Stress impairs decision-making in rats

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Stress influences various types of memory, but its effects on other cognitive functions are relatively unknown. We investigated the effects of uncontrollable stress on subsequent decision-making in rats, using a computer vision-based water foraging choice task. Stress impaired the animals' ability to bias their responses toward the larger reward when transitioning from equal to unequal quantities, and this stress effect was dependent on the amygdala.

It is now well documented that stress, a biologically significant and pervasive environmental factor, can produce alterations in brain-memory systems[1,2]. In humans, impairments in verbal recall tasks have been observed in posttraumatic stress disorder patients[3], and in healthy individuals exposed to stress[4]. In rodents, stress impedes spatial[5] memory, while potentiating aversive conditioning[6,7]. Further, various stress-associated neurobiological changes have been identified in brain structures (e.g., hippocampus[1,2], medial prefrontal cortex[8], amygdala[9]) subserving memory functions.

Although stress effects on memory have been extensively studied, far less is known about whether (and in what manner) stress influences other cognitive functions. The present study investigated the effects of acute, uncontrollable stress on subsequent decision-making performance in rats. Decision-making was assessed using an automated Figure-8 maze in which rats were motivated to forage for water rewards in two different locations under equal and unequal quantity conditions (**Fig. 1)**. Detailed methods are provided in **Supplementary Methods** online.

Rats readily learned to forage for water, and when left (L) and right (R) sides of the maze provided equal quantity and probability (0.04 ml, 80%) of water, animals made comparable numbers of L/R visits that were stable across three baseline days (**Fig. 2a**). When the reward volume on one side only was tripled (0.12 ml, 80%), unstressed ('control') animals readily made more visits to the larger reward. In contrast, ('stress') rats that experienced 60 min restraint+60 intermittent tailshocks on the previous day displayed a slower rate of bias toward the larger reward than did the controls ($P = .007$). Although stress rats eventually showed a reliable bias toward the larger reward by the fourth day of bias testing ($P = .006$), even after six days, their bias (132 ± 7.2%, means ± s.e.m.) did not reach the level of controls' third day bias (181 ± 12.5%). Animals that received daily corticosterone ('CORT') injections prior to testing chose the larger reward more frequently (173 ± 6.7%, Bias day 3), and did not differ from the controls ($P > .9$). Animals with their amygdalae inactivated during stress ('AMYG'), via infusions of the $GABA_A$ receptor agonist muscimol (**Supplementary Fig. 1**), behaved like controls ($P > .9$) and visited the larger reward more frequently (174 ± 13.0%, Bias day 3).

We then examined whether stress altered motor, motivation or reference memory that hindered the ability to bias responses toward the larger reward. The latency to complete the first bias test (**Fig. 2b**) showed a trend of stress animals finishing faster than the other groups ($P = .154$). Stress also did not impair the animals' reference memory: after making a L or R choice, stressed animals readily re-entered the center runway to start the next trial, whereas other groups more often investigated the other side before re-entering the center runway, particularly as bias testing progressed ($P = .032$, group x day; **Supplementary Fig. 2a**).

Our results indicate that rats clearly demonstrate the capacity to change their foraging behavior to acquire a larger reward, and that such decision-making is vulnerable to stress. This effect was not due to any lingering post-stress motivational or motor effects, as the latency to complete the bias test did not differ between stress and control rats. Daily corticosterone injections did not interfere with this task, indicating that corticosterone elevation alone cannot reproduce behavioral stress effects on decision-making. Similar to previous stress-memory studies[2,6], amygdalar inactivation effectively blocked stress effects on decision-making. This suggests that the amygdala plays a crucial role in mediating stress effects across different cognitive domains.

Although stress might have directly affected the brain systems underlying decision-making, thus altering ensuing behavior, alternate possibilities should be considered. For instance, the impairment of decision-making might be a consequence of stress effects on spatial working memory. The stress paradigm used here is known to alter hippocampal synaptic plasticity[2] and hinder spatial memory[5]. Therefore, contributions of stress-associated changes in learning cannot be excluded. Another possibility is that the "prudent" foraging behavior after stress is to maintain habitual behavior even if deviation may result in higher benefit. The fact that stressed rats less frequently investigated other parts of the maze is consistent with this explanation. The evolutionary history of the animal in foraging behavior[10] is clearly a crucial factor to be considered with regard to decision-making and adaptive behavioral responses to stress. It is also possible that stress disrupted the reward circuitry and impaired the ability to discriminate between the two reward values **(Supplementary Fig. 2b)**, in which case stress effects on a dopamine-related reward circuit[11] need to be explored.

If acute, uncontrollable stress influences subsequent decision-making, what is the neural basis for this effect? To address this, future studies need to investigate brain structures implicated in decision-making, including the prefrontal and the parietal cortices[12], for their susceptibility to stress. Regardless, the present findings, to our knowledge, provide the first direct evidence that uncontrollable stress impairs decision-making performance in rats and that this effect is dependent upon amygdalar activity during stress.

References

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Figure legends

Figure 1. Decision-making task. (a) Rats were trained to forage for water on a figure-eight maze. A computer algorithm controlled the four gates (rectangles) and water delivery (blue circles), while tracking the animal's location. During baseline testing, left and right rewards were equal in volume (V) and probability (P). During bias testing, one reward (counterbalanced) was increased in volume relative to the other reward. (b) Example visit maps of rats during baseline, control and stress conditions (40 laps each).

Figure 2. Stress and decision-making. (a) All groups showed comparable visits to left and right rewards during baseline testing. When transitioning from equal to unequal reward trials, stressed rats (n = 7) displayed an impaired ability to bias their responses toward the larger reward side compared to control (n = 10), AMYG (n = 7) and CORT (n = 7) rats, $F_{6,54} = 4.142$, $P = .002$, group x bias day interaction. (b) During bias testing, all groups took similar latencies to complete the 40 laps.

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Author contributions

J.J.K., L.K.J., and T.Y. designed research; L.K.J., T.Y., and J.J.K. performed research; L.K.J., T.Y., and J.J.K. analyzed data; and J.J.K. and L.K.J. wrote the paper.

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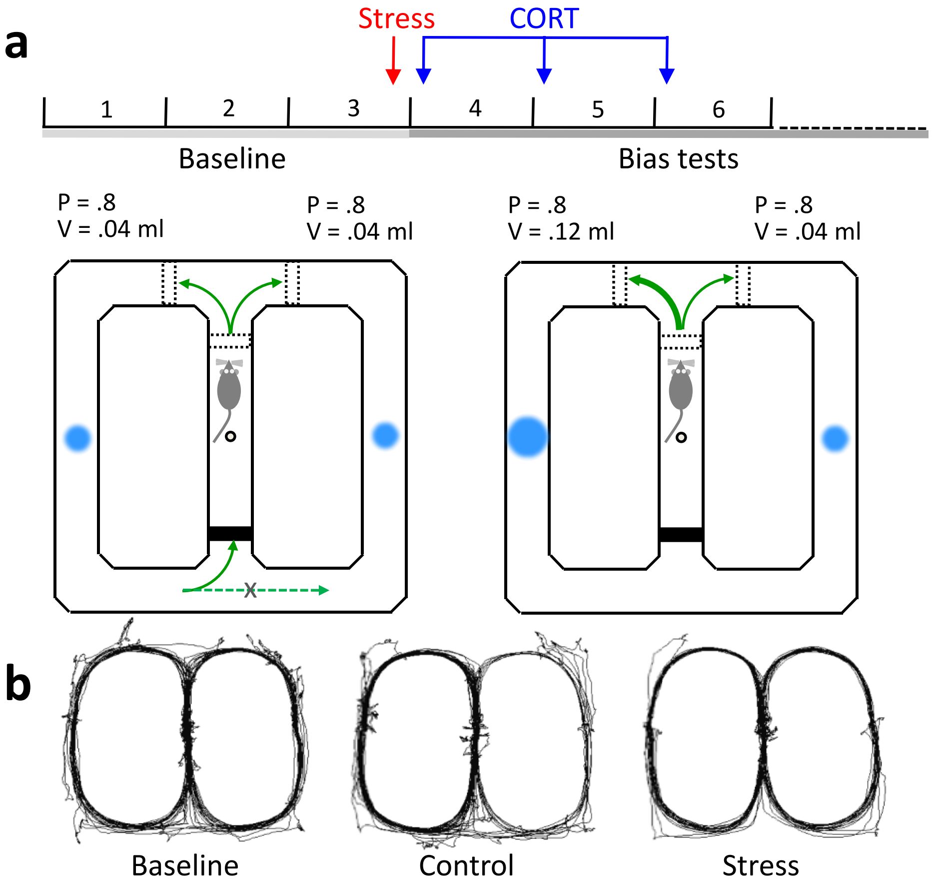
The authors declare that they have no competing financial interests.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V = .12 ml
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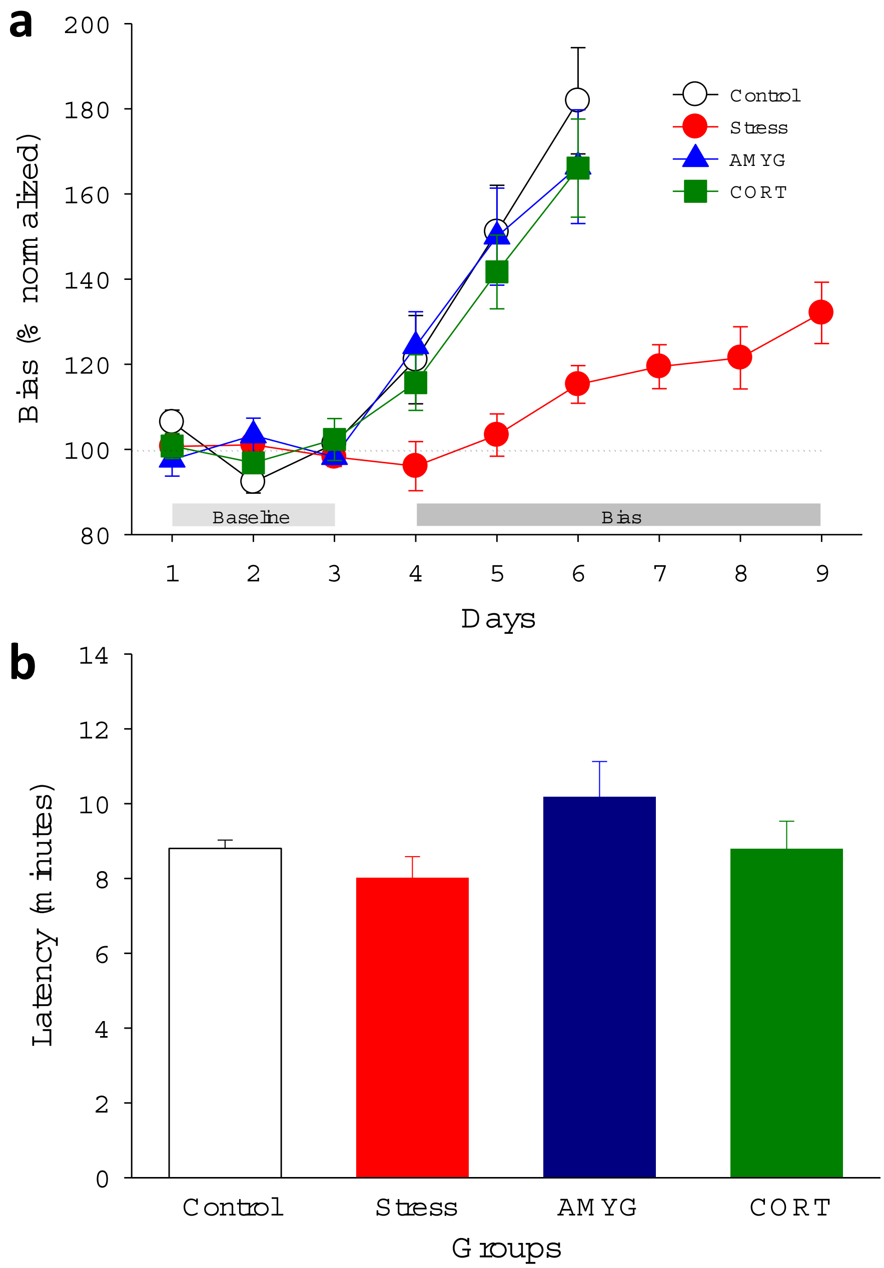
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