

The relationship between glucocorticoid levels at baseline and during an acute stress response

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ABSTRACT

During unpredictable events, vertebrates initiate a physiological stress response, in part mediated by corticosterone (CORT) released by the hypothalamic-pituitary-adrenal (HPA) axis. In circulation, CORT generally remain at baseline levels, with mild fluctuations reflecting predictable energetic demands. During stress, however, CORT levels become elevated above baseline, which functions to mobilize glucose reserves and inhibit nonessential functions. Once the stressor has passed, homeostasis is restored and CORT levels recover to baseline. An acute stress response, then, can generally be simplified to three CORT levels: baseline, stress-induced rise, and homeostatic-recovery. Here, we studied Japanese quail (*Coturnix japonica*) using a standard bag-restraint protocol to investigate relationships between baseline CORT and either the stress-induced rise of CORT, or the homeostatic-recovery of CORT levels. Specifically, we used dexamethasone, a synthetic glucocorticoid that causes negative feedback on the HPA axis, to measure homeostatic-recovery. We found that baseline CORT correlated positively with both stress-induced and dexamethasone recovery levels. Controlling for prior CORT levels, there was no relationship between baseline CORT levels and the increase in circulating CORT during an acute stress response. But, birds with lower baseline CORT had a faster decrease in CORT after the stressor was removed. Our results suggest that an individual's baseline CORT level relates to their ability to turn off a stress response.

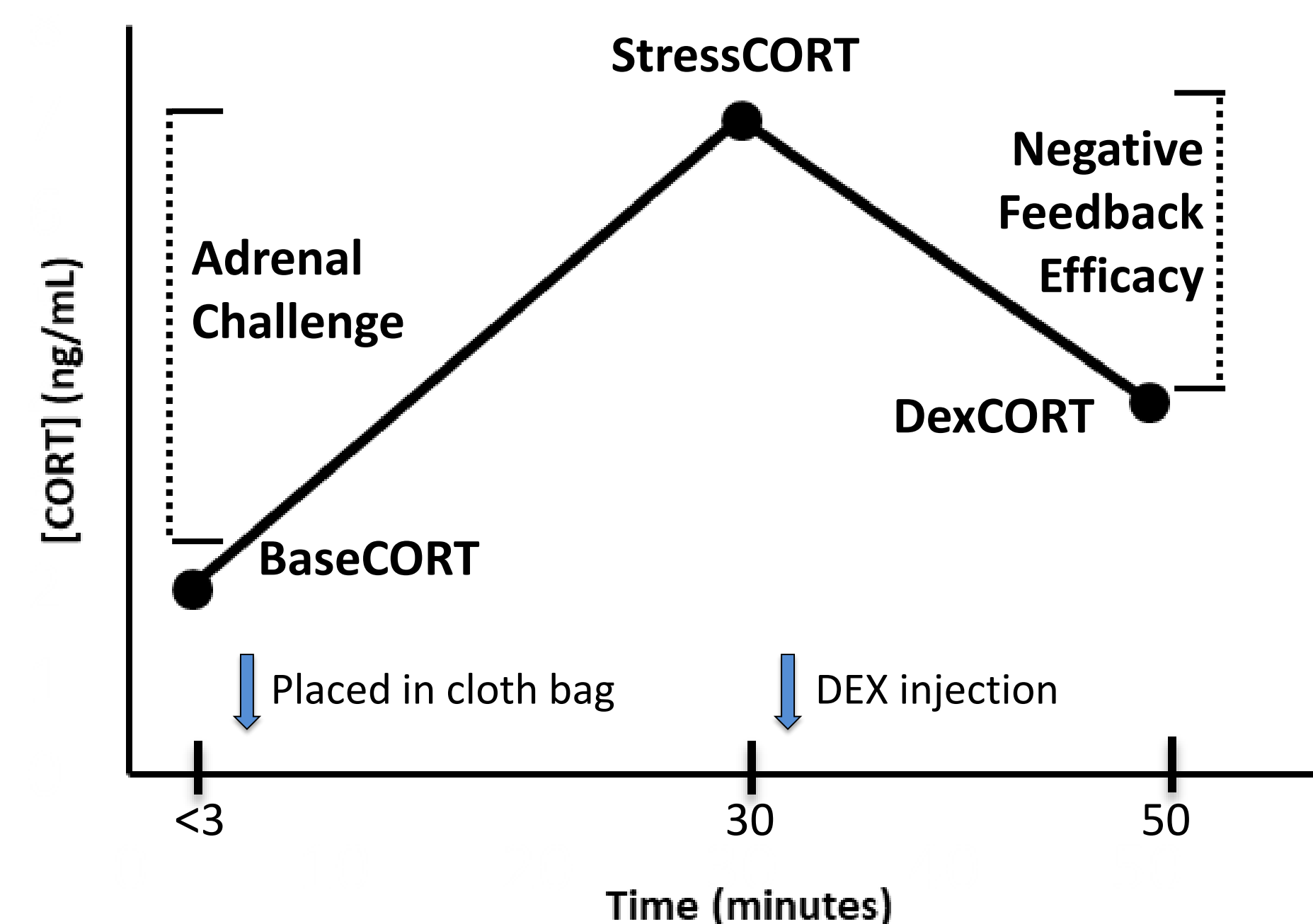
BACKGROUND and METHODS: Stress assessment

- In birds, stress causes a hormonal cascade through the Hypothalamic-Pituitary-Adrenal (HPA) axis resulting in the release of corticosterone (CORT).
- We measured CORT through three distinct phases of an acute stress response:
 - BaseCORT (Baseline CORT):** Sample within 3 min of disturbance
 - StressCORT (Stress-Induced CORT):** Sample 30 min after initiation of bag restraint
 - DexCORT (Dexamethasone-CORT):** Sample 20 min after dexamethasone injection (1mg/kg s.c.) and bag restraint
- We used two measurements to help assess variation in the three phases of an acute stress response:
 - Adrenal Challenge** (StressCORT – BaseCORT): Ability of adrenals to secrete CORT in response to bag restraint
 - Negative Feedback Efficacy** (StressCORT – DexCORT): The strength of negative feedback on the HPA axis in response to DEX in the presence of a stressor

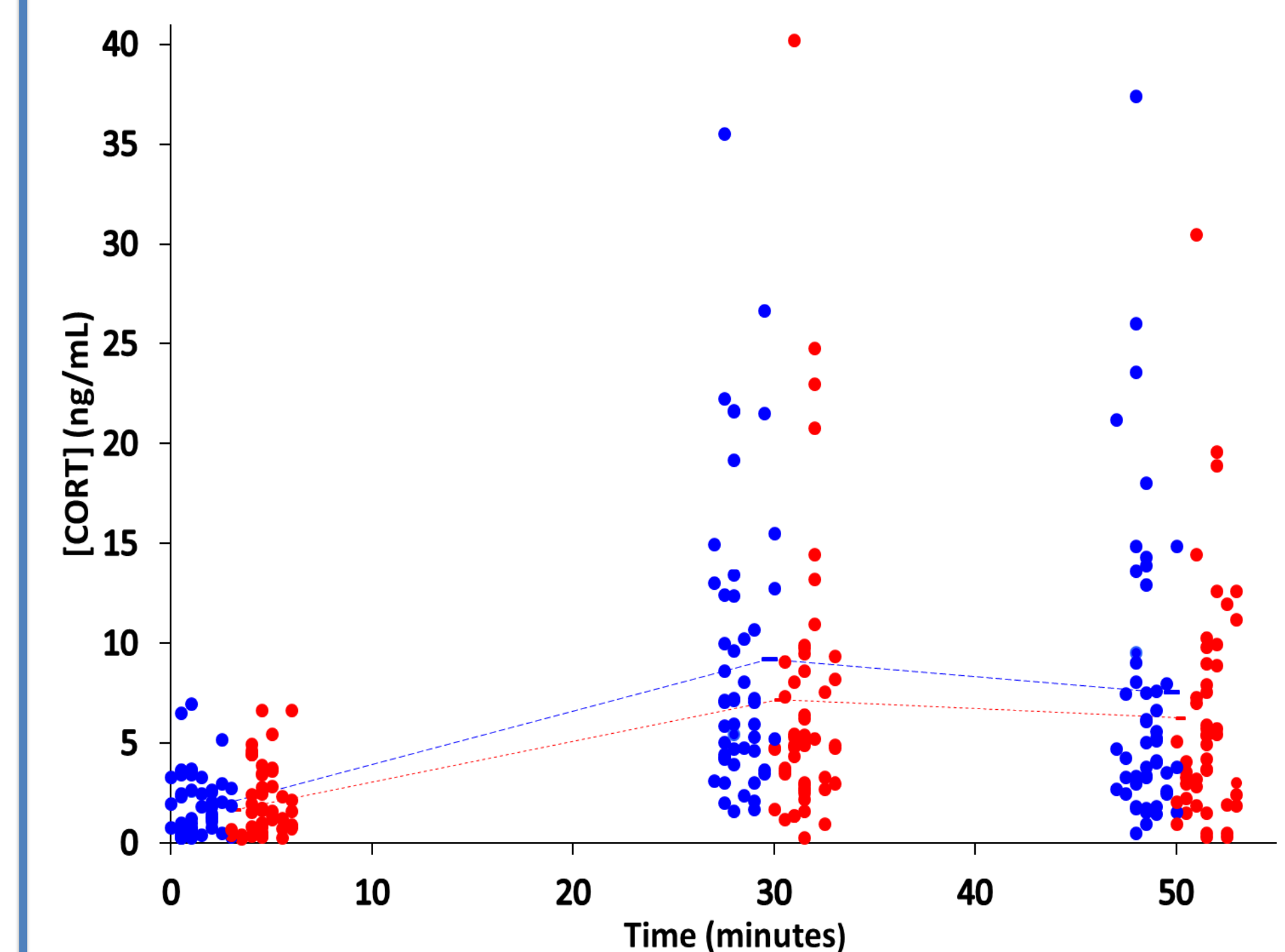
Objective: We manipulated the HPA axis in Japanese quail (*Coturnix japonica*) to explore how baseline corticosterone levels relate to variation in corticosterone during the different phases of an acute stress response.

ANIMAL and LAB METHODS

- 100, six-month old, Japanese quail (*Coturnix japonica*) in this study were from two groups:
 - Prenatal CORT exposure:** Freshly laid eggs were injected with 5ng/ml CORT in sesame oil (n = 50)
 - Control:** Freshly laid eggs were injected with sesame oil vehicle (n = 50)
- Plasma CORT was measured by radioimmunoassay
- Log CORT levels were analyzed using Mixed Effect Models, but untransformed CORT values are shown



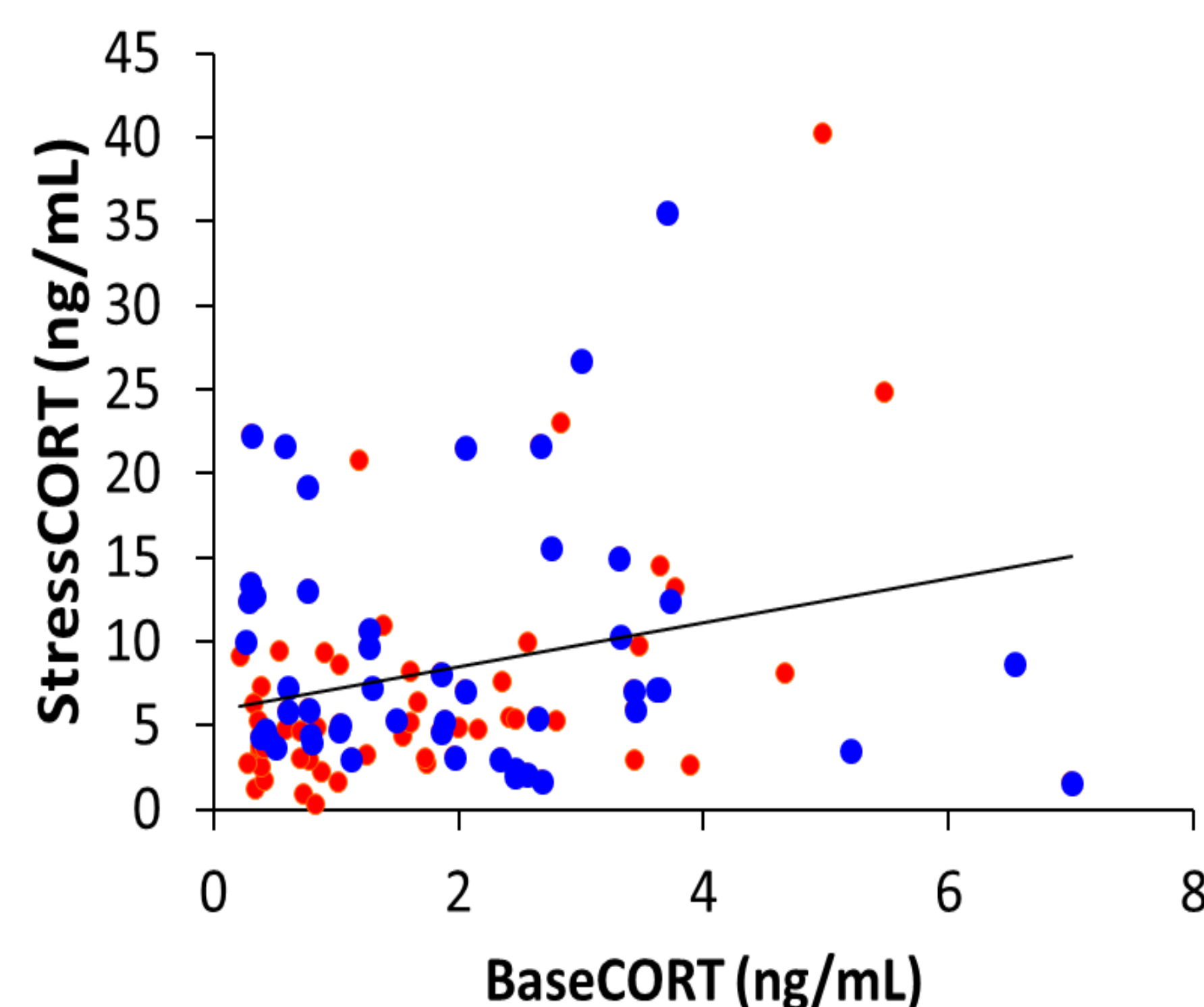
CORT levels during the stress assessment



RESULTS

- CORT levels differed by time ($F = 36.4$, $p < 0.0001$).
 - 91 birds increased from BaseCORT to StressCORT
 - 66 birds decreased from StressCORT to DexCORT
 - BaseCort values were lower than both StressCort and DexCort values, but StressCort and DexCort did not differ.
- Prenatal CORT exposure did not affect acute stress CORT ($F = 3.6$, $p = 0.06$), but 5ng birds tended to have lower CORT levels.

Baseline CORT is positively correlated with Stress-induced CORT



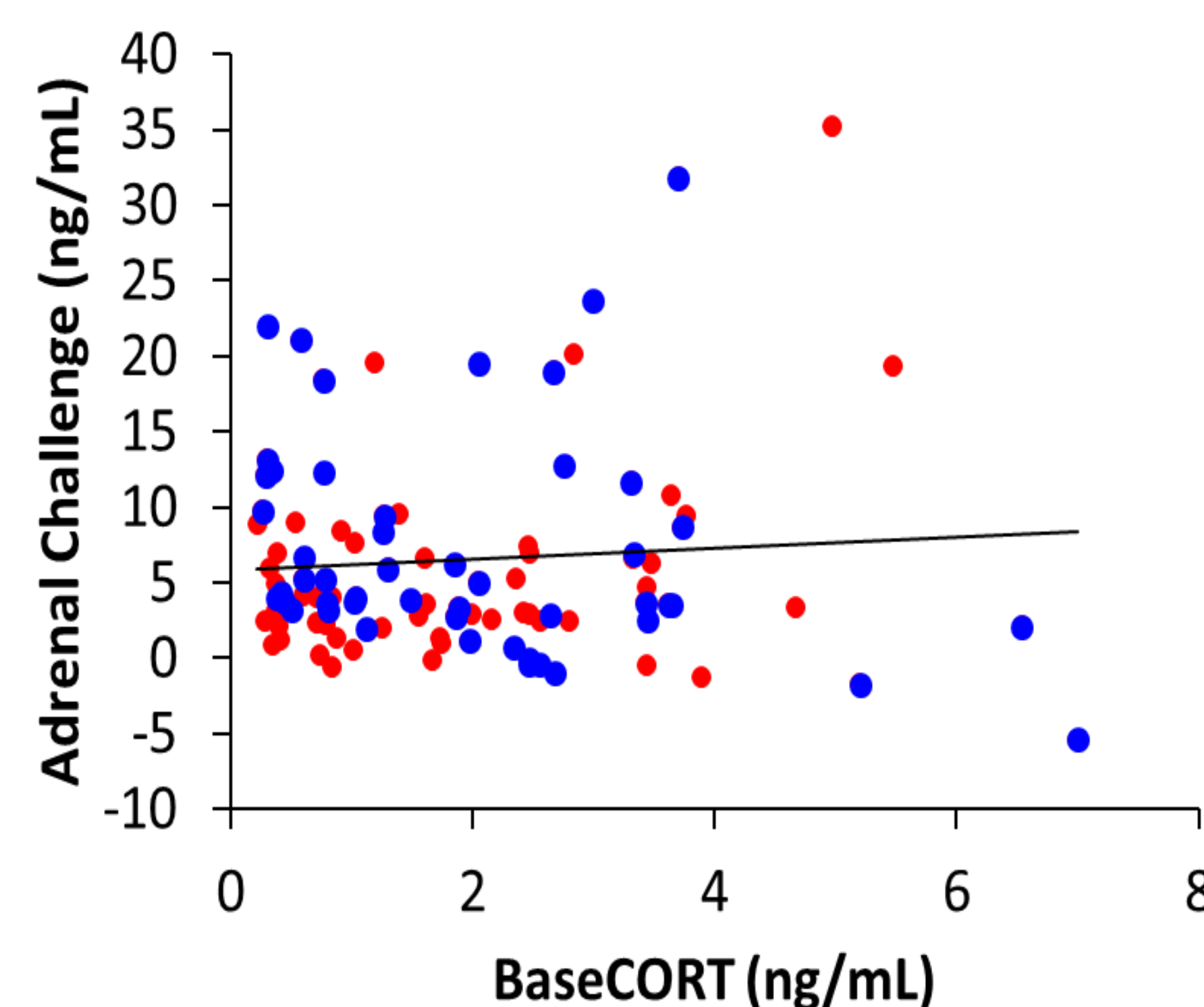
RESULTS

- Individuals with higher BaseCORT levels also had higher levels of CORT during restraint stress ($R^2 = 0.07$, $p = 0.01$).

DISCUSSION

- Because StressCORT levels are a function of both BaseCORT levels and the stress-induced rise in CORT, it is difficult to determine how much each of these is driving this relationship.

Baseline CORT is not correlated with the change in CORT during restraint stress



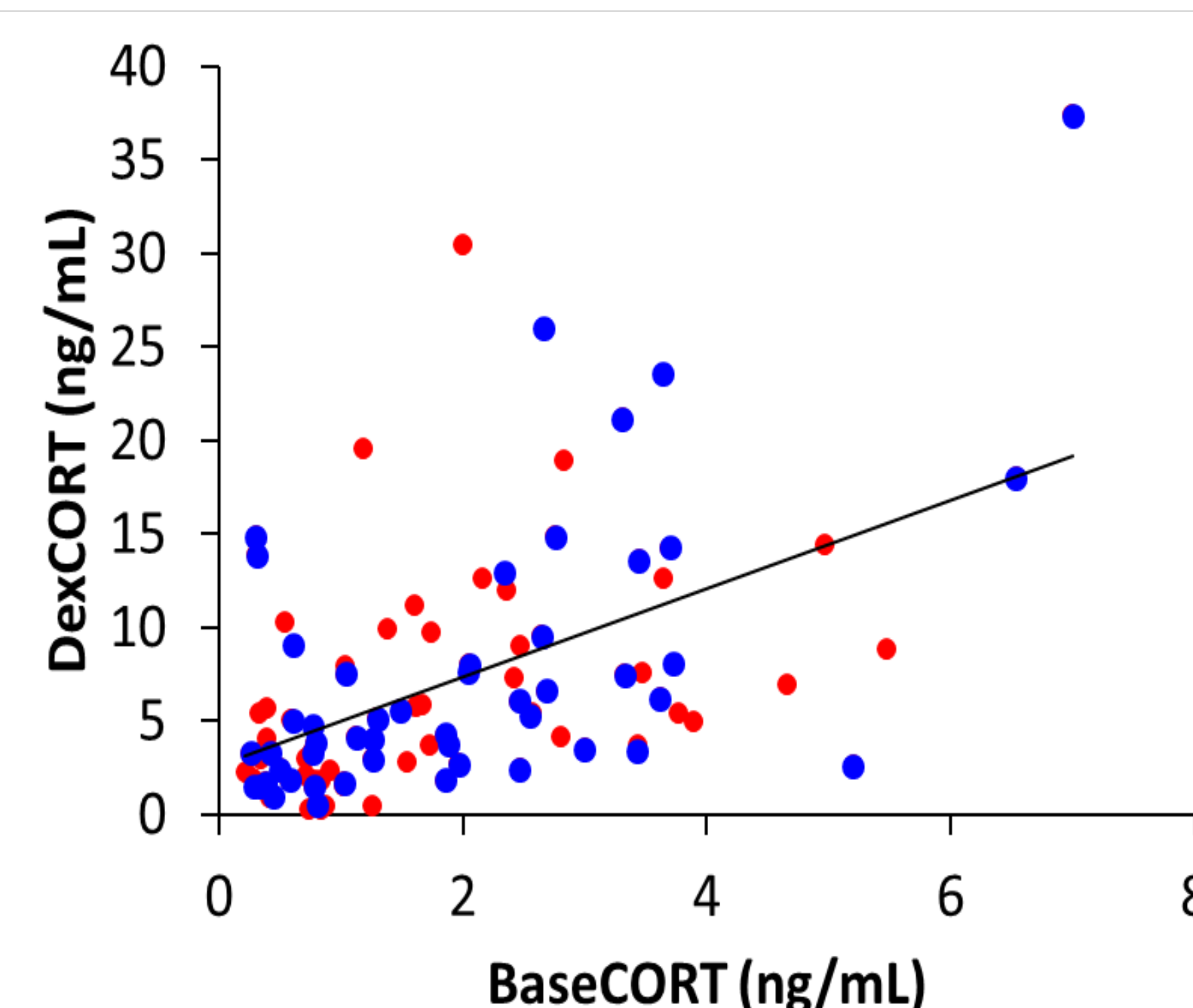
RESULTS

- BaseCORT levels were not significantly related to Adrenal Challenge CORT levels (StressCORT – BaseCORT; $R^2 = 0.004$, $p = 0.52$).

DISCUSSION

- The lack of relationship suggests that these two measures represent different physiological states and predictable energetic demands (baseline) do not strongly influence energetic demands during stress.

Baseline CORT is positively correlated with Dexamethasone-CORT



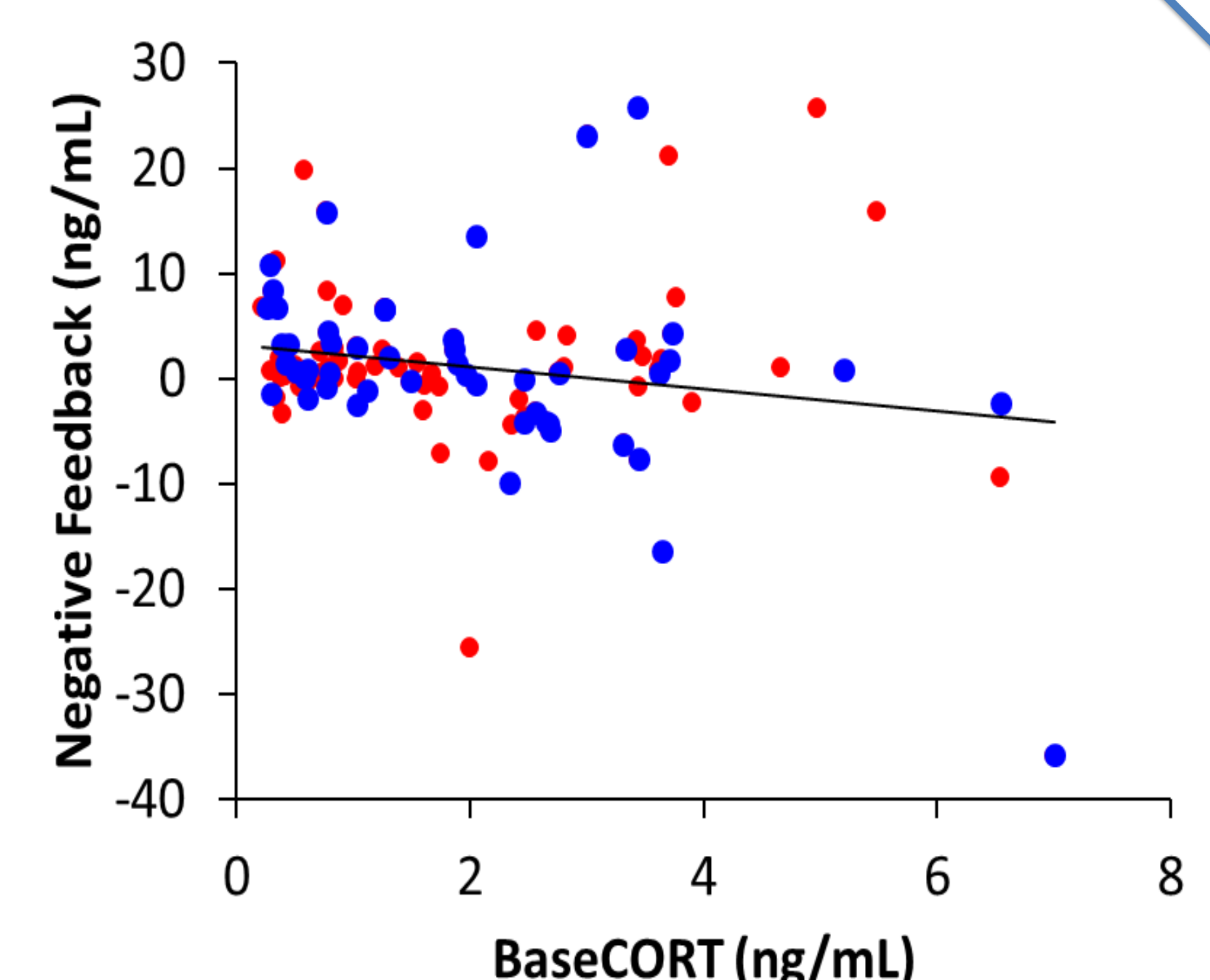
RESULTS

- Individuals with higher BaseCORT levels also had higher CORT levels 20 min after receiving a DEX injection ($R^2 = 0.24$, $p < 0.0001$).

DISCUSSION

- This suggests that after stress, negative feedback will help to return individuals to the same baseline CORT level they experienced before a stressor.

Baseline CORT is negatively correlated with Negative Feedback Efficacy



RESULTS

- Individuals with higher BaseCORT did not decrease CORT levels as quickly (StressCORT – DexCORT; $R^2 = 0.024$, $p < 0.05$).

DISCUSSION

- Interestingly, these data suggest that individuals with higher CORT levels at baseline were not able to return to those baseline levels as quickly using negative feedback.
- Taken together, while baseline CORT does not appear to influence a bird's magnitude to turn-on a stress response, it does relate to their ability to turn-off a stress response.



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