

**Supplemental Digital Content (SDC)** for: MacCormack, J. K., Armstrong-Carter, E. L., Gaudier-Diaz, M. M., Meltzer-Brody, S., Sloan, E. K., Lindquist, K. A., & Muscatell, K. A. (2021). Beta-adrenergic contributions to emotion and physiology during an acute psychosocial stressor. *Psychosomatic Medicine*.

Herein, we provide additional details regarding prior literature, methods, results, and discussion that supplement the main text and provide further insights and details. We hope that this additional information will not only increase this study's transparency but also its utility for future research and meta-analyses.

### **Supplementary Background**

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### **Supplementary References**

**Table S1. Summary of prior literature on propranolol and affect in healthy adults, organized chronologically.**

| Study                           | Propranolol Dosage | Sample Size  | Context   | Affect or Stress Measures  | Findings  |
|---------------------------------|--------------------|--|---|--|---|
| <b>Turner et al. (1965)</b>     | 5 mg               | Crossover design with:<br><b>8</b> with thyrotoxicosis<br><b>8</b> in an anxiety state   | All patients across 4 days given either 5 ml placebo saline, 5 mg propranolol, 5 mg phentolamine, vs. 62.5 mg amylobarbitone sodium | Heart rate during anxiety state (no subjective measure)  | Propranolol significantly blunted heart rate during anxiety state compared to placebo or other drugs  |
| <b>Lader &amp; Tyrer (1972)</b> | 120 mg             | Cross-over design with <b>6</b> subjects on 120 mg propranolol, 240 mg sotalol, vs. placebo across three separate days           | Various cognitive tests such as reaction time, key tapping, card-sorting, digit symbol substitution test, symbol copying test, etc. | Mood rating scale (16-items) with sedation, contentedness, and anxiety subscales                             | Propranolol increased drowsiness, “muzziness,” and feeling troubled, but not anxiety  |
| <b>Stone et al. (1973)</b>      | 6 doses of 10 mg   | <b>12</b> propranolol<br><b>12</b> placebo   | Acute stressor of speech task where participants discussed life events that upset, worried or evoked anxiety for them               | Post-stressor interview; two independent coders rated verbal samples of the interviews for anxiety           | Propranolol reduced anxiety reports post-stressor   |
| <b>Tyrer &amp; Lader (1974)</b> | 120 mg             | <b>8</b> placebo<br><b>8</b> propranolol<br><b>8</b> propranolol (racemic)<br><b>8</b> diazepam                                  | Three stressors including click-shock task, exposure to phobic objects, etc.  | Mood rating scale (16-items) with sedation, contentedness, and anxiety subscales                             | Propranolol reduced anxiety ratings relative to placebo but was less effective than diazepam  |
| <b>Gottschalk et al. (1974)</b> | 60 mg              | <b>12</b> propranolol<br><b>12</b> placebo   | Pre- to post-drug at rest; 10-min stress interview  | Anxiety ratings  | Propranolol reduced anxiety at rest but anxiety during the stressor was equivalent across groups  |
| <b>Ashton et al. (1976)</b>     | 60 mg              | <b>27</b> propranolol<br><b>27</b> diazepam<br><b>27</b> placebo   | Pre- to post-drug at rest; Acute stressor of mental arithmetic in front of peers  | VAS ratings of anxiety   | No effect of propranolol on anxiety at rest or post-stressor  |
| <b>Nakano et al. (1978)</b>     | 40 mg              | <b>24</b> healthy young men<br><b>12</b> propranolol<br><b>12</b> placebo  | Mental stressors: mirror drawing test & Stroop  | STAI measures of anxiety pre-drug at rest and post-drug/post-stressor<br><br>Subjective mood ratings         | No effect of propranolol on changes in anxiety or mood post-stressor  |
| <b>Landauer et al. (1979)</b>   | 80 mg              | Cross-over design with <b>18</b> healthy young men across 3 days receiving either 100 mg atenolol, 80 mg propranolol, or placebo | Variety of motor and cognitive tests 18 hrs after each dose   | “How you feel” measure (22 bipolar adjectives, e.g. sad-happy, lethargic-energetic)<br><br>POMS mood ratings | When on propranolol, participants rated feeling more gregarious, optimistic, less sorry for themselves, less anxious and less tense compared to when on placebo |

| Study (Continued)                  | Propranolol Dosage                 | Sample Size  | Context  | Affect or Stress Measures  | Findings  |
|------------------------------------|------------------------------------|--|--|--|---|
| <b>Taylor et al. (1981)</b>        | 80 mg                              | Cross-over design with <b>12</b> healthy young adults on two separate days with propranolol vs. placebo  | Experimental stress induced by having participant hold right leg with knee extended above a chair for as long as possible  | VAS ratings of anxiety, alertness, and concentration   | No effect of propranolol on ratings of anxiety, alertness, and concentration after experimental stress  |
| <b>Brantigan et al. (1982)</b>     | Not reported                       | Cross-over design with <b>29</b> music students who on separate days received propranolol vs. placebo  | Musical performances in front of other peers and judges  | Stage fright self-reports on overall performance, nervousness, & physical symptoms<br>STAI ratings of anxiety                              | Propranolol reduced state anxiety during the stage performance but did not alter trait anxiety at rest<br><br>Propranolol reduced nervousness & physical symptoms of stage fright   |
| <b>Hartley et al. (1983)</b>       | 40 mg                              | Study 1: Cross-over design with <b>16</b> health young adults (8 males, 8 females) high in self-rated trait anxiety; separate lab visits with placebo vs. 40 mg propranolol<br><br>Study 2 & 3: Cross-over design with <b>12</b> healthy young adults high in self-rated state and trait anxiety vs. <b>12</b> healthy adults low in state/trait anxiety; separate lab visits with placebo vs. 40 mg propranolol | One minute to prepare for a speech and then 3-min to give a speech in front of a video camera about counterbalanced topics (e.g., anxiety-provoking life experiences; feelings on administering electric shocks to volunteers) | STAI ratings of anxiety<br><br>Three independent raters also scored the videos for how anxious participants appeared to be from scale 1-20 | Study 1: Propranolol reduced both self-reported state anxiety and independently observed anxiety<br><br>Study 2: Propranolol reduced self-reported state anxiety across both the trait-anxious and non-anxious participants. However, propranolol appeared to reduce independently observed anxiety in the trait-anxious group but not in the non-anxious group |
| <b>Salem &amp; McDevitt (1984)</b> | 40 mg<br>80 mg<br>160 mg<br>320 mg | Cross-over design with <b>6</b> young men on 40, 80, 160, and 320 mg of propranolol vs. placebo  | Various cognitive tests (e.g., reaction time, digital copying test, symbol digit modalities test, etc.)  | VAS ratings of alertness, tension, detachment, and anxiety measured after the cognitive testing ended                                      | At 40 mg, propranolol increased ratings of detachment, and at 80 and 320 mg doses, decreased alertness, but no impact on tension or anxiety   |
| <b>Drew et al. (1985)</b>          | 120 mg                             | Cross-over design with <b>35</b> medical students who took either propranolol or placebo on two different exam days  | Mental arithmetic and verbal reasoning exams   | Asked to indicate (post-exam) if they had felt no, mild, moderate, or severe anxiety right before the exam                                 | Propranolol improved exam performance, especially in those who reported that they felt more anxious before the exam   |

| Study (Continued)               | Propranolol Dosage       | Sample Size   | Context  | Affect or Stress Measures  | Findings  |
|---------------------------------|--------------------------|---|--|--|---|
| <b>File &amp; Lister (1985)</b> | 80 mg                    | Cross-over design with <b>17</b> participants on lorazepam vs. propranolol vs. placebo  | Various cognitive tests (e.g., reaction time, digit-symbol substitution, & symbol copying tasks) as well as a 9-min stressor "IQ test" | Mood rating scale (16-items) with sedation, contentedness, and anxiety subscales<br>STAI measure of anxiety post-stressor                  | No effect of propranolol on mood or post-stress anxiety ratings   |
| <b>Krantz et al. (1987)</b>     | .2 mg/kg                 | Cross-over design with <b>12</b> healthy young men on propranolol vs. isoproterenol vs. placebo   | Structured interview (speech) and mental arithmetic task   | Multiple Affect Adjective Checklist<br>State-Trait Personality Inventory (state-form)  | No effect of propranolol (bolus injection) on anxiety, hostility, or anger ratings after a speech and math task |
| <b>Mazzuero et al. (1987)</b>   | 120 mg                   | Male patients with history of myocardial infarction<br><b>16</b> propranolol<br><b>16</b> atenolol<br><b>16</b> chlordesmethyldiazepam<br><b>16</b> placebo | Acute stressor of mental arithmetic plus the Sacks & Levy sentence completion test   | STAI measure of anxiety both pre- and post-stressor  | No effect of propranolol on anxiety either at rest nor post-stressor  |
| <b>Currie et al. (1988)</b>     | 40 mg<br>80 mg<br>160 mg | Cross-over design with <b>12</b> healthy young men taking 40, 80, and 160 mg of propranolol vs. placebo   | Cognitive and executive functioning tasks  | VAS ratings of wakefulness, tension, calm, energetic, alert, concentration, efficient, irritable, aggressive, sociable, depressed, anxious | Propranolol blunted anxiety   |
| <b>Dyck &amp; Chung (1991)</b>  | 80 mg                    | Women undergoing surgery<br><b>31</b> diazepam<br><b>32</b> propranolol<br><b>30</b> placebo  | Prior to a surgical operation  | STAI ratings of anxiety pre- and post-surgery  | No significant differences in anxiety between groups  |
| <b>Jakobsson et al. (1995)</b>  | 40 mg                    | Women undergoing surgery<br><b>30</b> ketobemidone<br><b>30</b> lorazepam<br><b>30</b> propranolol<br><b>30</b> placebo                                     | Prior to a surgical operation  | Anxiety rated on the Linear Analogue Anxiety Scale   | No significant differences in anxiety between groups  |

| Study (Continued)                                 | Propranolol Dosage | Sample Size  | Context   | Affect or Stress Measures   | Findings   |
|---|--------------------|--|---|---|--|
| <b>Head et al. (1996)</b>                         | 40 mg<br>80 mg     | Cross-over design with <b>20</b> young adults, taking placebo, 50 mg metaprolol, 100 mg metaprolol, 40 mg propranolol, & 80 mg propranolol | Treadmill walking exercise  | POMS mood and STAI anxiety ratings assessed pre- and post-exercise  | Compared to placebo, those on propranolol reported greater tension, depression, and mood disturbances at rest and greater fatigue and confusion both pre- and post-exercise; no drug effect on anxiety |
| <b>Mealy et al. (1996)</b>                        | 10 mg              | Patients undergoing same-day surgery<br>~ <b>25</b> propranolol<br>~ <b>25</b> placebo   | Same-day surgical procedure   | Hospital Anxiety and Depression Scale   | Propranolol reduced anxiety on the day of surgery  |
| <b>Elman et al. (1998)</b>                        | 40 mg              | <b>3</b> young male medical residents performing 40 surgeries on propranolol vs. <b>33</b> on placebo (double-blinded)                     | Surgery performance   | Sliding scale rating of how anxious the resident seemed as rated by an attending surgeon observer                               | For surgeries conducted under propranolol, third-person blinded anxiety ratings were lower than for surgeries conducted under placebo  |
| <b>Harmer et al. (2001)</b>                       | 80 mg              | <b>10</b> propranolol<br><b>10</b> placebo   | Emotion perception task   | VAS ratings of tense, angry, sad, happy, alert, & tired<br><br>Befindlichkeits Scale as additional mood measure                 | No effect of propranolol on subjective ratings of mood, alertness, or task speed at rest nor when completing an emotion perception task  |
| <b>Rogers et al. (2004)</b>                       | 80 mg              | <b>15</b> propranolol<br><b>17</b> placebo   | Mood ratings taken at rest pre- and post-drug but before a gambling task      | PANAS ratings of state negative and positive affect<br><br>VAS ratings of mental sedation, physical sedation, tranquility, etc. | Propranolol increased feelings of tranquility at rest post-drug, but no effects of propranolol on PANAS ratings at rest  |
| <b>Alexander et al. (2007)</b>                    | 40 mg              | Cross-over design with <b>16</b> healthy young adults who took propranolol vs. placebo   | Acute stressor of the TSST vs. non-stressful control task (reading, counting) | Anticipated stressfulness of the task (pre-TSST but after being informed about it)  | No effect of propranolol on anticipated stressfulness of the TSST  |
| <b>Andrews &amp; Pruessner (2013)<sup>a</sup></b> | 80 mg              | <b>15</b> propranolol<br><b>15</b> placebo   | Acute stressor of TSST  | Subjective stress rated on a VAS  | No effect of propranolol on ratings of stress  |
| <b>Dreifus et al. (2014)</b>                      | 60 mg              | <b>24</b> propranolol<br><b>25</b> placebo<br><b>24</b> no drug  | Pre- to post-drug at rest; Acute stressor as TSST                             | German versions of the PANAS, SAM ratings of valence and arousal, STAI anxiety ratings, as well as other mood measures          | Propranolol blunted state anxiety and arousal ratings at rest. Propranolol reduced TSST-related anxiety, nervousness, and TSST-related changes to well-being and SAM arousal and valence ratings       |

| Study (Continued)                    | Propranolol Dosage     | Sample Size   | Context   | Affect or Stress Measures  | Findings  |
|--------------------------------------|------------------------|---|---|--|---|
| <b>Ernst et al. (2016)</b>           | 40 mg                  | 20 propranolol<br>20 methylphenidate<br>20 placebo  | Working memory tasks under cognitive load and with conditions of safety vs. threat of shock | STAI anxiety ratings   | Propranolol had no effect on changes in anxiety across the tasks  |
| <b>Ali et al. (2017)<sup>b</sup></b> | 80 mg                  | 22 both dexamethasone and propranolol<br>22 placebo | Acute stressor of TSST  | VAS on “How stressed do you feel right now?”<br>POMS mood ratings  | Combined dexamethasone and propranolol group were not significantly different from placebo on stress or mood ratings across time, including post-TSST |
| <b>Stephoe et al. (2018)</b>         | 80 mg for 7 days prior | 32 propranolol<br>32 placebo                        | Stress tasks of TSST and mirror tracing   | HADS (Hospital Anxiety & Depression Scale) to assess anxiety<br><br>Positive affect subscale of PANAS<br><br>7-point single item scale measures of subjective stress and task difficulty | No effect of propranolol on anxiety, positive affect, subjective stress, or task difficulty ratings   |

**Note:** We have striven to only include studies here that focused on healthy adults without diagnosed anxiety, phobic, panic, or chronic mood disorders. See Steenen et al. (2016) *Journal of Psychopharmacology* for a review and meta-analysis on the effectiveness of propranolol in treating anxiety and related disorders. <sup>a</sup> **Andrews & Pruessner (2013)** also administered appraisal measures such as the Primary and Secondary Appraisal Questionnaire and the COPE Inventory, but do not report any findings with regards to appraisals (as far as we can find). <sup>b</sup> **Ali et al. (2017)** reported that they likely had sufficient power to detect propranolol effects on subjective ratings by taking the mean of effect sizes for drug effects on physiology (salivary alpha amylase, heart rate, and cortisol) and generating a hypothetical effect size for subjective ratings. This assumes that propranolol impacts psychological phenomenon to the same degree as physiology and that there is close coupling between psychology and physiology. We suggest that the effect size of propranolol on mood is likely much smaller than that of propranolol on physiology, given that drug works directly on physiology but states like emotion or appraisals reflect multiple intra-individual processes besides just physiology. As such, propranolol samples larger than  $n \sim 20$  are likely needed to detect reliable effects on mood/emotion.

## Supplemental Information on Study Procedure

### Recruitment

Participants were told that the study assessed “physiology and cognition,” that propranolol is used to treat hypertension, and that common side effects include feeling lightheaded or dizzy. Participants completed an initial visit to ensure they met health eligibility criteria (i.e., did not have low heart rate or blood pressure) and provided written informed consent. The lab visit occurred three to seven days after this prescreening visit. We were careful to avoid mentioning stress or emotion throughout the study prescreening, intake, and procedures, so as not to bias participants’ expectations.

**Table S2.** Additional sample characteristics compared by condition.

| <b>Demographics</b>                          | <b>Placebo</b> | <b>Propranolol</b> | <b>Total</b> | <b>p-value</b> |
|--|----------------|--------------------|--------------|----------------|
| <i>Mean Depressive symptoms</i> <sup>a</sup> | 1.40 ± 1.64    | 1.30 ± 1.44        | 1.36 ± 1.54  | .755           |
| <i>Mean Anxiety symptoms</i> <sup>b</sup>    | 37.07 ± 9.20   | 34.77 ± 7.58       | 35.96 ± 8.49 | .204           |
| <i>Mean Perceived stress</i> <sup>c</sup>    | 10.62 ± 4.92   | 10.24 ± 4.60       | 10.44 ± 4.75 | .709           |
| <i>Mean Fear of evaluation</i> <sup>d</sup>  | 31.28 ± 8.52   | 33.86 ± 8.86       | 32.49 ± 8.73 | .165           |

**Note:** Difference tested with independent samples t-tests. <sup>a</sup>PHQ-9 (Kroenke, Spitzer, & Williams, 2001); <sup>b</sup> State-Trait Anxiety Inventory (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), <sup>c</sup> 14-item Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983); <sup>d</sup> brief Fear of Negative Evaluation Scale (Leary, 1983).

### Trier Social Stress Test

Participants met two interviewers who were supposedly “experts in the fields of persuasion and nonverbal communication.” Participants had 2-min to mentally prepare alone for a 10-min speech about “Why I would be a good candidate for my dream job.” After preparation, the interviewers entered the room, sat at a table facing the participant, ostensibly started a video recorder, and the speech began, lasting for 10-min. After the speech ended, the interviewers surprised the participant with an impromptu mental arithmetic task that supposedly assessed their “cognitive capabilities.” Participants counted backwards out loud from the number 996 in steps of seven, as quickly as possible. If they made a mistake or lost their place, they were instructed to start again. This task lasted for 5-min. Interviewers wore white laboratory coats and remained neutral and stoic throughout the TSST, providing no feedback but taking copious notes about the performance.

## Supplemental Information on Study Measures

### Autonomic Psychophysiology

For ECG, three non-invasive spot electrodes were placed on the torso (- on the collarbone, + and ground on the lower ribs). For ICG, two non-invasive spot electrodes were placed on the torso and two on the back. ECG and ICG were collected continuously at a sampling rate of 1000 Hz. Two of the authors (EAC, MMG) visually inspected and independently scored all data, with disagreements resolved by the first author (JKM). Initial agreement between the two scorers was 97.5% for ECG (based on the number of R-spikes identified per segment) and 87.6% for ICG (based on PEP values per segment). RSA was calculated from high frequency HRV after parsing out respiration. Respiration was estimated from ICG; all ECG segments were visually inspected to ensure that respiratory values remained within appropriate respiratory bands.

### Emotion Reports

Items within each quadrant of the affective circumplex within each timepoint demonstrated acceptable internal reliability ( $M\alpha = .80$ ).

- **Negative high arousal items (16-items):** *afraid, angry, annoyed, anxious, ashamed, distressed, embarrassed, frustrated, hostile, irritable, jittery, nervous, panicky, scared, stressed, upset*

- **Negative low arousal items (6-items):** *bored, disgusted, guilty, sad, unhappy, weary*
- **Positive high arousal items (8-items):** *amused, determined, enthusiastic, excited, happy, inspired, proud, strong*
- **Positive low arousal items (7-items):** *calm, content, attentive, interested, pleased, relaxed, quiet*

**Additional items measured but that were too neutral in valence and thus not included in the means (3-items):** *alert, hyper, sleepy*

### Appraisal Reports

The prospective/retrospective measure of challenge and threat appraisals included 6 challenge items (Pre-TSST  $\alpha = .79$ ; Post-TSST  $\alpha = .73$ ) and 6 threat items (Pre-TSST  $\alpha = .75$ ; Post-TSST  $\alpha = .73$ ). All challenge and threat appraisal items were rated on a Likert scale from 1 (*strongly disagree*) to 7 (*strongly agree*).

The negative appraisal questionnaire listed 25 negative internal/external appraisal descriptors, listed below (Pre-TSST  $\alpha = .93$ ; Post-TSST  $\alpha = .90$ ). This measure was included to capture core evaluations of personal responsibility for performance (internal attributions or self-evaluations) vs. appraisals about the situation's controllability and unexpectedness (external attributions or evaluations of the experimenters and the situational features), rated on a Likert scale from 1 (*not at all*) to 6 (*extremely*). These items were: *Defeated, Challenged, Abandoned, Disgraced, Insulted, Incompetent, Cheated, Loss, Failure, Bad news, Lonely, Made a mistake, Offended, Overwhelmed, Rejected, Threat, Thwarted, Wronged, Uncertain, Uneventful, Unfair, Uninteresting, Unknown, Unresolved, Vulnerable*

Finally, participants rated the nature of the TSST on a "Task Appraisal" measure with 6-items assessing how difficult, stressful, and enjoyable participants found the speech and math tasks, respectively:  $\alpha = .63$ . For example, participants rated both the speech and math tasks with wordings such as "The math task was difficult" "The speech task was stressful" or "The math task was enjoyable."

### Evaluation of Possible Covariates

At BL1, we assessed trait anxiety via the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), depressive symptoms via the PHQ-9 (Kroenke, Spitzer, & Williams, 2001), recent perceived stress via the 14-item Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983), and evaluation concerns via the brief Fear of Negative Evaluation Scale (Leary, 1983). These measures were included to confirm no group differences (i.e., no randomization failure) for subclinical mood symptoms, perceived life stress, and fear of evaluation. Given that the groups did not differ on any of these measures (see Table S2 above), they were ultimately not included as covariates

## **Supplemental Information on Study Results**

### The Problem of Single-Item Stress Reports

Given that prior beta-blockade studies have used single-item measures of stress and found null effects of propranolol (Alexander, Hillier, Smith, Tivarus, & Beversdorf, 2007; Andrews & Pruessner, 2013), we specifically examined task stressfulness ratings to compliment prior research. This measure was a mean score of two stress items from the "Task Appraisal" measure ("How stressful was the speech task you just completed?" "How stressful was the math task you just completed?"). There were no group differences on this measure between the drug vs. placebo groups  $t(88) = .60, p = .55$ , suggesting that participants found the TSST to be similarly stressful in nature regardless of drug condition. This underlines the importance of assessing emotions or more "internal" psychological states, rather than narrowly focusing on one or two-item



reports of stress, which may instead reflect appraisals and perceptions about the external environment (i.e., the task itself) in line with people's cognitive schemas, rather than their affective states per se.

### **Parasympathetic Nervous System Reactivity**

There were no effects of the TSST on RSA, nor was there an effect of propranolol on RSA at BL2 nor any other timepoint during or after the TSST (all  $ps > .10$ ; see Table 4 in main text). Beyond RSA, we also examined HR to be consistent with other studies exploring the effects of propranolol on reactivity to acute stress. HR results replicated PEP findings, wherein individuals on propranolol had a lower heart rate relative to placebo throughout the TSST prep, main tasks, and recovery periods. See Figure S2 and Tables S2-S3 for more details.

### **Hypothalamic-Pituitary-Adrenal (HPA) Axis Reactivity**

As would be expected in the context of an acute stressor, salivary cortisol was significantly higher at 15-min and 30-min post-TSST relative to BL2 ( $bs = .87, .60, SEs = .13, ps < .001$ ). We also observed a significant main effect of *drug* at BL2: cortisol was higher in the propranolol group relative to placebo ( $b = .45, SE = .18, p = .013$ ). There were no *drug x timepoint* interactions at any later timepoint ( $ps > .25$ ), suggesting that propranolol did not buffer against TSST-related cortisol reactivity (Table 4 in main text). However, it is worth noting that there was a small but significant difference in cortisol between the propranolol and placebo groups at BL1, suggesting randomization failure for this particular measure. As such, cortisol results should be interpreted with caution.

### **Additional Figures and Tables**

See below in this document for additional figures and tables.

## **Discussion**

It is worth observing that the specificity of effects of propranolol on SNS markers but not on RSA or cortisol is in line with degeneracy. *Degeneracy* is a common biological principle whereby a system includes mechanistic redundancies in order to promote survival (Edelman & Gally, 2001). For example, in the context of a stressor, it is likely adaptive for organisms to recruit multiple neurophysiological systems (e.g., HPA-axis) when managing metabolic resources to cope with stressful situations, even when one pathway (e.g., beta-adrenergic signaling) becomes disrupted.

**Supplementary References**

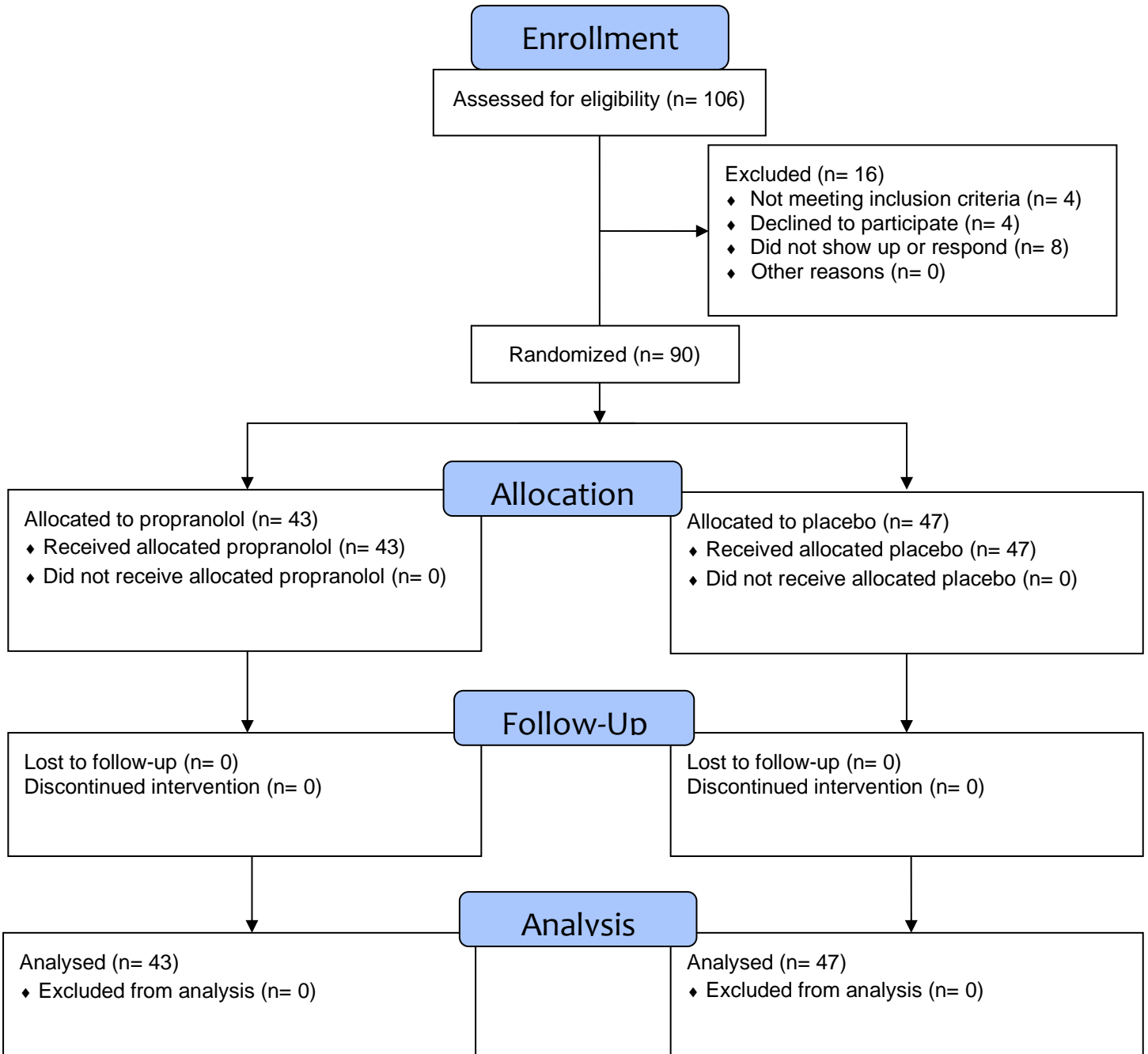
- Alexander, J. K., Hillier, A., Smith, R. M., Tivarus, M. E., & Beversdorf, D. Q. (2007). Beta-adrenergic modulation of cognitive flexibility during stress. *Journal of Cognitive Neuroscience*, *19*, 468–478. <https://doi.org/10.1162/jocn.2007.19.3.468>
- Andrews, J., & Pruessner, J. C. (2013). The combined propranolol/TSST paradigm – A new method for psychoneuroendocrinology. *PLoS ONE*, *8*, e57567. <https://doi.org/10.1371/journal.pone.0057567>
- Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*, 385. <https://doi.org/10.2307/2136404>
- Edelman, G. M., & Gally, J. A. (2001). Degeneracy and complexity in biological systems. *Proceedings of the National Academy of Sciences of the United States of America*, *98*, 13763–13768. <https://doi.org/10.1073/pnas.231499798>
- Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*, *16*, 606–613.
- Leary, M. R. (1983). A brief version of the fear of negative evaluation scale. *Personality and Social Psychology Bulletin*, *9*, 371–375. <https://doi.org/10.1177/0146167283093007>
- Spielberger, C. D., Gorsuch, R. L., Lushene, P. R., Vagg, P. R., & Jacobs, G. A. (1983). Manual for the State-Trait Anxiety Inventory. Consulting Psychologists Press.

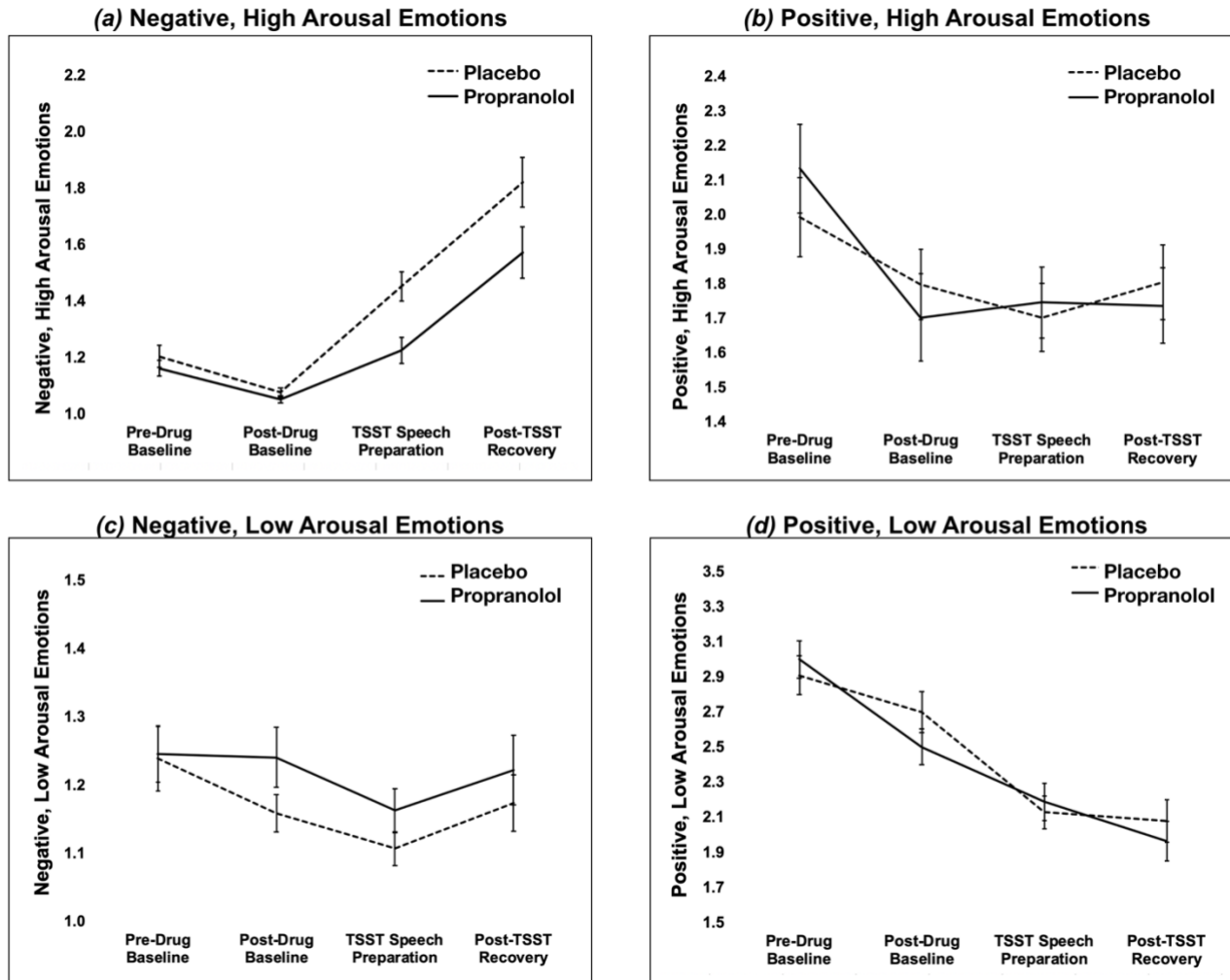


# CONSORT

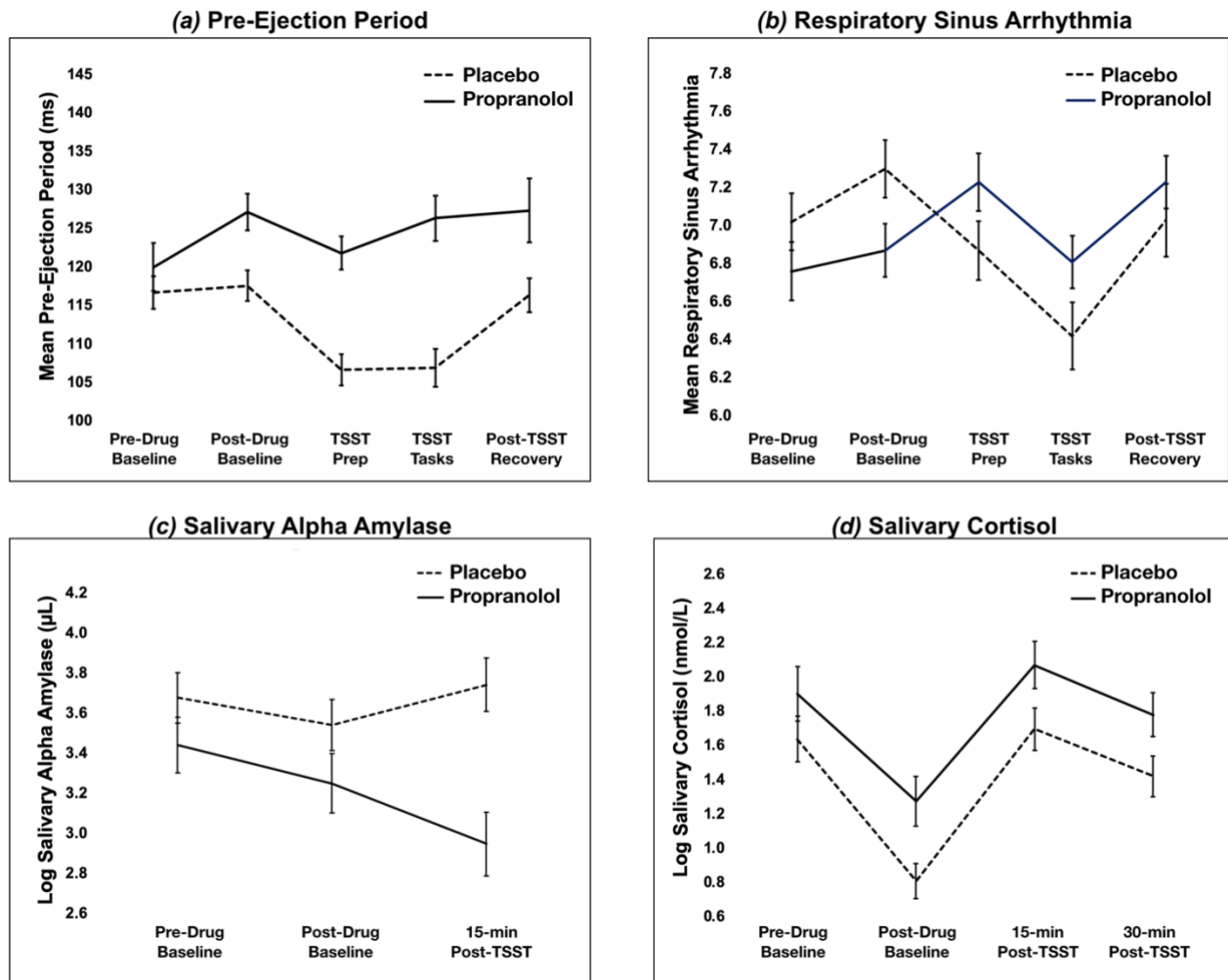
TRANSPARENT REPORTING of TRIALS

## CONSORT 2010 Flow Diagram





**Figure S1.** Findings showing effects on (a) negative, high arousal emotions, (b) positive, high arousal emotions, (c) negative, low arousal emotions, and (d) positive, low arousal emotions across measured timepoints with marginal means and standard errors. See Table 2 in the main text for multilevel models assessing statistical significance.



**Figure S2.** Findings showing effects on (a) pre-ejection period, (b) respiratory sinus arrhythmia, (c) salivary alpha amylase, and (d) salivary cortisol across measured timepoints with marginal means and standard errors. See Table 4 in the main text for multilevel models assessing statistical significance.

**Table S3.** RSA fixed effects unadjusted for HR, with the post-drug baseline (BL2) as the reference category.

| <i>Predictors</i>  | <i>b</i>     | <i>S.E.</i> | <i>p</i>        | <i>Lower<br/>95% CI</i> | <i>Upper<br/>95% CI</i> |
|--|--------------|-------------|-----------------|-------------------------|-------------------------|
| <b>Mean respiratory sinus arrhythmia, unadjusted</b>                                       |              |             |                 |                         |                         |
| <b>Intercept</b>   | <b>7.31</b>  | <b>0.16</b> | <b>&lt;.001</b> | <b>6.99</b>             | <b>7.63</b>             |
| Drug (at BL2)  | -0.22        | 0.23        | .336            | -0.68                   | 0.23                    |
| <b>TSST Prep</b>   | <b>-0.44</b> | <b>0.19</b> | <b>.019</b>     | <b>-0.80</b>            | <b>-0.07</b>            |
| <b>TSST Tasks</b>  | <b>-0.89</b> | <b>0.18</b> | <b>&lt;.001</b> | <b>-1.25</b>            | <b>-0.53</b>            |
| TSST Recovery  | -0.30        | 0.19        | .106            | -0.67                   | 0.06                    |
| <b>Drug x Prep</b>   | <b>0.58</b>  | <b>0.26</b> | <b>.028</b>     | <b>0.06</b>             | <b>1.10</b>             |
| <b>Drug x TSST</b>   | <b>0.58</b>  | <b>0.26</b> | <b>.028</b>     | <b>0.06</b>             | <b>1.10</b>             |
| Drug x Recovery  | 0.45         | 0.26        | .091            | -0.07                   | 0.97                    |
| <b>Mean respiratory sinus arrhythmia adjusted for all covariates except for heart rate</b> |              |             |                 |                         |                         |
| <b>Intercept</b>   | <b>8.58</b>  | <b>0.73</b> | <b>&lt;.001</b> | <b>7.15</b>             | <b>10.01</b>            |
| Drug (at BL2)  | -0.24        | 0.22        | .275            | -0.68                   | 0.19                    |
| <b>TSST Prep</b>   | <b>-0.43</b> | <b>0.17</b> | <b>.015</b>     | <b>-0.77</b>            | <b>-0.08</b>            |
| <b>TSST Tasks</b>  | <b>-0.88</b> | <b>0.17</b> | <b>&lt;.001</b> | <b>-1.22</b>            | <b>-0.54</b>            |
| TSST Recovery  | -0.29        | 0.18        | .103            | -0.63                   | 0.06                    |
| <b>Drug x Prep</b>   | <b>0.57</b>  | <b>0.25</b> | <b>.022</b>     | <b>0.08</b>             | <b>1.05</b>             |
| <b>Drug x TSST</b>   | <b>0.61</b>  | <b>0.25</b> | <b>.015</b>     | <b>0.12</b>             | <b>1.09</b>             |
| Drug x Recovery  | 0.43         | 0.25        | .083            | -0.06                   | 0.92                    |
| Sex  | -0.01        | 0.16        | .967            | -0.33                   | 0.32                    |
| BMI  | 0.00         | 0.06        | .963            | -0.11                   | 0.12                    |
| SES  | -0.08        | 0.04        | .076            | -0.16                   | 0.01                    |

**Note:** Significant effects ( $p < .05$ ) are bolded. Drug was coded 0=Placebo, 1=Propranolol. “TSST Tasks” are the Speech and Math tasks aggregated. Sex was coded 0=Female, 1=Male. Effects here are unadjusted for heart rate. Even after adjusting for the covariates of Sex, BMI, and SES (parental education), there are significant interaction effects of Drug x TSST that disappear when heart rate is added to the model (see Table 4 in main text).

**Table S4.** Emotion fixed effects, with the pre-drug baseline (BL1) as the reference category.

| <i>Predictors</i>                           | <i>b</i>     | <i>S.E.</i> | <i>p</i>        | <i>Lower<br/>95% CI</i> | <i>Upper<br/>95% CI</i> |
|---|--------------|-------------|-----------------|-------------------------|-------------------------|
| <b>Mean negative, high arousal emotions</b> |              |             |                 |                         |                         |
| <b>Intercept</b>                            | <b>1.28</b>  | <b>0.25</b> | <b>&lt;.001</b> | <b>0.79</b>             | <b>1.76</b>             |
| Drug  | -0.05        | 0.08        | .562            | -0.20                   | 0.11                    |
| <b>Post-Drug BL2</b>                        | <b>-0.13</b> | <b>0.06</b> | <b>.040</b>     | <b>-0.25</b>            | <b>-0.01</b>            |
| <b>TSST Prep</b>                            | <b>0.25</b>  | <b>0.06</b> | <b>&lt;.001</b> | <b>0.13</b>             | <b>0.37</b>             |
| <b>Post-TSST</b>                            | <b>0.62</b>  | <b>0.06</b> | <b>&lt;.001</b> | <b>0.50</b>             | <b>0.74</b>             |
| Drug x BL2                                  | 0.02         | 0.09        | .837            | -0.16                   | 0.19                    |
| Drug x TSST Prep                            | -0.17        | 0.09        | .065            | -0.34                   | 0.01                    |
| <b>Drug x Post-TSST</b>                     | <b>-0.20</b> | <b>0.09</b> | <b>.024</b>     | <b>-0.38</b>            | <b>-0.03</b>            |
| Sex   | 0.09         | 0.06        | .109            | -0.02                   | 0.20                    |
| BMI   | -0.00        | 0.02        | .843            | -0.04                   | 0.04                    |
| SES   | -0.01        | 0.02        | .616            | -0.04                   | 0.02                    |
| <b>Mean negative, low arousal emotions</b>  |              |             |                 |                         |                         |
| <b>Intercept</b>                            | <b>0.96</b>  | <b>0.19</b> | <b>&lt;.001</b> | <b>0.59</b>             | <b>1.34</b>             |
| Drug  | 0.02         | 0.06        | .732            | -0.09                   | 0.13                    |
| Post-Drug BL2                               | -0.07        | 0.04        | .091            | -0.15                   | 0.01                    |
| <b>TSST Prep</b>                            | <b>-0.12</b> | <b>0.04</b> | <b>.003</b>     | <b>-0.21</b>            | <b>-0.04</b>            |
| Post-TSST                                   | -0.06        | 0.04        | .174            | -0.14                   | 0.03                    |
| Drug x BL2                                  | 0.06         | 0.06        | .313            | -0.06                   | 0.18                    |
| Drug x TSST Prep                            | 0.04         | 0.06        | .546            | -0.08                   | 0.16                    |
| Drug x Post-TSST                            | 0.03         | 0.06        | .609            | -0.09                   | 0.15                    |
| Sex   | 0.04         | 0.04        | .414            | -0.05                   | 0.12                    |
| BMI   | 0.00         | 0.02        | .989            | -0.03                   | 0.03                    |
| SES   | 0.02         | 0.01        | .174            | -0.01                   | 0.04                    |
| <b>Mean positive, high arousal emotions</b> |              |             |                 |                         |                         |
| <b>Intercept</b>                            | <b>1.97</b>  | <b>0.60</b> | <b>.001</b>     | <b>0.79</b>             | <b>3.15</b>             |
| Drug  | 0.14         | 0.16        | .376            | -0.17                   | 0.44                    |
| <b>Post-Drug BL2</b>                        | <b>-0.25</b> | <b>0.09</b> | <b>.006</b>     | <b>-0.42</b>            | <b>-0.07</b>            |
| <b>TSST Prep</b>                            | <b>-0.29</b> | <b>0.09</b> | <b>.001</b>     | <b>-0.47</b>            | <b>-0.12</b>            |
| <b>Post-TSST</b>                            | <b>-0.19</b> | <b>0.09</b> | <b>.033</b>     | <b>-0.36</b>            | <b>-0.02</b>            |
| Drug x BL2                                  | -0.09        | 0.13        | .496            | -0.34                   | 0.17                    |
| Drug x TSST Prep                            | -0.10        | 0.13        | .449            | -0.35                   | 0.16                    |
| Drug x Post-TSST                            | -0.21        | 0.13        | .107            | -0.46                   | 0.05                    |
| <b>Sex</b>                                  | <b>0.33</b>  | <b>0.14</b> | <b>.017</b>     | <b>0.06</b>             | <b>0.59</b>             |
| BMI   | -0.03        | 0.05        | .562            | -0.12                   | 0.07                    |
| SES   | -0.01        | 0.04        | .827            | -0.08                   | 0.06                    |
| <b>Mean positive, low arousal emotions</b>  |              |             |                 |                         |                         |
| <b>Intercept</b>                            | <b>2.72</b>  | <b>0.56</b> | <b>&lt;.001</b> | <b>1.61</b>             | <b>3.82</b>             |
| Drug  | 0.10         | 0.16        | .526            | -0.21                   | 0.40                    |
| <b>Post-Drug BL2</b>                        | <b>-0.22</b> | <b>0.10</b> | <b>.034</b>     | <b>-0.42</b>            | <b>-0.02</b>            |
| <b>TSST Prep</b>                            | <b>-0.78</b> | <b>0.10</b> | <b>&lt;.001</b> | <b>-0.99</b>            | <b>-0.58</b>            |
| <b>Post-TSST</b>                            | <b>-0.83</b> | <b>0.10</b> | <b>&lt;.001</b> | <b>-1.03</b>            | <b>-0.63</b>            |
| Drug x BL2                                  | -0.28        | 0.15        | .063            | -0.57                   | 0.02                    |
| Drug x TSST Prep                            | -0.03        | 0.15        | .827            | -0.33                   | 0.26                    |
| Drug x Post-TSST                            | -0.19        | 0.15        | .218            | -0.48                   | 0.11                    |
| Sex   | 0.09         | 0.13        | .457            | -0.15                   | 0.34                    |
| BMI   | -0.07        | 0.05        | .149            | -0.16                   | 0.02                    |
| SES   | 0.01         | 0.03        | .710            | -0.05                   | 0.08                    |

**Note:** Significant effects ( $p < .05$ ) are bolded. Drug was coded 0=Placebo, 1=Propranolol. Sex was coded 0=Female, 1=Male. TSST Prep effects reflect emotion ratings immediately after the 2-min TSST preparatory period before giving the speech. Post-TSST effects reflect emotion ratings given immediately after the TSST completed.

**Table S5.** Physiology fixed effects, with the pre-drug baseline (BL1) as the reference category.

| <i>Predictors</i>                             | <i>b</i>      | <i>S.E.</i>  | <i>p</i>        | <i>Lower<br/>95% CI</i> | <i>Upper<br/>95% CI</i> |
|---|---------------|--------------|-----------------|-------------------------|-------------------------|
| <b>Mean pre-ejection period</b>               |               |              |                 |                         |                         |
| <b>Intercept</b>                              | <b>129.96</b> | <b>10.83</b> | <b>&lt;.001</b> | <b>108.67</b>           | <b>151.26</b>           |
| Drug  | 4.69          | 3.29         | .156            | -1.78                   | 11.15                   |
| Post-Drug BL2                                 | 1.63          | 2.29         | .476            | -2.86                   | 6.13                    |
| <b>TSST Prep</b>                              | <b>-9.09</b>  | <b>2.30</b>  | <b>&lt;.001</b> | <b>-13.62</b>           | <b>-4.56</b>            |
| <b>TSST Tasks</b>                             | <b>-9.09</b>  | <b>2.29</b>  | <b>&lt;.001</b> | <b>-13.59</b>           | <b>-4.59</b>            |
| TSST Recovery                                 | -0.11         | 2.31         | .963            | -4.66                   | 4.44                    |
| Drug x BL2                                    | 4.60          | 3.37         | .173            | -2.03                   | 11.22                   |
| <b>Drug x Prep</b>                            | <b>9.59</b>   | <b>3.40</b>  | <b>.005</b>     | <b>2.90</b>             | <b>16.27</b>            |
| <b>Drug x TSST</b>                            | <b>14.30</b>  | <b>3.36</b>  | <b>&lt;.001</b> | <b>7.69</b>             | <b>20.91</b>            |
| <b>Drug x Recovery</b>                        | <b>6.96</b>   | <b>3.39</b>  | <b>.041</b>     | <b>0.29</b>             | <b>13.63</b>            |
| <b>Sex</b>                                    | <b>5.07</b>   | <b>2.50</b>  | <b>.046</b>     | <b>0.15</b>             | <b>9.99</b>             |
| BMI   | 0.33          | 0.91         | .720            | -1.47                   | 2.12                    |
| SES   | -1.04         | 0.64         | .107            | -2.29                   | 0.21                    |
| <b>Mean respiratory sinus arrhythmia</b>      |               |              |                 |                         |                         |
| <b>Intercept</b>                              | <b>11.04</b>  | <b>0.69</b>  | <b>&lt;.001</b> | <b>9.68</b>             | <b>12.40</b>            |
| Drug  | -0.22         | 0.20         | .269            | -0.61                   | 0.17                    |
| Post-Drug BL2                                 | 0.17          | 0.16         | .275            | -0.14                   | 0.48                    |
| TSST Prep                                     | 0.31          | 0.16         | .061            | -0.01                   | 0.63                    |
| <b>TSST Tasks</b>                             | <b>0.37</b>   | <b>0.19</b>  | <b>.048</b>     | <b>0.00</b>             | <b>0.74</b>             |
| TSST Recovery                                 | -0.02         | 0.16         | .903            | -0.33                   | 0.29                    |
| Drug x BL2                                    | -0.03         | 0.22         | .878            | -0.48                   | 0.41                    |
| Drug x Prep                                   | 0.08          | 0.23         | .737            | -0.38                   | 0.53                    |
| Drug x TSST                                   | -0.21         | 0.24         | .397            | -0.68                   | 0.27                    |
| Drug x Recovery                               | 0.13          | 0.23         | .560            | -0.31                   | 0.58                    |
| <b>Heart rate</b>                             | <b>-0.04</b>  | <b>0.01</b>  | <b>&lt;.001</b> | <b>-0.05</b>            | <b>-0.04</b>            |
| Sex   | -0.23         | 0.14         | .103            | -0.51                   | 0.05                    |
| BMI   | 0.00          | 0.05         | .930            | -0.10                   | 0.10                    |
| SES   | -0.06         | 0.04         | .130            | -0.13                   | 0.02                    |
| <b>Log-transformed salivary alpha-amylase</b> |               |              |                 |                         |                         |
| <b>Intercept</b>                              | <b>2.38</b>   | <b>0.78</b>  | <b>.003</b>     | <b>0.85</b>             | <b>3.91</b>             |
| Drug  | -0.22         | 0.20         | .261            | -0.62                   | 0.17                    |
| Post-Drug BL2                                 | -0.13         | 0.13         | .290            | -0.38                   | 0.11                    |
| Post-TSST T15                                 | 0.07          | 0.12         | .601            | -0.18                   | 0.31                    |
| Drug x BL2                                    | -0.03         | 0.18         | .866            | -0.38                   | 0.32                    |
| <b>Drug x T15</b>                             | <b>-0.53</b>  | <b>0.18</b>  | <b>.003</b>     | <b>-0.88</b>            | <b>-0.18</b>            |
| Sex   | 0.12          | 0.21         | .564            | -0.30                   | 0.55                    |
| Menses Cycle                                  | 0.04          | 0.07         | .570            | -0.10                   | 0.18                    |
| BMI   | -0.07         | 0.06         | .280            | -0.19                   | 0.05                    |
| SES   | 0.08          | 0.05         | .095            | -0.01                   | 0.16                    |
| <b>Log-transformed salivary cortisol</b>      |               |              |                 |                         |                         |
| <b>Intercept</b>                              | <b>1.28</b>   | <b>0.65</b>  | <b>.050</b>     | <b>0.01</b>             | <b>2.55</b>             |
| Drug  | 0.29          | 0.19         | .129            | -0.08                   | 0.65                    |
| <b>Post-Drug BL2</b>                          | <b>-0.81</b>  | <b>0.14</b>  | <b>&lt;.001</b> | <b>-1.08</b>            | <b>-0.54</b>            |
| Post-TSST T15                                 | 0.05          | 0.14         | .710            | -0.22                   | 0.33                    |
| Post-TSST T30                                 | -0.22         | 0.14         | .120            | -0.49                   | 0.06                    |
| Drug x BL2                                    | 0.16          | 0.20         | .422            | -0.24                   | 0.56                    |
| Drug x T15                                    | 0.10          | 0.20         | .630            | -0.30                   | 0.49                    |
| Drug x T30                                    | 0.08          | 0.20         | .704            | -0.32                   | 0.47                    |
| Sex   | 0.30          | 0.18         | .092            | -0.05                   | 0.65                    |
| Menses Cycle                                  | 0.01          | 0.06         | .834            | -0.10                   | 0.13                    |
| BMI   | 0.05          | 0.05         | .291            | -0.05                   | 0.15                    |
| SES   | 0.01          | 0.04         | .839            | -0.07                   | 0.08                    |

**Note:** Significant effects ( $p < .05$ ) are bolded. Drug was coded 0=Placebo, 1=Propranolol. "TSST Tasks" are the Speech and Math tasks aggregated. Sex was coded 0=Female, 1=Male.



**Table S6.** Heart rate fixed effects with pre-drug baseline (BL1) vs. post-drug baseline (BL2) as the reference.

| <i>Predictors</i>  | <i>b</i>      | <i>S.E.</i> | <i>p</i>        | <i>Lower<br/>95% CI</i> | <i>Upper<br/>95% CI</i> |
|--|---------------|-------------|-----------------|-------------------------|-------------------------|
| <b>Mean heart rate with respect to BL1 or pre-drug baseline</b>  |               |             |                 |                         |                         |
| <b>Intercept</b>   | <b>61.26</b>  | <b>8.21</b> | <b>&lt;.001</b> | <b>45.11</b>            | <b>77.40</b>            |
| Drug   | 1.18          | 2.22        | .597            | -3.19                   | 5.54                    |
| Post-Drug BL2  | -2.40         | 1.39        | .084            | -5.13                   | 0.32                    |
| <b>TSST Prep</b>   | <b>10.18</b>  | <b>1.39</b> | <b>&lt;.001</b> | <b>7.45</b>             | <b>12.90</b>            |
| <b>TSST Tasks</b>  | <b>21.95</b>  | <b>1.38</b> | <b>&lt;.001</b> | <b>19.24</b>            | <b>24.66</b>            |
| TSST Recovery  | -0.51         | 1.40        | .713            | -3.26                   | 2.23                    |
| Drug x BL2   | -1.44         | 1.99        | .471            | -5.36                   | 2.48                    |
| <b>Drug x Prep</b>   | <b>-11.71</b> | <b>1.99</b> | <b>&lt;.001</b> | <b>-15.63</b>           | <b>-7.79</b>            |
| <b>Drug x TSST</b>   | <b>-18.92</b> | <b>1.99</b> | <b>&lt;.001</b> | <b>-22.82</b>           | <b>-15.01</b>           |
| <b>Drug x Recovery</b>   | <b>-7.12</b>  | <b>2.00</b> | <b>&lt;.001</b> | <b>-11.05</b>           | <b>-3.19</b>            |
| Sex  | <b>-4.81</b>  | <b>1.85</b> | <b>.011</b>     | <b>-8.44</b>            | <b>-1.18</b>            |
| BMI  | 0.25          | 0.67        | .711            | -1.06                   | 1.56                    |
| SES  | 0.47          | 0.49        | .335            | -0.48                   | 1.43                    |
| <b>Mean heart rate with respect to BL2 or post-drug baseline</b> |               |             |                 |                         |                         |
| <b>Intercept</b>   | <b>58.64</b>  | <b>8.90</b> | <b>&lt;.001</b> | <b>41.13</b>            | <b>76.14</b>            |
| Drug   | -0.18         | 2.35        | .939            | -4.79                   | 4.43                    |
| <b>TSST Prep</b>   | <b>12.67</b>  | <b>1.43</b> | <b>&lt;.001</b> | <b>9.85</b>             | <b>15.49</b>            |
| <b>TSST Tasks</b>  | <b>24.43</b>  | <b>1.42</b> | <b>&lt;.001</b> | <b>21.63</b>            | <b>27.23</b>            |
| TSST Recovery  | 2.08          | 1.44        | .151            | -0.76                   | 4.92                    |
| <b>Drug x Prep</b>   | <b>-10.37</b> | <b>2.04</b> | <b>&lt;.001</b> | <b>-14.39</b>           | <b>-6.35</b>            |
| <b>Drug x TSST</b>   | <b>-17.56</b> | <b>2.04</b> | <b>&lt;.001</b> | <b>-21.56</b>           | <b>-13.56</b>           |
| <b>Drug x Recovery</b>   | <b>-5.87</b>  | <b>2.05</b> | <b>.005</b>     | <b>-9.90</b>            | <b>-1.84</b>            |
| Sex  | <b>-5.27</b>  | <b>2.01</b> | <b>.010</b>     | <b>-9.21</b>            | <b>-1.32</b>            |
| BMI  | 0.18          | 0.72        | .807            | -1.24                   | 1.60                    |
| SES  | 0.50          | 0.53        | .346            | -0.54                   | 1.54                    |

**Note:** Significant effects ( $p < .05$ ) are bolded. Drug was coded 0=Placebo, 1=Propranolol. “TSST Tasks” are the Speech and Math tasks aggregated. Sex was coded 0=Female, 1=Male.

**Table S7.** Unadjusted fixed effects for all outcomes, provided for future meta-analyses.

| <i>Predictors</i>   | <i>b</i>      | <i>S.E.</i> | <i>p</i>        | <i>Lower<br/>95% CI</i> | <i>Upper<br/>95% CI</i> |
|---|---------------|-------------|-----------------|-------------------------|-------------------------|
| <b>Mean negative, high arousal emotions relative to BL2</b> |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>1.08</b>   | <b>0.06</b> | <b>&lt;.001</b> | <b>0.96</b>             | <b>1.19</b>             |
| Drug  | -0.02         | 0.08        | .778            | -0.19                   | 0.14                    |
| <b>TSST Prep</b>  | <b>0.38</b>   | <b>0.07</b> | <b>&lt;.001</b> | <b>0.24</b>             | <b>0.51</b>             |
| <b>Post-TSST</b>  | <b>0.75</b>   | <b>0.07</b> | <b>&lt;.001</b> | <b>0.61</b>             | <b>0.88</b>             |
| Drug x TSST Prep  | -0.18         | 0.10        | .067            | -0.38                   | 0.01                    |
| <b>Drug x Post-TSST</b>                                     | <b>-0.22</b>  | <b>0.10</b> | <b>.027</b>     | <b>-0.42</b>            | <b>-0.03</b>            |
| <b>Mean negative, low arousal emotions relative to BL2</b>  |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>1.16</b>   | <b>0.04</b> | <b>&lt;.001</b> | <b>1.09</b>             | <b>1.24</b>             |
| Drug  | 0.08          | 0.05        | .144            | -0.03                   | 0.18                    |
| TSST Prep   | -0.06         | 0.04        | .167            | -0.14                   | 0.02                    |
| Post-TSST   | 0.01          | 0.04        | .775            | -0.07                   | 0.09                    |
| Drug x TSST Prep  | -0.02         | 0.06        | .731            | -0.13                   | 0.09                    |
| Drug x Post-TSST  | -0.03         | 0.06        | .651            | -0.14                   | 0.09                    |
| <b>Mean positive, high arousal emotions relative to BL2</b> |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>1.74</b>   | <b>0.11</b> | <b>&lt;.001</b> | <b>1.53</b>             | <b>1.94</b>             |
| Drug  | 0.06          | 0.15        | .684            | -0.24                   | 0.36                    |
| TSST Prep   | -0.03         | 0.09        | .717            | -0.21                   | 0.15                    |
| Post-TSST   | 0.07          | 0.09        | .459            | -0.11                   | 0.25                    |
| Drug x TSST Prep  | -0.02         | 0.13        | .886            | -0.28                   | 0.24                    |
| Drug x Post-TSST  | -0.13         | 0.13        | .328            | -0.39                   | 0.13                    |
| <b>Mean positive, low arousal emotions relative to BL2</b>  |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>2.69</b>   | <b>0.11</b> | <b>&lt;.001</b> | <b>2.48</b>             | <b>2.9</b>              |
| Drug  | -0.19         | 0.16        | .225            | -0.49                   | 0.12                    |
| <b>TSST Prep</b>  | <b>-0.56</b>  | <b>0.10</b> | <b>&lt;.001</b> | <b>-0.76</b>            | <b>-0.36</b>            |
| <b>Post-TSST</b>  | <b>-0.61</b>  | <b>0.10</b> | <b>&lt;.001</b> | <b>-0.81</b>            | <b>-0.41</b>            |
| Drug x TSST Prep  | 0.25          | 0.15        | .096            | -0.04                   | 0.54                    |
| Drug x Post-TSST  | 0.09          | 0.15        | .549            | -0.20                   | 0.38                    |
| <b>Mean challenge appraisals relative to TSST Prep</b>      |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>4.66</b>   | <b>0.14</b> | <b>&lt;.001</b> | <b>4.39</b>             | <b>4.93</b>             |
| Drug  | 0.06          | 0.20        | .773            | -0.34                   | 0.45                    |
| <b>Post-TSST</b>  | <b>-0.55</b>  | <b>0.12</b> | <b>&lt;.001</b> | <b>-0.79</b>            | <b>-0.32</b>            |
| Drug x Post-TSST  | -0.10         | 0.18        | .574            | -0.45                   | 0.25                    |
| <b>Mean threat appraisals relative to TSST Prep</b>         |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>4.10</b>   | <b>0.15</b> | <b>&lt;.001</b> | <b>3.81</b>             | <b>4.39</b>             |
| Drug  | -0.27         | 0.22        | .206            | -0.70                   | 0.15                    |
| Post-TSST   | 0.04          | 0.12        | .754            | -0.20                   | 0.27                    |
| Drug x Post-TSST  | 0.11          | 0.17        | .510            | -0.23                   | 0.45                    |
| <b>Mean negative appraisals relative to TSST Prep</b>       |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>1.46</b>   | <b>0.08</b> | <b>&lt;.001</b> | <b>1.31</b>             | <b>1.62</b>             |
| Drug  | -0.05         | 0.11        | .658            | -0.27                   | 0.17                    |
| <b>Post-TSST</b>  | <b>0.38</b>   | <b>0.07</b> | <b>&lt;.001</b> | <b>0.24</b>             | <b>0.52</b>             |
| Drug x Post-TSST  | -0.17         | 0.10        | .112            | -0.37                   | 0.04                    |
| <b>Mean pre-ejection period relative to BL2</b>             |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>117.55</b> | <b>2.40</b> | <b>&lt;.001</b> | <b>112.84</b>           | <b>122.26</b>           |
| <b>Drug</b>   | <b>9.93</b>   | <b>3.52</b> | <b>.005</b>     | <b>3.01</b>             | <b>16.85</b>            |
| <b>TSST Prep</b>  | <b>-10.84</b> | <b>2.53</b> | <b>&lt;.001</b> | <b>-15.82</b>           | <b>-5.86</b>            |
| <b>TSST Tasks</b>   | <b>-10.75</b> | <b>2.52</b> | <b>&lt;.001</b> | <b>-15.69</b>           | <b>-5.80</b>            |
| TSST Recovery   | -1.69         | 2.55        | .509            | -6.70                   | 3.33                    |
| Drug x Prep   | 4.84          | 3.72        | .194            | -2.47                   | 12.15                   |
| <b>Drug x TSST</b>  | <b>9.58</b>   | <b>3.68</b> | <b>&lt;.001</b> | <b>2.35</b>             | <b>16.81</b>            |
| Drug x Recovery   | 2.10          | 3.72        | .572            | -5.20                   | 9.41                    |
| <b>Mean respiratory sinus arrhythmia relative to BL2</b>    |               |             |                 |                         |                         |
| <b>Intercept</b>  | <b>7.31</b>   | <b>0.16</b> | <b>&lt;.001</b> | <b>6.99</b>             | <b>7.63</b>             |
| Drug  | -0.22         | 0.23        | .336            | -0.68                   | 0.23                    |
| <b>TSST Prep</b>  | <b>-0.44</b>  | <b>0.19</b> | <b>.019</b>     | <b>-0.80</b>            | <b>-0.07</b>            |

|   |               |             |                 |               |              |
|---|---------------|-------------|-----------------|---------------|--------------|
| <b>TSST Tasks</b>   | <b>-0.89</b>  | <b>0.18</b> | <b>&lt;.001</b> | <b>-1.25</b>  | <b>-0.53</b> |
| TSST Recovery   | -0.30         | 0.19        | .106            | -0.67         | 0.06         |
| <b>Drug x Prep</b>  | <b>0.58</b>   | <b>0.26</b> | <b>.028</b>     | <b>0.06</b>   | <b>1.10</b>  |
| <b>Drug x TSST</b>  | <b>0.58</b>   | <b>0.26</b> | <b>.028</b>     | <b>0.06</b>   | <b>1.10</b>  |
| Drug x Recovery   | 0.45          | 0.26        | .091            | -0.07         | 0.97         |
| <b>Log-transformed salivary alpha-amylase relative to BL2</b> |               |             |                 |               |              |
| <b>Intercept</b>  | <b>44.76</b>  | <b>5.26</b> | <b>&lt;.001</b> | <b>34.38</b>  | <b>55.15</b> |
| Drug  | -7.48         | 7.54        | .322            | -22.37        | 7.40         |
| Post-TSST T15   | 7.27          | 4.93        | .143            | -2.48         | 17.01        |
| <b>Drug x T15</b>   | <b>-15.63</b> | <b>7.01</b> | <b>.027</b>     | <b>-29.46</b> | <b>-1.80</b> |
| <b>Log-transformed salivary cortisol relative to BL2</b>      |               |             |                 |               |              |
| <b>Intercept</b>  | <b>3.06</b>   | <b>0.88</b> | <b>.001</b>     | <b>1.32</b>   | <b>4.80</b>  |
| Drug  | 2.16          | 1.28        | .093            | -0.36         | 4.68         |
| <b>Post-TSST T15</b>  | <b>3.92</b>   | <b>0.10</b> | <b>&lt;.001</b> | <b>1.96</b>   | <b>5.89</b>  |
| Post-TSST T30   | 1.92          | 1.00        | .057            | -0.05         | 3.90         |
| Drug x T15  | 1.57          | 1.44        | .277            | -1.27         | 4.40         |
| Drug x T30  | 0.59          | 1.44        | .684            | -2.25         | 3.43         |

**Note:** Please reach out to the first author (JKM) or senior author (KAM) if you need more details or other effect information for meta-analyses.

**Table S8.** Bivariate correlations between emotions and appraisals within the TSST Prep and TSST Task timepoints.

|                   | During TSST Prep       |        |       |       |                          |         |          | Immediately after TSST Speech and Math |        |       |        |                          |         |          |
|-------------------|------------------------|--------|-------|-------|--------------------------|---------|----------|--|--------|-------|--------|--------------------------|---------|----------|
|                   | Self-Reported Emotions |        |       |       | Self-Reported Appraisals |         |          | Self-Reported Emotions                 |        |       |        | Self-Reported Appraisals |         |          |
|                   | NegHi                  | NegLo  | PosHi | PosLo | Challenge                | Threat  | Negative | NegHi                                  | NegLo  | PosHi | PosLo  | Challenge                | Threat  | Negative |
| <i>Emotions</i>   |                        |        |       |       |                          |         |          |  |        |       |        |                          |         |          |
| NegHi             | -                      | .49*** | .02   | -.23* | -.39***                  | .68***  | .69***   | -                                      | .54*** | -.10  | -.28** | -.50***                  | .59***  | .79***   |
| NegLo             |                        | -      | .03   | -.09  | -.35***                  | .28**   | .50***   |  | -      | -.22* | -.26*  | -.42***                  | .15     | .47***   |
| PosHi             |                        |        | -     | .66*  | .32**                    | -.31**  | -.08     |  |        | -     | .70*** | .37***                   | -.27**  | -.12     |
| PosLo             |                        |        |       | -     | .40***                   | -.48*** | -.21     |  |        |       | -      | .50***                   | -.36*** | -.26*    |
| <i>Appraisals</i> |                        |        |       |       |                          |         |          |  |        |       |        |                          |         |          |
| Challenge         |                        |        |       |       | -                        | -.43*** | -.36***  |  |        |       |        | -                        | -.32*** | -.40***  |
| Threat            |                        |        |       |       |                          | -       | .57***   |  |        |       |        |                          | -       | .58***   |

**Note:** NegHi= negative, high arousal emotions; NegLo= negative, low arousal emotions; PosHi= positive, high arousal emotions; PosLo= positive, low arousal emotions; Challenge= challenge appraisals; Threat= threat appraisals; Negative= negative internal and external evaluative appraisals.

\*\*\* $p < .001$ , \*\* $p < .01$ , \* $p < .05$

**Table S9.** Bivariate correlations between physiological markers in response to the TSST.

|     | RSA  | sAA   | Cortisol |
|-----|------|-------|----------|
| PEP | .26* | -.27* | .02      |
| RSA | -    | -.24* | -.11     |
| sAA |      | -     | -.13     |

**Note:** These measures reflect the raw timepoint inter-correlations between markers' peak response to the stressor. For autonomic physiology measures of pre-ejection period (PEP) and respiratory sinus arrhythmia (RSA), this was during the TSST speech and math tasks. For salivary markers, this was 15-min post-TSST for salivary alpha amylase (sAA) and 30-min post-TSST for salivary cortisol. Both PEP and RSA decreased under stress (indicative of greater effort or "stress") whereas sAA and cortisol tended to increase. As might be expected, we found a small correlation between PEP and RSA. Similarly, greater sAA peak was associated with greater PEP and RSA decreases in response to the TSST. Cortisol was unrelated to any other markers. \* $p < .05$