This study revealed a remarkable synergistic effect of common polymorphisms on acute stress response in healthy males.

- 5HTTLPR SS carriers showed higher overall cortisol concentrations than L carriers in response to intense, realistic stress.
- 5HTTLPR S carriers showed higher overall diastolic blood pressure (DBP) values than noncarriers (LL), Bcl1 GG were higher than C carriers, and -2C/G G carriers exceeded noncarriers (CC).
- A “high” genotype group revealed substantially higher overall cortisol concentrations than a “low” genotype group, as was the case for DBP.

**RESULTS**

- Tests of a recessive model of the short variant of 5HTTLPR showed cortisol concentrations were significantly higher in SS than L carriers (F(1,133) = 5.4, \( p < 0.05 \), \( \eta^2_p = 0.04 \)).
- HR recovery was superior in 5HTTLPR L carriers compared with short variant (SS) carriers (relative T2-T3: -37.0% vs. -27.9%, F(139) = 3.3, \( p < 0.001 \)).
- DBP was influenced by all three polymorphisms:
  - 5HTTLPR S variant carriers (SS+SL) had higher DBP than noncarriers (CC; \( p < 0.05 \)).
  - For Bcl1 in a recessive model for allele G showed higher DBP for GG carriers than CC (\( p < 0.05 \)).
  - For -2C/G, a dominant model for allele G showed higher DBP in G carriers (GG+GC) than CC (\( p < 0.05 \)).
- High (n = 8) genotype group had significantly higher cortisol concentrations than low genotype group (n = 18) at all three time points (Figure 2, F(1,24) = 18.4, \( p < 0.001 \), \( \eta^2_p = 0.43 \)).
- High (n = 8) genotype group had significantly higher DBP than low genotype group (n = 12) at all three time points (Figure 3, F(1,29) = 8.0, \( p < 0.05 \), \( \eta^2_p = 0.22 \)).

**CONCLUSIONS**

- The results of this study indicate that the adrenocortical and cardiovascular stress responses in healthy male service members are influenced by both distinct and additive effects of polymorphisms in the serotonin transporter (5HTTLPR L/S), glucocorticoid receptor (Bcl1 C/G), and mineralocorticoid (-2C/G) receptor genes.
- Most notably, remarkable differences between high and low genotype groups on cortisol and DBP trajectories were observed, implying a synergistic effect.
- Pending additional study, these findings may have implications for drug discovery, gene therapy, and stress inoculation strategies.

**REFERENCES**