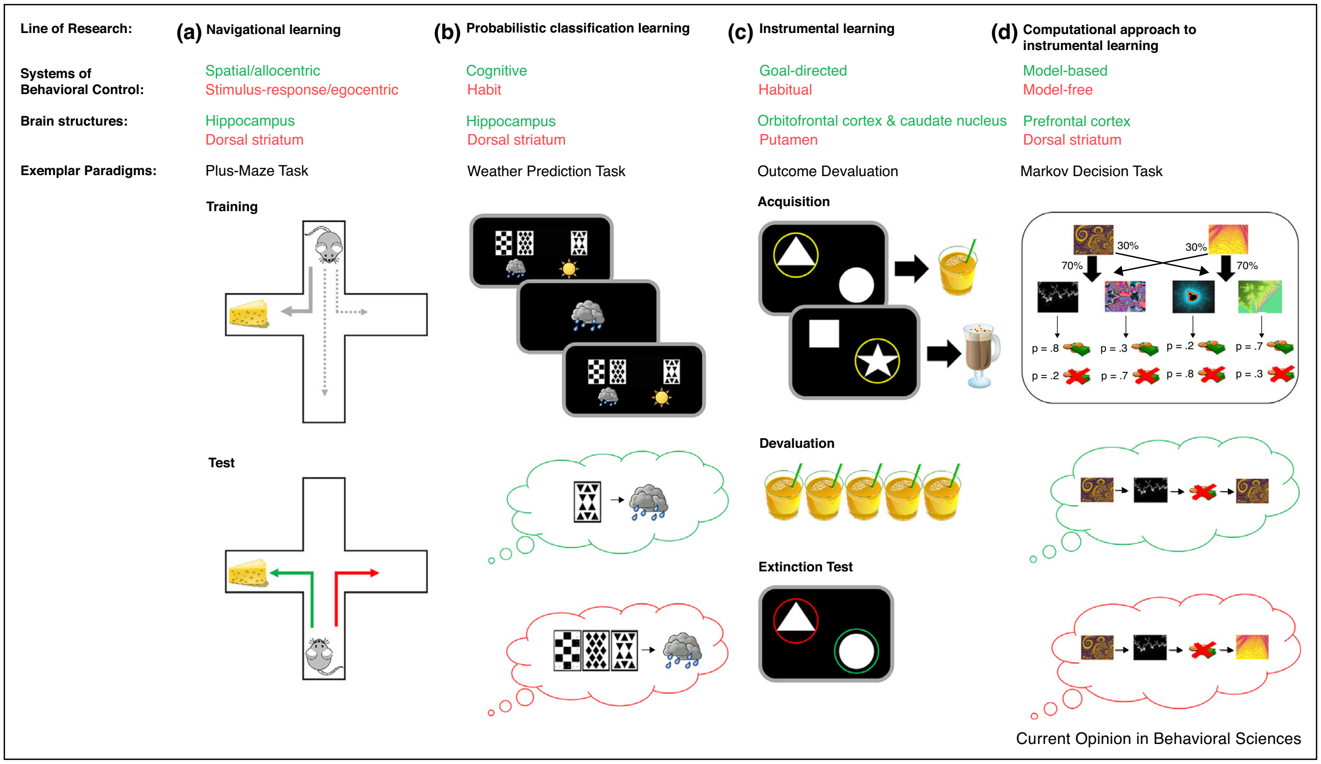
Introduction

Adaptive behavior requires an intricate balance of thoughtful processing and efficient responding. Whereas the deliberate evaluation of our environment enables behavioral flexibility, crystallizing repeatedly successful actions into habits promotes behavioral autonomy that frees up cognitive resources. The idea that behavior can be controlled by more reflective or more reflexive processes is shared by several lines of scientific inquiry (Figure 1). Research on navigational learning, dating back to early work of Edward Tolman [1], distinguished between a hippocampus-dependent spatial ('cognitive') memory system that uses the relationship between multiple cues in the environment to build a 'cognitive map' and a dorsal striatum-dependent stimulus-response (S-R; 'habit') memory system that learns associations between responses and single stimuli [2–4] (Figure 1a). Inspired by neuropsychological data, a similar distinction was made between a hippocampus-dependent 'cognitive' system and a dorsal-striatum-dependent 'habit' system in probabilistic classification learning [5] (Figure 1b). A parallel strand of research in instrumental learning developed a set of elegant paradigms, allowing the experimental dissociation of goal-directed learning that processes the causal relationship between an action and its consequences, and habitual learning that associates responses with the preceding stimuli without links to the consequences [6] (Figure 1c). Although originally studied in rodents, these modes of instrumental control were shown in humans as well. Corroborating previous lesion data in rodents, these human studies identified the orbitofrontal cortex and dorsomedial striatum as key regions for goal-directed action and the dorsolateral striatum as a locus of habitual responding [7,8]. Most recently, the concepts of goal-directed and habitual behavior were further developed by computational models suggesting a distinction between model-based and model-free learning [9,10] (Figure 1d). Model-based control, dependent on prefrontal cortex (PFC) areas, is characterized by a collection of flexible but complex strategies which build an internal model of the environment that aids future planning of actions and their potential outcomes. The dorsal striatum-dependent model-free system involves inflexible and rigid strategies that are driven solely by past outcomes. Specifically, in model-based learning approaches, participants use the task structure to maximize their rewards, whereas in model-free learning, choices are guided by recent experiences instead of the overall task structure.

While these different research traditions are only partly overlapping and important differences exist (e.g. with respect to the operational definition of a habit or to the neural underpinnings of the two modes of behavioral control, in particular the involvement of the dorsolateral versus dorsomedial striatum in habitual forms of behavior; [7,11,12]) a key question for all of these conceptualizations is how the 'cognitive' and 'habit' systems are coordinated. In other words, what factors determine which system may dominate behavior? Overtraining and dual-tasking are known to bias behavior toward the 'habit system' [13,14]. In addition, there is accumulating evidence that stress may be a factor that critically modulates the balance of 'cognitive' and 'habit' behavior, putatively by accelerating the shift that would otherwise occur after extensive practice [15••]. Stressful events are known to influence a broad range of cognitive functions, including attention, memory and decision-making [16–18]. These stress effects are mediated through the actions of

Figure 1



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Different lines of research on reflective versus reflexive systems. **(a)** In *navigational learning*, a distinction is made between hippocampus-dependent spatial or allocentric learning and dorsal striatum-dependent stimulus-response (S-R) or egocentric learning. These types of learning can be separated in a plus maze task, in which the animal starts from the north arm during training but from the south arm at test. Moving to the spatial location where a reward had been during training indicates flexible spatial or allocentric learning, whereas simply repeating the same movement performed during training (i.e. turning right at the intersection) is indicative of rather rigid egocentric learning. **(b)** *Probabilistic classification learning* can also be guided by a hippocampus-dependent, cognitive system or a dorsal striatum-dependent, habit system. The engagement of these systems is reflected in the use of either explicit learning strategies (focusing on single cues) or rather implicit strategies (focusing on cue patterns) in tasks such as the weather prediction task, in which participants learn how to classify stimuli into categories based on (probabilistic) trial-by-trial feedback. **(c)** *Instrumental learning* can be controlled by a goal-directed system that is supported by the orbitofrontal cortex and caudate nucleus or by a habit system subserved by the putamen. The contributions of these systems can be tested in an outcome devaluation paradigm, in which goal-directed learning would be sensitive and habit learning insensitive to changes in the motivational value of the outcome (e.g. due to satiation with the specific food outcome). **(d)** The computational analog of goal-directed learning is model-based learning, whereas the analog of habit learning is model-free learning. These systems can be dissociated, for example, in a Markov decision task with multiple decision states. In this task, outcomes are partly probabilistic and partly under the control of the individual. Participants that use a model-based learning approach employ the task structure to maximize their rewards. In participants using simpler model-free learning, in turn, choices are guided by recent experiences rather than the overall task structure. Processes, brain structures and task solutions associated with the more cognitive, reflective systems are indicated in green, while those linked to the more habitual, reflective systems are indicated in red.

neurotransmitters and hormones, such as noradrenaline and glucocorticoids (mainly cortisol in humans). In particular, noradrenaline, released within seconds after a stressful event from noradrenergic brain stem nuclei and the adrenal medulla, triggers a reorientation of large scale networks toward the processing of salient stimuli, at the expense of executive control processes [19]. Cortisol, acting via brain glucocorticoid (GRs) and mineralocorticoid receptors (MRs), initially enhances and later reverses the effects of noradrenaline [20].

Here, we review recent evidence showing that stress may modulate the preferential engagement of 'cognitive' and 'habitual' systems in different domains of learning and memory, ranging from navigational and classification to instrumental learning. We will argue that stressful events promote, mediated through the actions of noradrenaline and glucocorticoids, a shift from flexible 'cognitive' toward more rigid 'habit' behavior. The implications of this shift will be briefly discussed.

'Cognitive' versus 'habit' learning under stress

First evidence for a stress-induced shift from 'cognitive' toward 'habitual' memory came from a study showing that rats that were stressed before a cued-water maze task used a dorsal striatum-dependent S-R learning strategy more and a hippocampus-dependent spatial strategy less often than non-stressed rats [21]. These findings were translated to humans in a study using a spatial dual-solution task. In this task, participants could acquire the location of a win-card either by learning that it was always next to a proximal cue (S-R) or by learning the spatial position relative to other cues inside the room (spatial). Following a psychosocial stressor, participants used S-R strategies significantly more and spatial strategies significantly less often compared to non-stressed controls [22]. Recently, this stress-induced bias toward S-R learning was replicated in a virtual navigation task [23]. Following stress, participants predominantly relied on landmark cues indicating S-R learning, as opposed to boundary cues reflecting spatial learning. In addition to navigation tasks, the preferential engagement of hippocampal or dorsal striatal learning strategies can be assessed in probabilistic classification tasks in which participants are required to categorize stimuli based on trial-by-trial feedback [5] (Figure 1b). In these tasks as well, stress favored dorsal striatal over hippocampal learning [24,25]. Using functional magnetic resonance imaging (fMRI), it was shown for the first time that stress may actually change learning from hippocampal to dorsal striatal control in the human brain [24]. Subsequent studies replicated these findings [20,34••]. Together, they demonstrate that stress induces a shift from a hippocampal system required for flexible and integrative learning [3,26], toward a dorsal striatal system implicated in more reflexive learning [4]. Interestingly, this effect was also observed after chronic stress or stress during critical periods of brain development [27,28]. For instance, prenatal stress led, in healthy individuals, to a preferential engagement of dorsal striatal learning strategies in adulthood [29].

Goal-directed action versus habitual responding under stress

After demonstration of a stress-induced modulation of hippocampal 'cognitive' and dorsal striatal 'habit' learning in navigation, it was hypothesized that stress might also affect the balance of goal-directed and habitual processes in instrumental learning tasks in which habits can be assessed by an outcome devaluation procedure, a canonical assay to dissociate goal-directed versus habitual processes (Figure 1c). Indeed, research has mainly confirmed this prediction. Participants that were stressed before learning became insensitive to changes in outcome value, which indicates habitual responding [30]. Likewise, rats exposed to stress before outcome devaluation showed a shift toward habitual behavior [31]. Another study found a very similar shift from goal-directed toward habitual behavior when stress was administered after outcome devaluation, before the critical extinction test (thus ruling out effects on initial task acquisition; [32]). These findings suggest that stress mainly affects the flexible adaptation of behavior after alterations in outcome value. Recent data suggest that this reduced behavioral flexibility is mainly due to impaired goal-directed control, since performance on trials dependent only on the habit system was unimpaired [33]. Similarly to hippocampal versus dorsal striatal learning, control of instrumental behavior was also affected by chronic and early life stress, both of which resulted in more habitual responding [34••,35]. The bias toward habitual responding after prolonged stress was accompanied by opposite structural and functional changes in the medial PFC and the putamen [36].

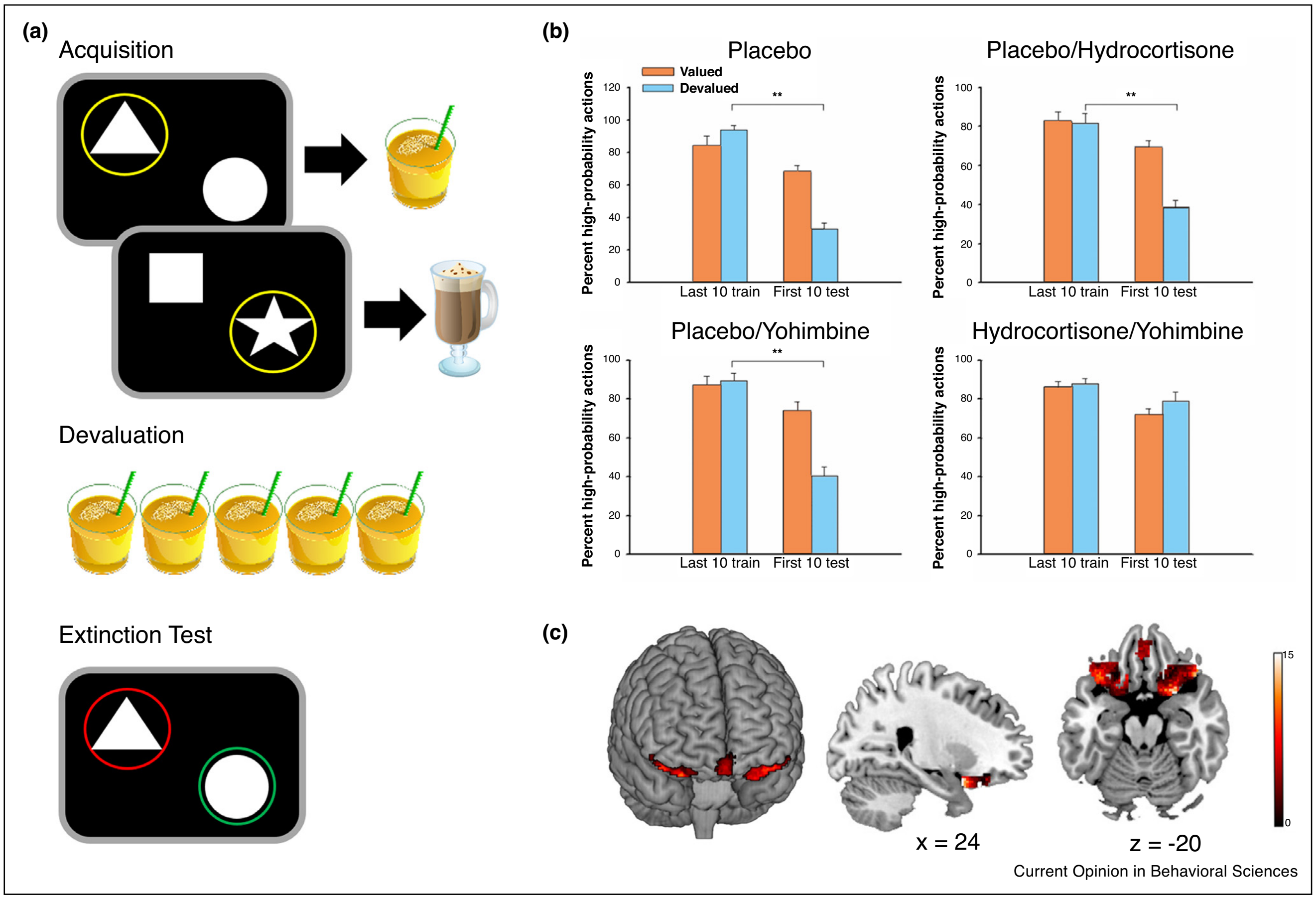
These findings, suggesting that stress favors habit learning at the cost of goal-directed learning, were extended by the latest 'generation' investigating reflective versus reflective forms of behavior, focusing on model-based and model-free reinforcement learning [10] (Figure 1d). Specifically, acute stress has been shown to decrease model-based contributions to behavior, particularly in participants with low working memory capacity or high chronic stress level [37,38].

Stress and the shift from reflective to reflexive behavior: mechanistic insights

As outlined above, there is strong evidence indicating that stress modulates the balance of cognitive and habitual forms of learning and memory. Across species, tasks, and types of learning, stress led to a shift from cognitively demanding forms of learning, including spatial and goal-directed learning, toward habitual forms of learning. The parallels across domains are striking and recent research targeting the neuroendocrine basis of the stress-induced bias toward habit behavior points to a common mechanism underlying the impact of stress on behavioral control.

Using fMRI, two studies reported that stress may decrease hippocampal activity during probabilistic classification learning [24,25] and another recent study found evidence for increased dorsal striatal activity after stress [39••]. Beyond the direct modulation of the systems supporting cognitive and habit learning, several studies showed a stress-induced modulation of the connectivity of these systems with the amygdala. Specifically, stress resulted in increased amygdala-dorsal striatum and reduced amygdala-hippocampus connectivity [23,25,39••,40]. These data suggest a critical role of the amygdala in the stress-induced modulation of hippocampal and dorsal striatal learning, in line with prior animal data showing that injections of anxiogenic drugs directly into the amygdala are sufficient to produce the stress-induced shift toward habit learning [12]. Together, these findings point to a critical role of noradrenergic arousal in the amygdala for the stress-induced shift toward habit learning. In support of a role of noradrenaline, a recent human neuroimaging study showed that a deletion variant of the gene coding for the α2b-adrenoceptor modulated the stress-induced shift toward dorsal striatum-dependent habitual learning and affected the

Figure 2



Concurrent glucocorticoid and noradrenergic activity impairs goal-directed action. **(a)** Participants received either a placebo, hydrocortisone, yohimbine, an α2-adrenoceptor antagonist leading to increased noradrenergic stimulation, or both drugs before the acquisition of two instrumental actions leading to distinct food outcomes. After acquisition, one of the food outcomes was devalued (by satiation with that specific food) and the sensitivity to the change in outcome value was tested in an extinction test. **(b)** Results showed that participants who received either hydrocortisone or yohimbine acted, same as those that had received a placebo, in a goal-directed manner as reflected in a sharp decrease in the choice of the action that led to the now devalued outcome. However, participants that had received both hydrocortisone and yohimbine were insensitive to the change in outcome value, which indicates habitual behavior. **(c)** Functional magnetic resonance imaging showed that this effect of concurrent glucocorticoid and noradrenergic was paralleled by a decrease in orbitofrontal and medial prefrontal areas, those regions that support goal-directed action.
Adapted from [46].

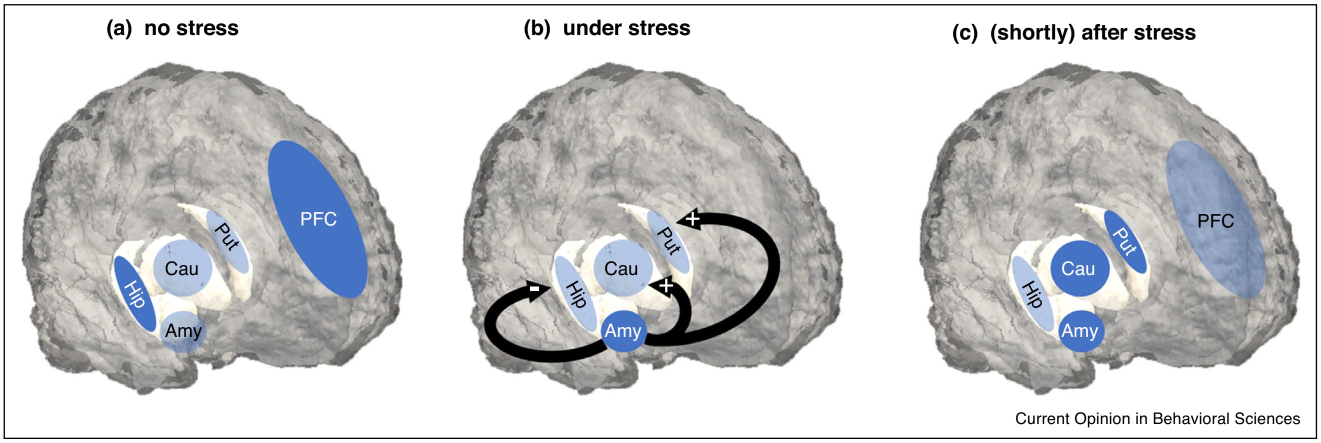
connectivity of the amygdala with the hippocampus and dorsal striatum [39••].

In addition to noradrenaline, there is strong evidence for a critical involvement of glucocorticoids in the stress-induced shift toward habit learning. A recent study in rodents showed that glucocorticoid injections into the dorsolateral but not dorsomedial striatum following training in a spatial maze task accelerated the training-dependent shift toward S-R learning [40]. This finding suggests that, similarly to instrumental learning tasks investigating goal-directed versus habitual learning, it is the dorsolateral striatum (putamen in humans) that is critical for stress-induced increases in habit learning. In addition, glucocorticoid administration was sufficient to shift learning toward habits and the pharmacological blockade of the MR prevented the stress-induced bias toward habit learning in mice [41]. The MR-dependency of the shift from hippocampal to dorsal-striatal learning after stress was confirmed in humans [23,25]. Although glucocorticoids may exert direct effects on hippocampal and striatal functioning [42,43], these studies showed that it were specifically the effects of stress on amygdala crosstalk with the hippocampus and the dorsal striatum that were abolished by an MR antagonist, suggesting that amygdalar MRs might be essential for the shift to dorsal striatal learning. Thus, noradrenergic and glucocorticoid activity (via the MR) in the amygdala appear to be key mechanisms for the stress-induced bias toward habitual behavior in navigation and classification tasks. However, whether noradrenaline and glucocorticoids do indeed interact in the amygdala to modulate the preferential engagement of multiple memory systems, as established for stress effects on memory consolidation and retrieval [18], remains to be shown.

Direct evidence for interactive effects of glucocorticoids and noradrenaline on behavioral control comes from pharmacological studies that investigated the role of glucocorticoids and noradrenaline in the balance of goal-directed and habitual instrumental learning. Administration of both hydrocortisone and yohimbine, but not of either drug alone, resulted in a significant insensitivity to outcome devaluation, that is, habitual performance [44]. While these data showed that the simultaneous activity of glucocorticoids and noradrenaline is sufficient to bias instrumental control toward habitual responding, another study showed that the stress-induced shift toward habit behavior was prevented by the administration of a β-adrenergic antagonist, suggesting that noradrenergic activity is necessary for stress effects on instrumental behavior [45]. Moreover, stress-induced cortisol was found to be directly correlated with the extent of habitual behavior. A subsequent neuroimaging study confirmed that the simultaneous activity of noradrenaline and glucocorticoids renders instrumental behavior habitual and further revealed that this interactive effect was associated with reduced activity of medial prefrontal and orbitofrontal areas [46], those areas that subserve goal-directed action [7] (Figure 2a–c). Together, these studies indicate that the stress-induced bias toward habit behavior is owing to the interactive actions of glucocorticoids and noradrenaline, resulting in an impairment of the goal-directed system. Although there is first evidence for a role of the GR in the effect of chronic stress on instrumental action [47], whether the GR mediates the rapid effects of acute stress on the balance of goal-directed and habit behavior is still unknown.

In sum, converging evidence from navigational, classification, and instrumental learning indicates that, firstly, glucocorticoids and noradrenaline are critically involved in the stress-induced shift from cognitive to habitual forms of learning and that, secondly, stress interferes in particular with systems supporting the cognitive control of learning (i.e. medial temporal and prefrontal areas). At least in navigational and classification learning, there is strong evidence that the amygdala orchestrates learning and memory systems in favor of habitual systems and at the cost of cognitive systems. Given the timescale of these stress effects, usually within 20–30 min, we further propose that glucocorticoids exert their actions through binding to membrane-associated MRs, which allow for rapid, non-genomic glucocorticoid actions [20]. These rapid glucocorticoid effects most likely act synergistically with noradrenergic activity in the amygdala [20], the recruitment of which is facilitated by large-scale reorganizations of brain networks in favor of the salience network [19,48,49]. The amygdala appears to exert an inhibitory influence on cognitive systems, thus enabling the habitual systems to dominate behavior (Figure 3).

Figure 3



Model of stress-induced changes in brain systems underlying flexible cognitive and efficient habitual learning and memory. **(a)** In non-stressful situations, learning and memory can be guided by the prefrontal cortex (PFC) and the hippocampus (Hip), enabling flexible, goal-directed learning. **(b)** Under acute stress, noradrenergic and glucocorticoid activity promote a shift from 'cognitive' to 'habit' learning that is orchestrated by the amygdala (Amy) which facilitates dorsal striatal (Put-putamen, Cau-caudate nucleus) processing but hampers hippocampal (and most likely also prefrontal) processing. **(c)** As a consequence, behavior is dominated by the dorsal striatum, at the cost of prefrontal and hippocampal areas, in the aftermath of a stressful encounter. Differences in color intensity represent proposed changes in the strength of the respective systems.

Habitual behavior under stress: from adaptation to risk

The distinction between cognitive and habitual processes is highly relevant in several cognitive domains, including attention or decision-making [50••,51••]. Although we focused here on multiple systems in learning and memory and stress effects on reflective versus reflexive processes in other cognitive domains are less well studied, we propose that there is a general mechanism that favors well established habits and routines over flexible but cognitively demanding processes under stress [52]. This shift may be highly adaptive, as it helps the organism to save cognitive resources and avoid hesitations or delays during threatening situations [53]. Indeed, there is direct evidence showing that the shift toward habitual learning is beneficial for performance under stress, whereas cognitive learning in the face of stress impairs performance [24,41]. While being generally adaptive, the shift toward habitual learning under stress comes at a cost. It may result in rather rigid, inflexible memories that are difficult to generalize to novel situations or to link to existing knowledge structures [54••,55,56]. Thus, the ability to shift back and forth between cognitive and habitual forms of behavioral control, depending on the environmental demands, is crucial. Lack of this ability may ultimately promote the development of mental disorders, such as post-traumatic stress disorder, as well as the relapse to maladaptive behaviors in addiction or obsessive-compulsive disorders, both of which can be triggered by stressful events [57–60]. Elucidating the mechanisms involved in the stress-induced shift from cognitive to habitual behavior may hence aid our understanding of these disorders and eventually the development of new treatment opportunities.

Conflict of interest statement

Nothing declared.

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Using a cross maze task in which rats were trained to find a reward, this study provides evidence for differential roles of the dorsolateral and dorsomedial striatum in the impact of glucocorticoids on spatial versus S-R memory. Specifically, posttraining infusion of corticosterone into the dorsolateral striatum led to an accelerated shift toward S-R strategies, whereas a similar infusion into the dorsomedial striatum had no such effect. These findings indicate that it is specifically the dorsolateral part of the striatum that is critical for the impact of glucocorticoids on the preferential engagement of spatial versus S-R memory processes.

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