Stress-induced attenuation of acoustic startle in low-saccharin-consuming rats.

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ABSTRACT

Exposure to stress can lead to either increased stress vulnerability or enhanced resiliency. Laboratory rats are a key tool in the exploration of basic biobehavioral processes underlying individual differences in the effect of stress on subsequent stressors’ impact. The Occidental low (LoS) and high (HiS) saccharin-consuming rats, which differ in emotional reactivity, are useful in this effort. In the present study, footshock affected acoustic startle amplitude 4 h later among LoS but not HiS rats. Surprisingly, shock attenuated startle rather than sensitizing it, a finding not previously reported for male rats exposed to shock. Attenuation was blocked by administering the anxiolytic drug alprazolam prior to stress, implicating anxiety in the effect. Preliminary tests provided no evidence of mediation by adenosine or corticosterone. This novel result encourages further study of the stressor and dispositional variables that modulate the timecourse of effects of stress on startle and identification of its mechanisms.

Stressful events can affect reactivity to subsequent stressors, either increasing stress vulnerability or enhancing resilience (Heim et al., 2003; Levine, 2005; McEwen, 2004). In humans, alterations in stress vulnerability have been implicated in depression (Gutman and Nemeroff, 2003; Nolen-Hoeksema, 2001), post-traumatic stress disorder (PTSD; Silva et al., 2000; Stam, 2007), substance abuse (Dawes et al., 1999; Koob, 2006), and schizophrenia (Mueser et al., 2002). Both heightened and attenuated stress reactivity from prior stress also have been documented in other mammals (Koolhaas et al., 2006). Milder stressors tend to attenuate later stress responses, whereas trauma tends to enhance them. However, the same stressor can affect various stress response systems differently (e.g., sympathetic versus hypothalamic-pituitary-adrenal activity, Schommer et al., 2003). Furthermore, situational and dispositional variables moderate the impact of prior stress on subsequent vulnerability (e.g., Gunnar and Vasquez, 2006; Moore et al., 2006).

A useful paradigm for studying sequential stress effects in laboratory rats centers on modulation of acoustic startle amplitude. Startle is a defensive reflex, and startle testing after earlier stress constitutes a mild stressor reexposure (Commissaris et al., 2004; Cranney, 1988). Prior experimental stress, such as inescapable shock, usually sensitizes startle. Sensitization has been observed seconds (Pilz et al., 1999), minutes (Davis, 1989), and days (Servatius et al., 1995) after shock. As stressor severity increases, sensitization emerges later and lasts longer. Sensitization emerges a few minutes after ten 0.5-s, 0.6-mA footshocks and is gone within 40 min; at 1.0 or 1.4 mA, sensitization emerges in 20–30 min and is robust at 40 min (Davis, 1989). Sensitization is detectable a week after one session of forty 3-s, 2-mA tailshocks, but not until 10 days after three sessions (Servatius et al., 1995; see also Matuszewich et al., 2007).

The degree to which shock sensitizes startle also varies among rats. Sprague-Dawley rats sensitize more than Wistars (Pilz et al., 1999; also see, Faraday, 2002). Using startle nonhabituation after shock as a PTSD model, Garrick et al. (2001) observed nonhabituation only in rats with low baseline startle amplitudes. Milde et al. (2003) also found sensitization after shock in a subset of rats, those with low plasma corticosterone (CORT).

Compared to sensitization, stress-induced startle attenuation seems rarer and more circumscribed. Beck and Servatius (2005, 2006) observed attenuation 2 h after shock but not after restraint, and only in intact females, concluding that attenuation depends on nociception and ovarian hormones. However, Conti and Printz (2003) observed attenuated startle 24 h after restraint in males of some rat strains. Stress-attenuated startle appears to be a potentially important phenomenon in need of further study.

Accounting for individual differences in stress-induced changes in startle requires approaches in which dispositional variables are well characterized. Selective breeding is such an approach: Lines are developed on a clearly operationalized phenotype, after which phenotypic correlates and functional relationships are examined. For example, Roman low (RLA) and high (RHA) avoidance rats are...
selectively bred on an avoidance phenotype, and excessive anxiety has been implicated in RLA rats’ poor avoidance (Driscoll et al., 1998; Steiner and Driscoll, 2003; see also Brush, 2003). The line difference in anxiety manifests as greater baseline startle and greater shock-induced startle sensitization among RLA rats (Schwegler et al., 1997).

In the present study, Occidental high (HiS) and low (LoS) saccharin-consuming rats were used to further explore the role of dispositional emotionality in sequential stress effects. Selectively breeding on a taste phenotype has yielded lines that differ in emotional reactivity. Relative to HiS rats, LoS rats hyperstartle, defecate more in a novel open field, show stronger stress–induced hypoalgesia and anorexia, and are more affected by food deprivation and glucocorticoids (Dess et al., 2000; Dess and Minor, 1996; VanderWeele et al., 2002); similar relationships exist in humans (Craig et al., 2003; Dess and Edelheit, 1998). Stress usually sensitizes startle, more so in the anxiety-prone RLA rats (Schwegler et al., 1997), so the most straightforward prediction regarding startle after stress is greater sensitization among LoS rats. On the other hand, sensitization is greater among rats with lower baseline startle (Garrick et al., 2001) or lower CORT (Milde et al., 2003), both of which characterize HiS rats (Dess et al., 2000; VanderWeele et al., 2002). Thus, contrary to other measures of stressor reactivity to date, HiS rats could show greater sensitization. Finally, because startle attenuation has been reported for some male rats (Conti and Printz, 2003), differential attenuation was yet another possible outcome.

1. Experiment 1

Experiment 1 assessed the effect of stress on startle in LoS and HiS rats and the mediating role of anxiety in any effect. No standard protocol exists for studying stress-induced changes in startle. Diverse stressors, parameters, and rat strains are used. In light of our prior research, the relationship between stressor severity and onset of altered startle, and ethical and practical considerations, we selected twenty 5-s 0.6-mA footshocks as a stressor and a 4-h stress–startle interval. This shock regime is more severe than that after which Davis (1989) observed sensitization for at least 40 min and is less severe than startles that delay sensitization for days (Servatius et al., 1994, 1995). The pre-stress anxiolytic treatment was alprazolam, which is short acting and should have minimal direct effects more than 4 h later (Lau and Heatherington, 1997). Alprazolam functions much like other benzodiazepines in anxiety paradigms (e.g. Griebel et al., 1996; Isogawa et al., 2005; Lobarinas and Falk, 2000). It reduces startle sensitization (Commissaris et al., 2004; Hijzen et al., 1995) via anxiety reduction (Gifkins et al., 2002; Joordens et al., 1998).

This and the following experiments employed nested designs (Winer et al., 1991). Complete factorial designs often provide superfluous information and thus are not always the most efficient or ethical choice. Our designs provided sufficient power for key comparisons while minimizing rat numbers and distress. In Experiment 1, because this stressor was not expected to affect HiS rats, only LoS rats received alprazolam pretreatment. If anxiety mediates any effect of stress on startle, alprazolam should block the effect, yielding startle in drug-pretreated stressed LoS rats comparable to that of non-stressed LoS controls. Together, those groups should startle differently from stressed LoS rats given no anxiolytic.

1.1. Method

1.1.1. Rats

Experimentally naïve male Occidental HiS (N = 20) and LoS (N = 25) rats aged 60–80 days from, respectively, eight and nine litters in Generations 27–28 were tested. Body weight averaged 412 ± 5 g (mean ± S.E.M.) and did not differ between groups. Rats were housed individually on a 12:12 light:dark cycle (lights off at 7 p.m.) with Purina 5001 chow and water freely available. Rats’ care and use conformed to Public Health Service and institutional policies for humane treatment.

1.1.2. Apparatus and materials

The footshock apparatus was a 16 cm × 32.5 cm × 19.5 cm (w × l × h) clear acrylic box. Two stainless steel plates lined the sides of the box and angled toward the bottom to create a 1.5-cm gap that the rat had to straddle, thus completing the circuit when current was applied to the plates. The box was placed in an illuminated sound-attenuating chamber. Footshocks were generated by constant current generators (Model 82400, Lafayette Instruments, Lafayette, IN). Shock delivery was computer controlled.

Acoustic startle testing was conducted in a commercial startle chamber (Model SR-Pilot, San Diego Instruments, San Diego, CA) with dimensions of 14 cm × 21 cm × 23 cm (w × l × h). The startle stimulus was a 40-ms, 95-dB white noise burst. Startle amplitude was detected with a piezoelectric sensor and was displayed digitally in arbitrary units (20–2000). Trial initiation and data recording were manual. The startle apparatus was housed in a sound-attenuating box with a 7-W light bulb and 65-dB ambient masking white noise, located in the same large room as the footshock apparatus.

Alprazolam (Sigma–Aldrich Inc., St. Louis, MO) was prepared with glycol/ethanol/saline vehicle. A dose of 2 mg/kg or vehicle was injected i.p. at a volume of 1 ml/kg.

1.1.3. Experimental design

A five-group nested design was used. Line (HiS versus LoS) and stress condition (Stress versus No Stress) were completely crossed. Drug treatment was nested within the LoS/Stress condition: Eight LoS/Stress rats were injected with alprazolam (LoS/Stress/APZ), and nine were injected with vehicle (LoS/Stress). All HiS/Stress rats (n = 10) were injected with vehicle. Remaining rats (LoS/No Stress, n = 8; HiS/No Stress, n = 10) were not stressed. Within a line, rats were assigned randomly to groups.

1.1.4. Procedure

Rats received brief gentle handling for 4 days before testing. Beginning at 9:30 a.m. on the test day, LoS/Stress/APZ were injected with alprazolam and LoS/Stress and HiS/Stress rats were injected with vehicle. Twenty-five min later, these groups were exposed to twenty 5-s 0.6-mA footshocks on a variable time 60-s schedule. Afterwards, they were returned to their home cages. LoS/No Stress and HiS/No Stress rats remained in their home cages.

Four hours after the stress session ended, startle testing began. Rats were individually placed in the startle chamber. After a 3-min adaptation period, 30 startle trials occurred on a fixed-time 10-s schedule. The rat then was returned to his home cage, and the inside of the chamber was cleaned with 5% ammonium hydroxide solution.

Squads of rats were staggered to hold injection-stress and stressor-startle intervals roughly constant at, respectively, 25 min and 4 h. Groups were balanced in the testing order.

1.2. Results and discussion

Startle amplitude in 10 three-trial blocks is shown in Fig. 1. To minimize undue influence of outlying values, the median value in each block of three trials for each rat was used in the present experiments, as elsewhere (Dess et al., 2000). Startle among LoS rats given alprazolam before footshock was comparable to that of non-stressed LoS controls. Startle among stressed LoS rats given
vehicle was lower than in those groups—indeed, it was as low as among HiS rats.

The data were subjected to a 5 (group) × 10 (trial block) analysis of variance (ANOVA). Greenhouse-Geisser corrections were used for tests of trial block effects. Test statistics significant at $\alpha = 0.05$ are reported in the text, along with partial eta squared ($\eta_p^2$) as a measure of effect size. Startle declined over trials [trial block main effect, $F(9,360) = 5.40$, $\eta_p^2 = 0.12$]. The group × trial block interaction was not significant. The main effect of group was significant, $F(4,40) = 5.17$ ($\eta_p^2 = 0.34$). Two-tailed planned comparisons (Winer et al., 1991, pp. 166–167) showed that LoS/No Stress and LoS/Stress/APZ did not differ from each other and, together, startled more than LoS/Stress, $t(40) = 2.37$. LoS/Stress startled as little as HiS rats, the two groups of which did not differ from each other.

Elevated startle amplitude among non-stressed and anxiolytic-pretreated LoS relative to HiS rats and the greater impact of stress on LoS than HiS rats add to previous evidence of LoS rats’ greater emotional reactivity. That shock attenuated startle in LoS rats was surprising. Startle attenuation has been observed in females 2 h after shock (Beck and Servatius, 2005, 2006) and in some males 24 h after repeated restraint (Conti and Printz, 2003), but we know of no other study in which shock attenuated later startle in male rats at any testing interval.

Alprazolam blocked the effect of stress on LoS rats. The drug’s impact on startle is inconsistent with lingering anxiolysis or sedation, which available literature indicates would have reduced startle rather than increasing it (Commissaris et al., 2004; Hijzen et al., 1995; Joordens et al., 1998; Rodriguez-Fornells et al., 1999). Thus, elicitation of anxiety by the stressor is necessary to attenuation of startle later in the day.

2. Experiment 2

The chief purpose of Experiment 2 was to replicate startle attenuation in LoS rats. A preliminary test of adenosine’s role was included. Caffeine, a nonselective adenosine antagonist, blocks learned helplessness when given before the escape test (Minor et al., 2001) and normalizes LoS rats’ impaired response to glucoprivation (VanderWeele et al., 2002), theoretically by blocking inhibition triggered by cellular energy depletion (Minor and Hunter, 2002). The dose selected (10 mg/kg) was intermediate to doses that normalize metabolic stress and block helplessness (respectively, 15 mg/kg and 7 mg/kg). If shock attenuates startle via adenosine-mediated inhibition, caffeine treatment should reduce attenuation. Any stimulant effect (Antoniou et al., 1998) was evaluated by giving caffeine to non-stressed controls.

2.1. Method

2.1.1. Rats

Experimentally naïve male Occidental HiS (N = 16) and LoS (N = 34) rats aged 60–80 days from, respectively, eight and seven litters in Generations 29–30 were maintained as in Experiment 1. Body weight averaged 432 ± 6 g (mean ± S.E.M.) and did not differ between groups.

2.1.2. Apparatus and materials

The apparatuses were the same as above. Caffeine sodium benzoate (50% caffeine by weight; Sigma Chemical Inc., St. Louis, MO) was prepared with isotonic saline. Caffeine (10 mg/kg) or vehicle was injected i.p. at a volume of 1 ml/kg.

2.1.3. Experimental design

A six-group nested experimental design was used (n = 8–9). Line (HiS versus LoS) and drug treatment (Vehicle versus Caffeine) were completely crossed between-group variables. Because stress had no effect on HiS rats in Experiment 1, stress condition (No Stress versus Stress) was nested within the LoS line. Rats were assigned randomly to groups within a line.

2.1.4. Procedure

The procedure was the same as above except for drug treatment. Vehicle or caffeine was injected 20 min prior to startle testing. Squads of rats were staggered to hold stressor-startle and injection-startle intervals roughly constant at, respectively, 4 h and 20 min. Groups were balanced in the testing order.

2.2. Results and discussion

Startle amplitude is shown in Fig. 2. No effect involving caffeine approached significance (p > 0.60), so LoS/No Stress, LoS/Stress, and HiS/No Stress conditions are shown collapsed across drug condition. Startle was initially higher in both LoS conditions relative to HiS controls but decreased rapidly among stressed LoS rats to a level comparable to HiS controls.

A 3 (Group LoS/No Stress, LoS/Stress, HiS/No Stress) × 2 (vehicle, caffeine) × 10 (trial block) mixed-design ANOVA yielded main effects of group, $F(2,44) = 8.96$ ($\eta_p^2 = 0.29$), and trial block, $F(9,396) = 11.22$ ($\eta_p^2 = 0.20$), and a group × trial block interaction, $F(18,396) = 2.35$ ($\eta_p^2 = 0.10$). Planned comparisons
on group marginal means showed that LoS/No Stress startled more than LoS/Stress, $t(44) = 2.27$, which did not differ from HiS/No Stress. The group $\times$ trial block interaction was interpreted with Bonferroni-corrected group contrasts for each trial block. LoS/No Stress startled more than HiS/No Stress in every block except Block 10 and more than LoS/Stress in 5 of 10 blocks (Blocks 3, 5, 6, 8, and 9). LoS/Stress startled more than HiS/Stress only in Block 1.

Experiment 2 replicates stress-induced attenuation of startle in LoS rats. It also shows that the footshock session, and not injection, comprises the effective stressor because no rats were injected in the morning. Caffeine in a dosage range that blocks effects of stronger stressors (Minor et al., 2001; VanderWeele et al., 2002) had no effect. A higher dose of caffeine or a selective $A_2$ adenosine receptor antagonist (Minor et al., 1994) might yield different results. Alternatively, cellular exhaustion or other debilitation may play no role in the attenuation of startle by stress. Startle attenuation could reflect adaptation rather than distress, an idea considered further in Section 4.

3. Experiment 3

Experiment 3 comprised a final replication of startle attenuation by stress. Preliminary probes of the role of corticosterone were included. LoS rats are hypercorticosteronemic (VanderWeele et al., 2002), indicating a line difference in hypothalamic-pituitary-adrenal (HPA) function. Inhibiting CORT synthesis and release with mifepristone (MIF, also known as RU486) blocks a stress-induced reduction in startle sensitization (Adamec et al., 2006). Thus, CORT could play a role in stress-induced attenuation in LoS rats, possibly through fast-feedback downregulation of the HPA axis (Thrivikraman et al., 2000). If so, CORT treatment in the morning should simulate the effect of footshock on startle, and MIF pretreatment should reduce startle attenuation.

3.1. Method

3.1.1. Rats

Experimentally naïve male Occidental HiS ($N = 9$) and LoS ($N = 28$) rats aged 60–80 days from, respectively, eight and nine litters in Generations 31–32 were maintained as in Experiments 1 and 2. Body weight averaged 445 $\pm$ 8 g (mean $\pm$ S.E.M.) and did not differ between groups.

3.1.2. Apparatus and materials

The apparatuses were the same as above. CORT (2.5 mg/kg i.p.) and MIF (10 mg/kg s.c.) (Sigma Chemical Inc., St. Louis, MO) were prepared with a glycol/ethanol/saline vehicle and injected at a volume of 1 ml/kg. These doses and routes of administration are effective in adult male rats (Aisa et al., 2007; Caggiula et al., 1993; Dong et al., 2006; Haller et al., 1997; Orr and Mann, 1992; Steketee and Goeders, 2002; Xu et al., 1998).

3.1.3. Experimental design

The design included a HiS control group (HiS/No Stress, $n = 9$) and three LoS groups: CORT to simulate footshock (LoS/No Stress/CORT, $n = 10$), MIF followed by footshock (LoS/Stress/MIF, $n = 10$), and a non-stressed control (LoS/No Stress, $n = 9$). In Experiments 1 and 2, no vehicle- or caffeine-treated LoS groups differed from HiS/NS rats, making a vehicle-treated LoS/Stress group unnecessary. Because MIF was used to examine whether blocking CORT would reduce startle attenuation by stress in LoS rats, MIF was not given to any non-stressed LoS or stressed HiS rats. LoS rats were assigned randomly to groups.

3.1.4. Procedure

The procedure was the same as above except for drug treatments. At 9:30 a.m. on the test day, LoS/No Stress/CORT rats were injected with CORT and returned to their home cages, and LoS/Stress/MIF rats were injected with MIF. LoS/Stress/MIF rats received a footshock session 25 min after injection. LoS/No Stress and HiS/No Stress rats remained in their home cages. Startle testing began 4 h later. Squads of rats were staggered to hold injection-stress and stressor-startle intervals roughly constant at, respectively, 25 min and 4 h. Groups were balanced in the testing order.

3.2. Results and discussion

Startle amplitude is shown in Fig. 3. Non-stressed LoS rats startled equally highly regardless of CORT treatment and, again, stressed LoS rats startled as little as HiS controls despite MIF pretreatment. A 4 (group) $\times$ 10 (trial block) mixed-design ANOVA yielded main effects of group, $F(3,33) = 3.70$ ($\eta^2 = 0.25$), and trial block, $F(9,297) = 9.24$ ($\eta^2 = 0.22$). The group $\times$ trial block interaction was not significant. Planned comparisons showed that LoS/No Stress and LoS/No Stress/CORT did not differ from each other. LoS/Stress and HiS/No Stress did not differ from each other and, together, startled less than non-stressed LoS groups, $t(33) = 3.04$.

Fig. 3. Mean acoustic startle amplitude ($\pm$S.E.M.) of LoS and HiS rats in Experiment 3. CORT, corticosterone; MIF, mifepristone.

In light of nonhomogeneity of variance in Block 1, the soundness of the ANOVA results was checked by reanalyzing the data nonparametrically. A Kruskal–Wallis test on marginal group means was significant, $H(4) = 12.06$, and Mann–Whitney $U$ tests yielded the same pattern of group differences as planned comparisons—i.e. non-stressed LoS groups did not differ, and LoS/Startle and HiS/No Stress did not differ, but these homogeneous subsets differed, $U(18,19) = 69.5$.

Experiment 3 establishes the reliability of stress-attenuated startle in LoS rats. CORT did not attenuate startle, and MIF did not block attenuation. In fact, both agents shifted startle slightly in the opposite direction. These initial tests are not definitive, of course. LoS rats’ hypercorticosteronemia may downregulate CORT receptors such that only a larger dose would exert an effect, and MIF might not have completely blocked CORT. Nonetheless, that neither CORT nor an inhibitor, respectively, simulates or reduces the stressor’s effect discourages the idea that CORT mediates attenuation. Other aspects of HPA regulation or other neurochemical systems (Charney, 2004) may be more important than an acute rise in CORT.

4. General discussion

Stress-attenuated startle in rats selectively bred on a taste phenotype is intriguing. Consistent with linkage of the taste and emotionality, LoS rats’ disposition toward anxiety contributes to...
the stress effect. Paradoxically, morning anxiety reduces startle later. When and how it does so are unclear. The key events do appear to precede onset of startle trials. Overall attenuation startle by stress was significant in all three experiments, despite some tendency toward recovery in stressed LoS rats. In contrast, change across trials in the pattern of group differences was reliable in only one experiment, and the effect was much smaller than the group main effect. Moreover, mean startle over Blocks 3–6 — where attenuation was clearest — accounted for 86–89% of the variance in mean startle in the three experiments, leaving little variance for initial startle to explain. These results do not favor an explanation of attenuation in terms of within-session dynamics.

Transformation of anxiety in the morning into attenuated startle later could involve arousal, affective state, attention, and cue-elicited emotion (Bradley et al., 2006; Davis, 1997). For instance, the shock and startle apparatuses were in the same large room, so shock-associated contextual cues could play a role (Grillon et al., 2006; Guscott et al., 2000; Richardson, 2000). However, in virtually all research on startle after stress, the phenomenon to be explained has been startle sensitization. Explaining startle attenuation in terms of associative or non-associative stress sequelae will require a different perspective on those processes.

A promising approach frames the present findings in terms of allostatic adaptation to stress (Charney, 2004; McEwen, 2004). Allostatic processes set in motion by stress increase or decrease stress vulnerability, depending on whether allostatic load exceeds coping resources. Recently, Korte et al. (2005) elaborated an evolutionary framework focused on individual differences in coping. They distinguished a bold, rapid, risky, flight–flight response (“Hawk”) from a cautious, deliberate, risk-averse, freeze-hide response (“Dove”). The latter comprises an accommodative bias that is adaptive in certain environments but also predisposes individuals to developing anxiety disorders as allostatic load increases.

The Dove strategy aligns well with characteristics of LoS rats. Applying the concept to the present results, shock-induced anxiety precipitated an allostatic shift among LoS rats, such that they experienced the startle test as innocuous, as HiS rats appear to (Helson, 1964; Walters, 1994). Rats spared anxiety in the morning — LoS rats by virtue of anxiolytic pretreatment, HiS rats by virtue of unflappable disposition — underwent no such shift and thus did not startle differently from nonshocked counterparts within their line. The nature of the hypothetical allostatic shift remains to be determined. It could, for instance, be stressor-specific or general (Pacak and Palkovits, 2001; Thrivikraman et al., 2000), and could reflect changes in perception of or responsiveness to startle stimuli (Beck and Servatius, 2005). Juxtaposing the present findings with other reports on startle attenuation does little to illuminate it. A critical role for ovarian hormones (Beck and Servatius, 2005, 2006) is inconsistent with attenuation in males (present study; Conti and Printz, 2003). Attenuation in males from strains that do not differ from others in overall startle but habituate faster (Conti and Printz, 2003) is inconsistent with attenuation only in LoS rats, who have higher baseline startle and do not consistently habituate faster than HiS rats.

While the few reports of attenuation are difficult to reconcile, all yielded attenuation in a subset of rats 2–24 h after stress, an interval for which we can find no reports of sensitization. This pattern hints at heretofore unexamined temporal dynamics of startle modulation by stress. Stressors are perturbations in a confluence of real-time processes that augment or reduce startle (Koch and Schnitzler, 1997; Koolhaas et al., 1997; Pilz and Schnitzler, 1996), and a startle probe reveals the momentary relative strength of those processes. From this perspective, the delay of sensitization with increasing stressor severity (Davis, 1989; Servatius et al., 1995) may reflect the early dominance of allostatic processes that reduce reactivity, with sensitization appearing if and when allostasis cannot be sustained. The stronger the allostatic response, the later sensitization appears. Alternatively, startle after stress could follow a nonmonotonic time-course reminiscent of Selye’s general adaptation syndrome, with sensitizing processes dominating at short and at long post-stress intervals and attenuating processes dominating in between. Different processes could subserve immediate versus delayed sensitization and attenuation. A model of this sort has been proposed for stress enhancement and impairment of memory (Diamond et al., 2007), and it might be usefully applied to startle modulation by stress.

In the current literature, short (seconds, minutes) and long (4–10 days) stress–startle intervals are overrepresented, and because they tend to be used in different laboratories, are largely confounded with stressor and rat strain. The main contribution of the present study, then, is to draw attention to stress-induced startle attenuation as a reliable phenomenon that occurs in an understudied post-stress period in dispositionally sensitive individuals. Doing so points the way to empirical work to fill and explore temporal gaps, laying the groundwork for development of real-time models of startle modulation that include individual-difference parameters.

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