MAXED Registered Report Doc

# Results

## Preliminary Analysis

*We will provide sample descriptive statistics for both ED and HC groups on variables of interest (e.g., age, ED diagnosis, BMI, compulsive exercise, Eating Disorder Examination subscales).*

Descriptive statistics for the sample are presented in [Table 1](#tbl-descriptives). Overall, the ED and HC group were well matched on key demographic variables as well as free-living activity levels. The ED group had higher levels of disordered eating symptoms and higher CET Total, CET Weight Control, and CET Avoidance scores compared to the HC group.

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| Table 1: Descriptive Statistics Across Eating Disorder (ED) and Healthy Control (HC) Groups  Descriptive Statistics Across Eating Disorder (ED) and Healthy Control (HC) Groups   | Variable | ED | HC | t value | p | Cohen’s d | | --- | --- | --- | --- | --- | --- | | Asexual | 1 | 0 | NA | NA | NA | | Bisexual/Pansexual | 6 | 6 | NA | NA | NA | | Lesbian/Gay | 2 | 2 | NA | NA | NA | | Heterosexual | 11 | 10 | NA | NA | NA | | Sex Orientation Not Reported | 0 | 2 | NA | NA | NA | | Woman | 20 | 17 | NA | NA | NA | | Nonbinary | 0 | 1 | NA | NA | NA | | Unsure | 0 | 0 | NA | NA | NA | | Gender Not Reported | 0 | 2 | NA | NA | NA | | White | 16 | 16 | NA | NA | NA | | Black/African American | 0 | 2 | NA | NA | NA | | Asian | 3 | 1 | NA | NA | NA | | Hispanic | 2 | 0 | NA | NA | NA | | Middle Eastern | 0 | 1 | NA | NA | NA | | South Asian | 1 | 0 | NA | NA | NA | | Southeast Asian | 0 | 0 | NA | NA | NA | | Age | 19.05 (2.56) | 19.91 (2.04) | -1.21 | 2.35e-01 | -0.38 | | BMI | 22.43 (3.11) | 22.32 (2.16) | -0.83 | 4.10e-01 | -0.26 | | Weight Suppression | 8.34 (12.27) | 3.79 (5.09) | 1.63 | 1.17e-01 | 0.53 | | EDE Global | 2.06 (0.68) | 0.24 (0.24) | 6.61 | 4.65e-07 | 2.09 | | EDE Restraint | 1.77 (1.12) | 0.02 (0.06) | 6.51 | 1.68e-06 | 2.20 | | EDE Eating Concern | 1.20 (0.83) | 0.05 (0.09) | 3.95 | 3.93e-04 | 1.30 | | EDE Shape Concern | 2.39 (1.47) | 0.55 (0.58) | 5.32 | 1.02e-05 | 1.68 | | EDE Weight Concern | 2.86 (1.08) | 0.35 (0.50) | 6.12 | 1.47e-06 | 1.99 | | LPA | 30.96 (23.41) | 51.53 (31.63) | -1.28 | 2.12e-01 | -0.45 | | MVPA | 27.80 (16.19) | 46.16 (23.51) | -0.07 | 9.44e-01 | -0.03 | | Distance | 5.03 (1.42) | 4.96 (1.79) | -0.38 | 7.05e-01 | -0.15 | | Karvonen Max Intensity | 49.19 (13.55) | 39.34 (20.97) | 1.08 | 2.89e-01 | 0.35 | | Max % HR | 68.00 (11.20) | 62.73 (12.93) | 0.81 | 4.22e-01 | 0.26 | | Average % HR | 63.95 (11.67) | 57.05 (10.83) | 1.04 | 3.06e-01 | 0.33 | | DFM | 2.04 (0.88) | 2.36 (0.83) | -0.81 | 4.24e-01 | -0.26 | | FAMB ANR | 2.86 (1.21) | 3.02 (1.21) | 0.90 | 3.73e-01 | 0.29 | | FAMB APR | 2.31 (0.94) | 2.35 (0.80) | 1.14 | 2.61e-01 | 0.37 | | FAMB SPR | 1.34 (0.61) | 1.24 (0.20) | 0.75 | 4.60e-01 | 0.24 | | FAMB SNR | 1.95 (1.25) | 1.82 (0.90) | 1.07 | 2.91e-01 | 0.34 | | EDS | 46.43 (19.65) | 45.09 (14.33) | 2.01 | 5.29e-02 | 0.65 | | CET | 11.59 (3.29) | 9.05 (3.72) | 3.26 | 2.48e-03 | 1.06 | | CET Avoidance | 1.12 (0.93) | 1.05 (0.95) | 2.85 | 7.26e-03 | 0.93 | | CET Weight Control | 2.97 (1.02) | 1.31 (1.18) | 4.59 | 5.46e-05 | 1.49 | | CET Mood | 2.83 (1.72) | 3.33 (0.93) | 0.10 | 9.21e-01 | 0.03 | | CET Lack of Enjoyment | 2.57 (1.78) | 1.73 (0.96) | 1.35 | 1.94e-01 | 0.53 | | CET Rigid | 2.10 (1.65) | 1.64 (1.35) | 1.62 | 1.14e-01 | 0.53 | |

We also compared affect ratings and disordered eating urges before and after milkshake ingestion on Day A to clarify the degree to which these variables were impacted my milkshake ingestion. Results are presented in Supplemental **?@tbl-milkshake**. Individuals with EDs reported feeling increased enthusiasm and decreases in fatigue after milkshake ingestion, along with increased urges to restrict, vomit, and exercise.

## **Aim 1: Feasiblity**

*We will confirm feasibility of our exercise-based tasks via a) study dropout at all timepoints, b) adverse events, c) completion rates of exercise task on Day B, d) completion rates of milkshake task across ED and HC participants. Over the course of the study, we expect both ED and HC groups to meet thresholds of < 20% dropout, zero adverse events, and > 80% task completion.*

Full study flow is outlined in Supplemental [Table 3](#tbl-aim1). There were 321 total screenings completed. Of these, 33 were ineligible and 70 went on to complete intakes. Of those who were eligible after intake, 15 chose not to enroll, and the most common reason for not enrolling was cited as time constraints. Ultimately, 39/40 individuals who enrolled in the study completed all study visits. There were no serious adverse events during the study. One participant became lightheaded after blood draw, but this resolved quickly with rest. 100% of participants who engaged in the Day B exercise task completed the task. On Day both days A and C, 97% participants completed drinking the milkshake, with one participant not completing the shake on each day. This was a different participant on Day A vs. Day C. In once instance, the participant finished 31% of the milkshake, in the other instance, the participant finished 63% of the milkshake.

## **Aim 2: Variability in Exercise Response**

*We will characterize changes during exercise in state body image, mood, and biological markers in both ED and HC groups; we will specifically characterize mean levels of, and variability in, biobehavioral response to exercise across the ED and HC groups. We will evaluate exercise-induced changes in DA, 5-HT, BDNF, leptin, and eCB biomarkers for the Prescribed Exercise Task. Shifts in affect, body image, and biomarkers will be evaluated descriptively with measures of central tendency, skew, and variance. We will further characterize shifts in affect and body image through linear mixed effect models.*

Specific models tested are noted in [Table 2](#tbl-params).

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| Table 2: General Models and Parameters   | Model Name | Parameters | | --- | --- | | **Overall Model: Affect and Body Image Variables** | DV ~ 1 + Age + Group + Time + BMI\*Condition + Time\*Condition + Time\*Group\*Condition + (1+Time | | **Within ED: Affect and Body Image Variables** | DV ~ 1 + Age + Time + BMI\*Condition + Time\*Condition + Time\*Condition + (1+Time | | **Overall Biomarker Model** | Biomarker ~ 1 + Age + Group + Time + BMI\*Condition + Time\*Condition + (1 + Time | | **Within ED: Biomarkers** | Biomarker ~ 1 + Age + Time + BMI\*Condition + Time\*Condition + (1 + Time | | **Heterogeneity of Variance across Groups in Exercise Response** | DV ~ 1 + Age + Group + Time + Time x Group, random = list(id = pdDiag(form = ~ Group)), weights = varIdent(form = ~ 1 | |

We estimated change over time using descriptives, and also ran overall and within ED models using the lme4 package. To evaluate heterogeneity of variance, we incorporated a random effect of group into a model with age, time, group, and group x time fixed effects. We then compared model fit of this model to the model without a random effect of group. To examine potential heterogeneity of within person, a level-1 random effect was then incorporated into the model and compared against a model with between-person (level 2) random effects only.

### Affect

#### Descriptives

Affective change across group and condition are presented in [Figure 1 (a)](#fig-ChangePlots-1). Visual depiction of raw changes in affect measurements during exercise across groups is presented in Supplemental **?@fig-AffectChange** along with variance in affect across group and condition. Specific values for average levels of change across groups (30 min vs. BL), maximum increases and maximum decreases from baseline, and variance are presented in Supplemental **?@tbl-affectChange**. Patterns of results indicate that individuals in the ED group consistently feel more positive and less negative emotion increases across the 30 mins of exercise. Fatigue increases in the ED group may be delayed, relative to HC.

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| |  | | --- | | (a) Affective Change during Exercise (30min vs BL) | |

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| |  | | --- | | (b) Body Image Change during Exercise (30min vs BL) | |

Figure 1: Description of Body Image and Affect Changes During Exercise

#### Overall Model

Model fit indices for each variable and task are presented in Supplemental **?@tbl-AffectModFit**.

Marginal values indicate that fixed effects specified in the current models are, together, accounting for 4-19% of variance in affect during the course of the task, depending on task and variable. Results from each variable in the overall model (see [Table 2](#tbl-params)) are presented in Supplemental **?@tbl-affect** with estimated marginal means for each timepoint presented in Supplemental **?@fig-affectemm**. Significant Time x Condition interactions indicate that, across both ED and Control groups, participants tended to feel increased fatigue and reduced calmness during exercise, relative to rest.

As noted, the current pilot trial was not sufficiently powered to detect small-to-moderate three-way interactions. One Group x Time x Condition emerged at nominal level of significance (*p* < 0.05) - feeling Crummy in the Self-Paced Task. The ED group exhibited higher negative affect (feeling crummy) in the Rest condition of the Self-Paced Task (i.e. when asked to ingest a milkshake and then rest), which may to be mitigated by the opportunity to exercise (see Supplemental **?@fig-affectemm**). While not detected in this pilot sample, there is also possible trend toward increased enthusiasm in the ED group in the Prescribed Task, relative to a decrease in enthusiasm in the control group.

Evaluations of the between and within subject variance across groups via introducing additional random effects and comparing nested models indicated potentially higher within subject variance in fatigue and calmenss during the Prescribed Task and enthusiasm and crumminess during the Self-Paced Task among the ED group, relative to the HC group (see Supplemental **?@tbl-affectHOV**).

#### Within ED Group Model

Model fit indices for each variable and task are presented in Supplmental **?@tbl-AffectModFit**. Marginal values indicate that fixed effects specified in the current models are, together, accounting for 5-22% of variance in affect during the course of the task, depending on task and variable. Results within the ED group are presented in Supplemental **?@tbl-affectED**. A Time x Condition effect emerged for calmness during the Prescribed Task and fatigue during the Self-Paced Task. Individuals with EDs reported feeling less calm and more fatigued over time during exercise vs. rest. Further, older age was associated with feeling less crummy during both tasks and less Fatigued during the Prescribed task. There were no BMI or BMI x Condition effects, indicating limited impact of BMI on affect during exercise among the ED group.

### Body Image

#### Descriptives

Average levels of change from 0 to 30 minutes is presented in [Figure 1 (b)](#fig-ChangePlots-2). Visual depiction of raw changes in body image changes during exercise across groups is presented in Supplemental **?@fig-BISSChange**, along with variance in body image across groups are presented. All specific values for average levels of change across groups (30 min vs. BL), maximum increases and maximum decreases from baseline, and variance are presented in Supplemental **?@tbl-BISSChange**. Patterns of results indicate that individuals in the ED group consistently feel worse about their bodies, although exercise does have some impact on body image. In all measures, the ED group had greater improvements in body image during exercise, as compared to controls. Change indicators suggest (ED vs. HC Cohen’s d > .2) that individuals with EDs specifically feel better about their weight, looks, and appearance, as well as feeling better on average and feeling better than the average person after self-paced exercise and better on average after prescribed exercise. Effect sizes favored self-paced vs. prescribed exercise – particularly for feeling better about weight and average scores – in the ED group.

#### Overall Model

Model fit indices for each variable and task are presented in Supplmental **?@tbl-BISSModFit**. Marginal values indicate that fixed effects specified in the current models are, together, accounting for 6-39% of variance in body image during exercise across variable and task. Results from each variable in the overall model (see [Table 2](#tbl-params)) are presented in Supplemental **?@tbl-bodyimage** with estimated marginal means for each timepoint presented in **?@fig-bissemm**. Group was a significant predictor of all body image items – with the HC group feeling better about their body, relative to the ED group. Higher BMI was associated with feeling less attractive than the average person, but there were no significant BMI x Condition effects, indicating that exercise did not influence this effect. There was an overall time effect several items during the Self-Paced Task, with individuals generally feeling better over time. There was also a Group x Time interaction for the BISS average and Weight during the Prescribed Task, such that individuals in the ED group had greater increases in average BISS scores along with feelings about their Weight relative to controls. Two Time x Condition x Group interactions emerged. Coupled with an interpretation of marginal means (Supplemental **?@fig-bissemm**) , these interactions indicate that the ED group had more positive increases in feelings about their weight and overall body image during self-paced exercise, relative to the HC group. Evaluations of variance across the two groups also indicates more within person variance in the ED group, as compared to the HC group, on most BISS measurements during exercise (see Supplemental **?@tbl-bissHOV**).

#### Within ED Group Model

Model fit indices for each variable and task within the ED group are presented in Supplmental **?@tbl-BISSModFit**. Marginal values indicate that fixed effects specified in the current models are, together, accounting for 4-15% of variance in body image during exercise across variable and task. Results for each model within the ED group are presented in Supplemental **?@tbl-biss-ed**. A Time effect emerged for Weight and Appearance in the Prescribed Task – individuals felt better about these aspects of body image as the task progressed, regardless of condition (Exercise vs. Rest).

### Biomarker Response

#### Descriptives

Biomakers were obtained for only a portion of the sample as this study served as a pilot trial and included ongoing phlebotemy training for study team members. Blood was therefore obtained only when a phlebotomist was available, and precautions were taken to ensure that participants were not overly distressed by the procedure. As such, the sample size for biomarker data (N = 58 successful blood draws with assays that passed initial quality control measures across pre- and post-exercise and pre- and post-rest; with complete data from 9 ED and 7 control participants) is smaller than the overall sample size. A visual depiction of biomarker response is presented in [Figure 2](#fig-biomarker). Detailed responses are presented in **?@fig-biomarker1**.

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| Figure 2: Biomarker Measurements Before and After Exercise |

#### Overall Model

Full t-test results across both exercise and rest conditions along with tests of heterogeneity of variance in exercise condition response across the ED and Control group using each outcome approach are presented in Supplementary **?@tbl-BiomarkerChange**.

#### Within ED Group Model

Full t-test results across both exercise and rest conditions using each outcome approach are presented in Supplementary **?@tbl-BiomarkerChangeED**. Although there were no significant differences between the ED and Control group in the overall model, effect sizes indicate that BNDF may show specific increases in the ED group post-exercise, relative to the Control group.

## **Aim 3: Exercise Response Correlations**

*Within the ED group, we will calculate correlations between acute exercise parameters/response and ED-related measures. We will conduct a linear regression to obtain slope estimates for affect and body image shifts for each individual, within exercise condition. We will also conduct a linear regression estimating post-biomarker scores across all individuals with EDs in the exercise condition, saving residuals.*

*We will quantify Pearson correlations with 95% confidence intervals between these slope estimates, biomarker residuals, Self-Paced Task exercise parameters (e.g., average bike speed, HR), functions of exercise subscales, self-report of compulsive exercise, and EDE global scores. We will estimate Pearson correlations and 95% confidence intervals for these correlations.*

### Exercise Response

Correlations between acute exercise response variables are presented in Supplemental **?@fig-exresponse**, and full correlation data with 95% CIs is presented in Supplemental **?@tbl-exresponsecorrs**. Average zero-order between exercise response variables in the control group is 0.14 and in the ED group is 0.19, indicating slightly stronger association between exercise response variables in the ED group, relative to the control group, with little evidence of collinearity across exercise response measures – indicating an independence and potential unique utility of exercise response measures across the three domains of assessment. Of the number of correlations tested, 6% reached p < 0.05 significance for controls (close to this alpha), while 14% reached p < 0.05 significance for the ED group, further supporting greater coherence of exercise response measures in the ED group.

### Correlations with Additional Variables

Correlations between body image response to exercise with key variables of interest are presented in [Figure 3](#fig-exresponse2). Full correlation data with 95% CIs is presented in **?@tbl-exresponsecorrs2**. Average zero-order between acute exercise response and key variables of interest in the control group is 0.08 and in the ED group is 0.09. For only those in the ED group only, greater body image response to acute exercise was associated with key variables, including higher self-reported drive for muscularity, lower social positive reinforcement of exercise, and lower body mass index. More improvement in feelings about Shape during exercise were *negatively* associated with EDE global scores for controls.

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| Figure 3: Correlations between Exercise Response and Individual Difference Variables |

# Supplement

### Study Flow

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| Table 3: **Study Flow**   | **Inflow/Retention** | Outflow | Reason | | --- | --- | --- | | **Eligibility Screenings (n = 321)** | Ineligible screenings (n = 41) | Duplicates (n = 8) Outside of age range (n = 11) Binge eating reported (n = 5) Unable to attend in-person visits (n = 5) Medical Exclusion (n = 3) Blood Draw (n = 3) Other (n = 6) | | **Intake (n = 70)** | Did not schedule Intake (n = 127) |  | |  | Ineligible intakes (n = 10) | Binge Eating Disorder (n = 7) ARFID (n = 1) Bipolar 1 Disorder (n = 1) Other (n = 1) | |  | Did not enroll (n = 15 - HC: 5, ED: 10) | No reason provided (n = 9) Time constraint (n = 4) Unforeseen circumstances (n = 2) | | **Day A (n = 40)** |  |  | | **Day B (n = 40)** |  |  | | **Day C (n = 39)** | Visit dropout (n = 1) | No reason provided (n = 1) | | **Completed Study (n = 39 - HC: 20, ED: 19)** |  |  | |