Greater Anhedonia Scores in Healthy Individuals are Associated with Less Decline in 24-hour Energy Expenditure with Fasting: Evidence for a Link Between Behavioral Traits and Spendthrift Phenotype.

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Highlights

- The spendthrift phenotype is more prone to weight-loss and resistant to weight-gain.
- Greater anhedonia traits were associated with the spendthrift metabolic phenotype.
- Healthy participants with anhedonia may respond better to their homeostatic needs.
- This association weakens when depressive symptoms increase

Abstract

Obesity rates are increasing and affecting mental health. It is important to understand how behavioural traits such as anhedonia are associated with physiologic traits that may predict weight-change in clinical and non-clinical populations. We studied whether 24-hour energy expenditure (24hEE) changes with fasting and overfeeding are associated with anhedonia in a healthy cohort. We performed behavioural assessments (physical anhedonia scale (PAS) and inventory for depressive symptoms (IDS)) followed by measures of 24hEE and urinary catecholamines in a whole-room indirect calorimeter (respiratory chamber) during energy balance, and then randomly during fasting and 2 different overfeeding diets. Participants (n=98) were medically healthy, between 18-55 years of age, with normal glucose regulation and weight-stable 6 months before admission. Women were premenopausal and not pregnant. Higher PAS was significantly associated with lesser decrease in 24hEE with fasting and higher urinary catecholamine excretion rates – consistent with spendthrift metabolism. As IDS increased, the association between anhedonia and the change in 24hEE from energy balance to fasting decreased (B-values were lower for change in EE). Here, higher PAS scores may reflect the ability to respond with appropriate homeostatic reactions which balance energy needs. IDS scores blunting this response may explain how anhedonia and depression can lead to weight gain.

Keywords: physical anhedonia, energy expenditure, energy metabolism, obesity, depressive symptoms, catecholamines, fasting

1. Introduction

Obesity and mental health disorders are substantial health problems that are bidirectionally related [1]. Pathologies such as major depressive disorder (MDD), bipolar disorder, schizophrenia, binge eating disorder, and bulimia nervosa are associated with weight gain [2-7]. Moreover, obesity worsens outcomes in many of these conditions [8-11]. Hence, it is critical to understand the relationship between mental health symptoms and weight gain.

Anhedonia – defined as decreased interest and capacity to be driven by pleasure or motivation – provides insight into the reward-motivation system [12], which is highly interconnected with eating behaviour [13]. However anhedonia has been associated with both weight gain [14, 15], and weight loss [16] a difference which may depend on the behavioral health of the population. Thus, studying metabolic measurements associated with anhedonia – which is considered a symptom in different psychiatric disorders and a personality trait found in healthy populations – may help understand its impact on weight change [12, 17] and has been encouraged in the mental health field [18].

The reward-motivation system, which can be in part assessed by measuring anhedonia, has been linked to sympathetic nervous system (SNS) responses [19]. SNS responses have also been associated with diet induced changes in 24-h energy expenditure (EE), a variable in weight-change studies [20]. Urinary catecholamines increase during fasting indirectly implying a role in future weight- change [21-23]. However, whether anhedonia traits are associated with energy metabolism and SNS responses is unclear. Our group has identified energy expenditure phenotypes that characterize individuals as spendthrift vs. thrifty. This spendthrift phenotype concept is based on previous work demonstrating that individuals who decrease their 24hEE less with fasting compared to energy balance lose more weight during calorie restriction and gain less weight during overfeeding and free-living conditions [24, 25]. Thus, we consider those individuals who decrease their 24hEE less with fasting more “spendthrift”. We have also demonstrated that those individuals who are more spendthrift have greater increases in urinary epinephrine excretion during fasting. Thus, we aimed to explore how anhedonia traits in healthy adults are related to 24-h EE and SNS responses in a secondary analysis from an energy expenditure phenotyping inpatient study.

2.Methods

This is a secondary analysis from a clinical trial (clinicaltrials.gov identifier: NCT00523627) aimed at analyzing metabolic responses of healthy individuals exposed to 24-h fasting and different overfeeding diets. The methodological details have been previously described [25].

Briefly, this inpatient study took place in the Clinical Research Unit at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in Phoenix, Arizona from 2008 to 2017. Enrolled individuals were between 18-55 years of age, medically healthy (assessed by medical history, physical exam, and routine blood tests), and weight stable (<10% variation in body weight) for the previous 6 months before admission. All women were premenopausal and not pregnant. The extensive list of exclusion criteria was previously published [26]. All volunteers provided written informed consent before initiating the study. The study was approved by the Institutional Review Board of the NIDDK.

Of 183 participants screened, 98 met eligibility criteria and were admitted to the Clinical Research Unit (Supplementary Figure 1). Upon admission, participants began a weight-maintaining diet (50% carbohydrates, 30% fat and 20% protein) using a unit-specific equation based on sex and weight [27]. Participants were weighed daily in the morning prior to breakfast. Body weight was maintained within 1% of the admission weight by adjusting the weight maintaining diet by ± 200 kcal/day if required. On day 2, a dual-energy X-ray absorptiometry (DXA) (Lunar prodigy or iDXA[28]) (Lunar Radiation, Madison, WI) was performed to assess body composition. DXA values were made comparable based on published formula [28]. After at least three days of weight-maintaining diet, a 75g oral glucose tolerance test was performed and only those participants with normal glucose regulation, according to American Diabetes Association criteria, continued the study [29]. Glucose concentrations were obtained by the glucose oxidase method (Beckman Glucose Analyzer, Beckman Instruments, Brea, CA, or Glucose analyzer GM9, Analox Instruments, Lunebertg, MA, USA).

2.1 Behavioral questionnaires

Following admission, participants were asked to answer a set of self-reported behavioral questionnaires including:

Physical Anhedonia Scale (PAS) [30]: a 61-item scale assessing sensitivity to reward. Items are responded as true or false, and each anhedonic response receives 1 point. Since the PAS does not specify a time frame, it describes anhedonic traits rather than symptoms belonging to a specific time or condition.

Examples: “1. I have usually found lovemaking to be intensely pleasurable; 2. When eating a favorite food, I have often tried to eat slowly to make it last longer; 3. I have often enjoyed the feel of silk, velvet or fur.”

Inventory for Depressive Symptomatology (IDS) [31]: evaluates signs and symptoms of depression in the last seven days through 30 questions with responses scored from 0-3 (least to most severe).

Three-Factor Eating Questionnaire (TFEQ) [32]: is a 51-item questionnaire assessing three factors of eating behavior: cognitive dietary restraint, dietary disinhibition, and susceptibility to hunger.

Emotional Appetite Questionnaire (EMAQ) [33]: assesses eating responses to 22 different positive and negative emotions and situations. Participants score whether they eat would less, the same, or more (Likert Scale from 1-9) when facing these specific circumstances.

Gormally Binge Eating Scale (BES) [34]: contains 16 items evaluating behavioral and cognitive aspects of binge eating to classify its severity.

2.2 Respiratory chamber

A whole-room indirect calorimeter (respiratory chamber) was used to measure 24-h EE. Detailed descriptions have been previously published [25]. To summarize, participants entered the respiratory chamber at 0730 AM (after breakfast if not a chamber under fasting conditions). In the chamber, meals were provided at 11 AM, 4 PM, and 7 PM through an airlock except for the 24-h fasting chamber. Any food remainders from chambers under non-fasting conditions were measured at the metabolic kitchen to calculate the actual energy intake inside the respiratory chamber (participants were instructed to eat all their food and only sessions with ≥ 95% of intake were included in analysis). Participants were instructed to not exercise but could move freely around the room, while CO_2 production and O_2 consumption rates were recorded every minute. Lusk’s equation was employed to calculate 24-h EE [35].

2.3 Dietary interventions

The dietary interventions protocol has been extensively described previously [25]. Two eucaloric 24-h sessions in the respiratory chamber were obtained to calculate 24-h energy balance (Enbal). In the first eucaloric session, the caloric intake was based on chamber specific equations as previously described [36]. Prescribed energy

intake during the second session two days later was the 24-h EE measured on the first chamber session. The EE measurements from the second eucaloric session were analyzed. Afterwards, volunteers underwent different dietary assessments which were given for 24-h in the respiratory chamber (fasting and 5 overfeeding diets) with a 3-day washout period during which time participants received the weight maintaining diet. The order of dietary interventions was randomized for each participant to reduce potential sequence effects. In this secondary analysis, we studied Enbal, fasting, and the low protein and high fat overfeeding as measures from these chambers previously predicted weight change [22].

During the 24-h chamber under fasting conditions, participants could drink water and noncaloric, noncaffeinated beverages ad libitum. Prescribed energy intake for the overfeeding diets equaled twice the baseline 24-h EE value of the second eucaloric session (200% of energy requirements). The overfeeding diets in this secondary analysis included: high-fat-overfeeding (FNP) (60% fat, 20% carbohydrate, and 20% protein), and low-protein-overfeeding (LPF) (51% carbohydrates, 46% fat, and 3% protein). Only sessions where participants consumed ≥ 95% of total energy intake provided on the diets were included in the analysis.

2.4 Sympathetic nervous system and cortisol responses

Twenty-four hour urine specimens were collected and stored in a refrigerator inside the calorimeter during each chamber session for cortisol and SNS hormones (dopamine, epinephrine, metanephrine, norepinephrine, and normetanephrine). Urine with added hydrochloric acid was stored at -70° C until analysis. High-performance liquid chromatography was used to measure epinephrine, norepinephrine and dopamine, and liquid chromatography–tandem mass spectrometry stable isotope dilution analysis was used for metanephrine and normetanephrine by the commercial Mayo Clinic laboratory. Due to logistical difficulties or significant return of interventional diets, not all the 98 subjects had valid measurements of sympathetic nervous system for all the dietary interventions (actual sample size reported on Table 1). Urinary free cortisol concentrations were measured using ELISA (Cayman Chemical Company, Ann Arbor, MI).

2.5 Statistical analysis

Data analyses were performed using SAS software (SAS 9.3, Enterprise guide version 5.1; SAS 9.4; SAS Institute Inc., Cary, NC, USA). Continuous data are expressed as mean ± SD, except for data with skewed distribution, which are expressed as median with interquartile range (IQR). Categorical data are expressed as counts and percentages. An alpha less than .05 (two-tailed) was considered statistically

significant. Catecholamines were log10 transformed to approximate normal distributions. General linear models (GLM) for each chamber condition were used to calculate residuals of 24-h EE with adjustments for known confounders [37]. 24-h EE models were adjusted for age, sex, race/ethnicity, fat mass, fat-free mass, and calorimeter ambient temperature. Differences and percentage change between chamber conditions (e.g., fasting) and Enbal were calculated for catecholamines and energy expenditure variables: change = value during intervention chamber-value during Enbal; percent change=(value during intervention-value during Enbal)/value during Enbal. Pearson correlation coefficients quantified the associations between behavioral questionnaires, body composition, demographics, catecholamines, and energy expenditure variables. Additionally, partial correlation coefficients adjusted for age and sex were also calculated for anhedonia's analyses with EMAQ and catecholamines. An interaction analysis was done considering anhedonia (PAS) as the independent variable, depressive symptoms (IDS) as the moderator, and residuals values of Adjusted 24-h EE (Fasting values minus Enbal) as the dependent variable. Significant interactions were probed using simple slopes, as this was a continuous-by-continuous interaction term; we defined the slopes by -1SD, mean, and +1SD difference in IDS.

3. Results

3.1 Clinical characteristics

Participant characteristics are shown in Table 1. Participants were mostly men, with a mean BMI of 26.6 ± 4.2 kg/m2. The PAS score mean was 13.3 ± 7.5 (range 1 -30 points) with the highest possible score of 61. Greater anhedonia (PAS scores) was negatively correlated with emotional eating scores (mean 3.98 ± 1.26, minimum 1.11, maximum 6.56) ($r= -0.27$ $p= 0.01$) (Figure 1 A), even after adjustment for age and sex (partial $r= -0.30$ $p=0.006$). There were no associations between anhedonia and IDS, BES or TFEQ (all $p > 0.3$).

3.2. Energy expenditure

PAS scores and adjusted EE during Enbal were negatively correlated (-58.8 kcal per 10 PAS points; $r= -0.28$ $p= 0.009$) (Figure 2A). Table 2 presents the correlation of PAS score with the absolute and percent changes in EE values for the dietary interventions. As expected, there was a wide variation in the difference between 24hEE measured during Enbal and fasting consistent with our previously identified thrifty (those who have a greater decrease in 24hEE during fasting compared to 24hEE during energy balance) versus spendthrift (those who have lesser decrease in

24hEE during fasting) phenotypes [21]. Participants with higher PAS score consistently had smaller decrease in 24hEE during fasting conditions (Table 2, Figure 2B) and this was not due to a correlation with adjusted EE during fasting (p=0.47). There was an interaction between IDS and PAS scores such that the association between PAS scores and decrease in 24hEE during fasting was stronger with lower IDS scores, indicative of more spendthrift phenotype. To illustrate the association between PAS score and decrease in 24hEE with fasting we modeled by IDS mean and ± 1 SD (IDS mean-1SD = 1.44, B = 6.01, SE = 1.92, p=0.002; IDS mean =9.09, B= 3.75, SE = 1.33, p=0.006; IDS mean +1SD = 16.75, B = 1.5, SE = 1.63, p=0.36) (Figure 1B [compare with Figure 2B]).

3.3 Sympathetic nervous system and cortisol

The 24-h urinary catecholamine and cortisol excretion rates during the Enbal chamber are presented in Table 1. None were correlated with PAS score, unadjusted and adjusted for age and sex (all p>0.26). As previously reported: fasting epinephrine excretion increased during fasting[23] . However, lower PAS score associated with greater reductions in catecholamine excretion rates during fasting (dietary interventions minus values from Enbal [Table 2, Figure 3, and Supplementary Figure 2]). PAS score was associated with fasting to Enbal changes in epinephrine and normetanephrine excretion rates (Table 2 and Supplementary Figure 2).

4. Discussion

In this secondary analysis of dietary interventions, we investigated the metabolic responses of participants with anhedonia traits as measured by the PAS. We found that participants with greater PAS score had both a smaller decrease in energy expenditure and greater sympathetic response during 24-h fasting compared with energy balance. These results indicate that greater anhedonia is associated with a more spendthrift metabolic profile. However, the strength of this association became weaker as depressive symptoms increased.

The thrifty and spendthrift metabolic phenotypes have been investigated to understand the

inter-individual propensity to either weight gain or weight loss[20, 21]. In this scenario, thriftiness

implies a conservation of energy use during different eating scenarios, such as undernutrition or dietary

protein restriction [20, 21]. Our phenotype is based specifically on 24-h EE changes under fasting conditions compared to 24h EE measured during energy balance [23], a change in 24hEE that has a large inter-individual variability. We have demonstrated, in both controlled inpatient and free-living outpatient settings, that a lesser decrease in 24-h EE (more spendthrift phenotype) during fasting from energy balance predicts greater diet-induced weight loss and less overfeeding-induced weight gain, respectively [25, 38]. As we have described, participants with spendthrift characteristics have a lower adjusted 24-h EE during energy balance and sedentary condition, but they also show lesser decrease in 24-h EE during prolonged fasting. Thus, our findings of negative association between anhedonia and adjusted 24-h EE during energy balance (higher the anhedonia scores, lower the adjusted 24-h EE) and a positive association between anhedonia and the decrease in 24-h EE with fasting (higher the anhedonia scores, less the 24hEE decrease with fasting) are consistent with the findings that in this population without clinical depression higher anhedonia appears to be part of a more spendthrift phenotype.

We observed consistent positive associations between PAS scores and the changes in catecholamine excretion rates from Enbal to fasting (Figure 3). We have previously demonstrated that higher urinary epinephrine during fasting is also associated with smaller decrease in 24-h EE during fasting [23]. Thus, our observation of anhedonia's relationship with epinephrine excretion rates and change in 24hEE with fasting is again consistent with higher anhedonia being associated with a more spendthrift metabolic profile.

Our findings regarding the changes in urinary catecholamines and higher PAS score require careful interpretation. Dopamine can be found in the central nervous system (CNS) and peripherally, but peripheral dopamine does not cross the blood-brain barrier [39]. Epinephrine is only produced outside the brain – in the medulla of the adrenal glands – and cannot cross the blood-brain barrier [40], but it has been associated with cognitive decline [41]. Norepinephrine production occurs both at the CNS and peripherally. Like dopamine and epinephrine, peripheral norepinephrine does not cross the blood-brain barrier [40]. However, in animal models stress induces central norepinephrine to stimulate the paraventricular nucleus of the hypothalamus, thus regulating the HPA, sympathoneural, and adrenomedullary systems [42, 43]. Normetanephrine excretion in urine has been observed to respond to both norepinephrine and epinephrine changes [40]. Fasting can be considered a stressor [44], and explain the expected rise in catecholamine levels [45]. The question arises: why would participants with greater anhedonia exhibit larger increases in catecholamine excretion during fasting? Greater anhedonia has been postulated to be linked with aspects of the motivation-reward system that result in reduced processing of hedonic information [46]. In healthy individuals, greater anhedonia may indicate greater situation awareness and

manifest as a greater SNS response in a stress condition (such as fasting). This might be a protective response in a food rich environment. We hypothesize that persons with non-clinical (e.g., no psychiatric diagnoses) anhedonia traits may have a "homeostatic response" more appropriate to their energy needs.

To investigate this hypothesis further, we investigated the relationship of PAS with IDS scores. PAS scores were not associated with the depression scores indicating that PAS signifies a trait, rather than a state-related or pathologic symptom, in a medically healthy population [46]. The EMAQ was negatively correlated with anhedonia, revealing that participants with higher anhedonia reported less emotional eating when facing negative emotions and situations (Figure 1A). This further supports the concept that participants with higher anhedonia respond to their energy needs instead of other eating cues. Further supporting our hypothesis was that the positive association between PAS score and the change in 24hEE from energy balance to fasting weakened depressive symptoms increased (Figure1B) indicating that depressive symptoms may interfere with the ability maintain energy balance and avoid weight gain. We consider this alteration in the relationship of PAS scores and 24hEE changes would provide one plausible mechanism for weight gain in the setting of depressive symptoms.

Anhedonia is considered a phenomenon arising from at least one of several mental functions: desire, effort/motivation, anticipation and consummatory pleasure, and learning from stimulus-reward associations [47, 48]. The neuroscience behind anhedonia and its assessment has been previously reviewed extensively [47, 48]. Prior evidence indicates that anhedonia is tied to the reward system [46, 48]. In general, brain structures involved in the reward system include the prefrontal cortex (PFC), the ventral tegmental area, insula, and the nucleus accumbens [48, 49]. A study in 26 healthy individuals without mental illness and with similar PAS scores (13.0 ± 8.5) to our population, found severity of anhedonia traits were negatively associated with activity in the medial PFC, left inferior and right middle temporal gyri, left cuneus, right superior parietal gyrus, and anterior cingulate [46]. In this same study, anhedonia scores were similar in patients with schizophrenia (14.1 ± 7.1, p=0.58) but the PAS scores were negatively correlated with other activity in brain regions not demonstrated in the healthy group. Thus, anhedonia may be differentially associated with hedonic response pathways differ in individuals who are health versus those with defined psychiatric illness. Interestingly, some authors have hypothesized that low positive affect mediates the relationship between anhedonia and binge eating [50]. This might explain our previous findings where anhedonia, moderated by depressive symptoms, was associated to weight gain at follow-up [14]. In that study, lower anhedonia and higher depression predicted weight loss [14].

Our study has several strengths, including employing gold-standard respiratory chamber procedures to accurately measure daily EE during highly controlled feeding conditions; assessing anhedonia with a widely validated questionnaire and measurement of sympathetic response with 24-h urinary catecholamines. Our limitations include few women; the use of questionnaires only at the beginning of the study; and that our measure of anhedonia did not assess for specific components of the reward system. Although psychiatric diagnoses and treatments were asked during the screening medical history and physical exam, a structured clinical interview was not performed.

5. Conclusions

In this secondary analysis of an inpatient dietary-intervention study with healthy participants, we found that higher anhedonia traits (PAS scores) were correlated with energy expenditure measurements which identify individuals who are more spendthrift. These measurements included smaller decrease in 24-h EE from energy balance to fasting and greater activation of sympathetic nervous system activity again from energy balance to fasting. This metabolic profile has been associated with greater weight-loss in controlled conditions, and less weight-gain in free living conditions. However, the presence of depressive symptoms reduced the association between anhedonia and the 24h-EE spendthrift characteristics. Even more, those with higher anhedonia reported less emotional eating during negative situations. These results expand our previously described energy expenditure phenotypes to include important behavioral characteristics that may provide additional explanations into the ability to maintain energy balance and avoid weight gain.

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Disclosures

Declaration of interests: none

Author contributions

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Table 1. Clinical Characteristics of the Study Group

	Total n=98	Women n=19	Men n=79
Age (years), mean ± SD, n=98	37.0 ± 10.6	33.3 ± 9.6	37.8 ± 10.7
Race/Ethnicity, n (%)	B 22 (22.5) W 31 (31.6) H 15 (15.3) I 30 (30.6)	B 5 (26.3) W 7 (36.8) H 3 (15.8) I 4 (21.1)	B 17 (21.5) W 24 (30.4) H 12 (15.2) I 26 (32.9)
Body weight (kg), mean ± SD, n=98	79.6 ± 13.8	72.4 ± 16.8	81.3 ± 12.5
BMI (kg/m^2), mean ± SD, n=98	26.6 ± 4.3	26.8 ± 5.6	26.6 ± 3.9
Fat mass (kg), mean ± SD, n=98	23.3 ± 10.3	29.7 ± 12.9	21.7 ± 9.1
Free-fat mass (kg), mean ± SD, n=98	56.3 ± 9.6	42.7 ± 5.4	59.6 ± 7.1
SPA (Enbal chamber) (%), n=96	6 ± 3.60	4.7 ± 3.2	6.3 ± 3.7
PAS, mean ± SD, n=86	13.3 ± 7.5	12.3 ± 8.1	13.6 ± 7.3
IDS, mean ± SD, n=93	9.1 ± 7.7	9.5 ± 8.5	9.0 ± 7.5
TFEQ Disinhibition, mean ± SD, n=88	3.3 ± 2.3	3.8 ± 3	3.2 ± 2.1
TFEQ Hunger, mean ± SD, n=88	3.3 ± 2.9	3.3 ± 2.8	3.3 ± 4.2
TFEQ Restraint, mean ± SD, n=88	8.0 ± 4.4	8.9 ± 4.8	7.7 ± 4.3
EMAQ Positive Mean Score, mean ± SD, n=86	5.1 ± 1.2	4.6 ± 1.5	5.2 ± 1.1
EMAQ Negative Mean Score, mean ± SD, n=87	4.0 ± 1.3	3.8 ± 1.4	4.1 ± 1.2
BES Mean Score, mean ± SD, n=87	4.4 ± 4.5	7.3 ± 5.5	3.6 ± 3.9
24-h EE (kcal/day during Enbal), mean ± SD, n=97	2033.1 ± 307.2	1741.0 ± 246.8	2104.0 ± 277.8
Percentage deviation from Enbal (%)	2.2 ± 5.4	1.4 ± 4.3	2.5 ± 5.8
EE change from Enbal (kcal/day)			
- Fasting, n=90	−167.3 ± 96.2	−158.6 ± 91.1	−169.6 ± 98.0
- FNP, n=79	148.9 ± 105.2	119.5 ± 69.5	• 157.0 ± 112.2
- LPF, n=77	52.8 ± 92.5	−0.6 ± 82.8	64.7 ± 90.9
Urinary Free Cortisol (µg/24-h) n=41	1.4 ± 0.2	1.3 ± 0.1	1.5 ± 0.2
Dopamine (µg/24-h) n=n=95	2.4 ± 0.2	2.4 ± 0.2	2.4 ± 0.2
Epinephrine (µg/24-h) n=95	0.6 ± 0.2	0.5 ± 0.2	0.6 ± 0.2
Metanephrine (µg/24-h) n=95	2.1 ± 0.2	2.0 ± 0.2	2.1 ± 0.2
Norepinephrine (µg/24-h) n=95	1.4 ± 0.2	1.3 ± 0.2	1.4 ± 0.2
Normetanephrine (µg/24-h) n=95	2.3 ± 0.2	2.3 ± 0.2	2.4 ± 0.2

SD, Standard Deviation; B, Black; W, White; H, Hispanic; I, Indigenous American; BMI, Body-mass index; SPA, Spontaneous Physical Activity; PAS, Physical Anhedonia Scale; IDS, Inventory of Depressive Symptoms; TFEQ, Three Factor Eating Questionnaire; EMAQ, Emotional Appetite Questionnaire; FNP, High Fat Overfeeding Diet; LPF, Low Protein Overfeeding Diet.

Table 2. Anhedonia Correlations with Energy Expenditure and Urinary Hormone Responses to Dietary Challenges

	PAS Correlation		
	Δ FST – Enbal	**Δ FNP – Enbal**	**Δ LPF – Enbal**
EE (kcal/day)	r=0.24 p=0.03	r=0.02 p=0.81	r=0.18 p=0.12
EE (%)	r=0.26 p=0.01	r=0.04 p=0.68	r=0.20 p=0.08
Adjusted EE Analyses	r=0.28 p=0.01	r=0.10 p=0.39	r=0.14 p=0.39
Urinary Free Cortisol (µg/24-h) n=41	*r*= −0.14 p=0.45	*r*= −0.08 p=0.63	*r*= −0.26 p=0.14
Dopamine (µg/24-h) n=95	r=0.21 p=0.06	r=0.18 p=0.18	r=0.28 p=0.01
Epinephrine (µg/24-h) n=95	r=0.26 p=0.01	r=0.12 p=0.37	r=0.12 p=0.31
Metanephrine (µg/24-h) n=95	r=0.18 p=0.1	r=0.29 p=0.03	r=0.29 p=0.03
Norepinephrine (µg/24-h) n=95	r=0.18 p=0.09	r=0.04 p=0.73	r=0.28 p=0.02
Normetanephrine (µg/24-h) n=95	r=0.28 p=0.01	r=0.14 *p* = 0.3	r=0.14 p=0.3

PAS, Physical Anhedonia Scale; Enbal, Energy balance; FST, Fasting; FNP, High Fat Overfeeding Diet; LPF, Low Protein Overfeeding Diet; EE, Energy Expenditure; SD, Standard Deviation. EE (%) deltas are the percent change between chamber and Enbal (e.g., delta = (FST – Enbal); percent = (FST – Enbal/Enbal) * 100). The adjusted EE analyses accounted for sex, race, fat mass, fat-free mass, and age.

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Figure 1. Behavioral Assessments and Anhedonia Relationships.
PAS, Physical Anhedonia Scale; EMAQ, Emotional Appetite Questionnaire; Enbal, Energy Balance; EE, Energy Expenditure; IDS, Inventory of Depressive Symptoms. Figure 1A shows the negative correlation between anhedonia and reports of eating more during negative emotions or situations. Figure 1B shows how a lesser decrease of adjusted EE during fasting (a spendthrift characteristic) is associated to anhedonia. However, this association becomes blunted as depressive symptoms increase (IDS score).

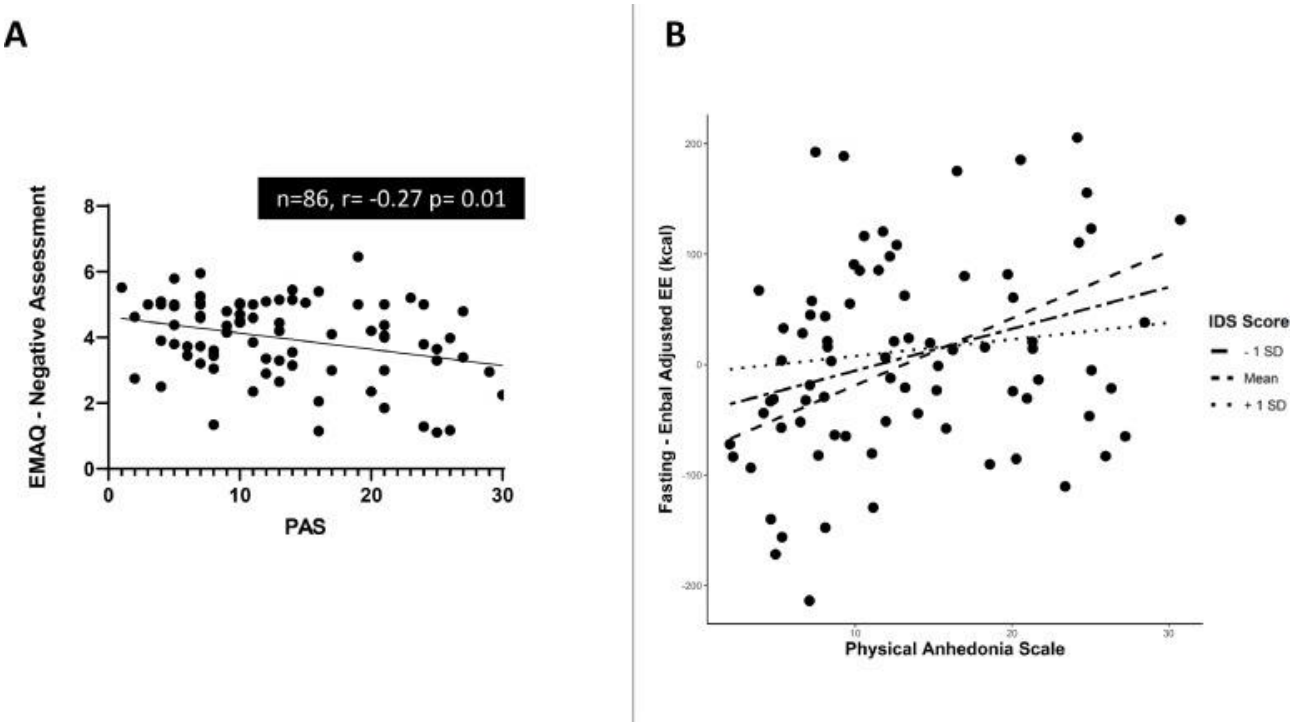


Figure 2. Correlations of Adjusted Energy Expenditure and Anhedonia.
EE, Energy Expenditure; Enbal, Energy Balance; FNP, High Fat Overfeeding Diet; LPF, Low Protein Overfeeding Diet. Figure 2A shows adjusted EE on the Y axis; Figures 2B, 2C and 2D show the difference in adjusted EE from Enbal and each dietary intervention.

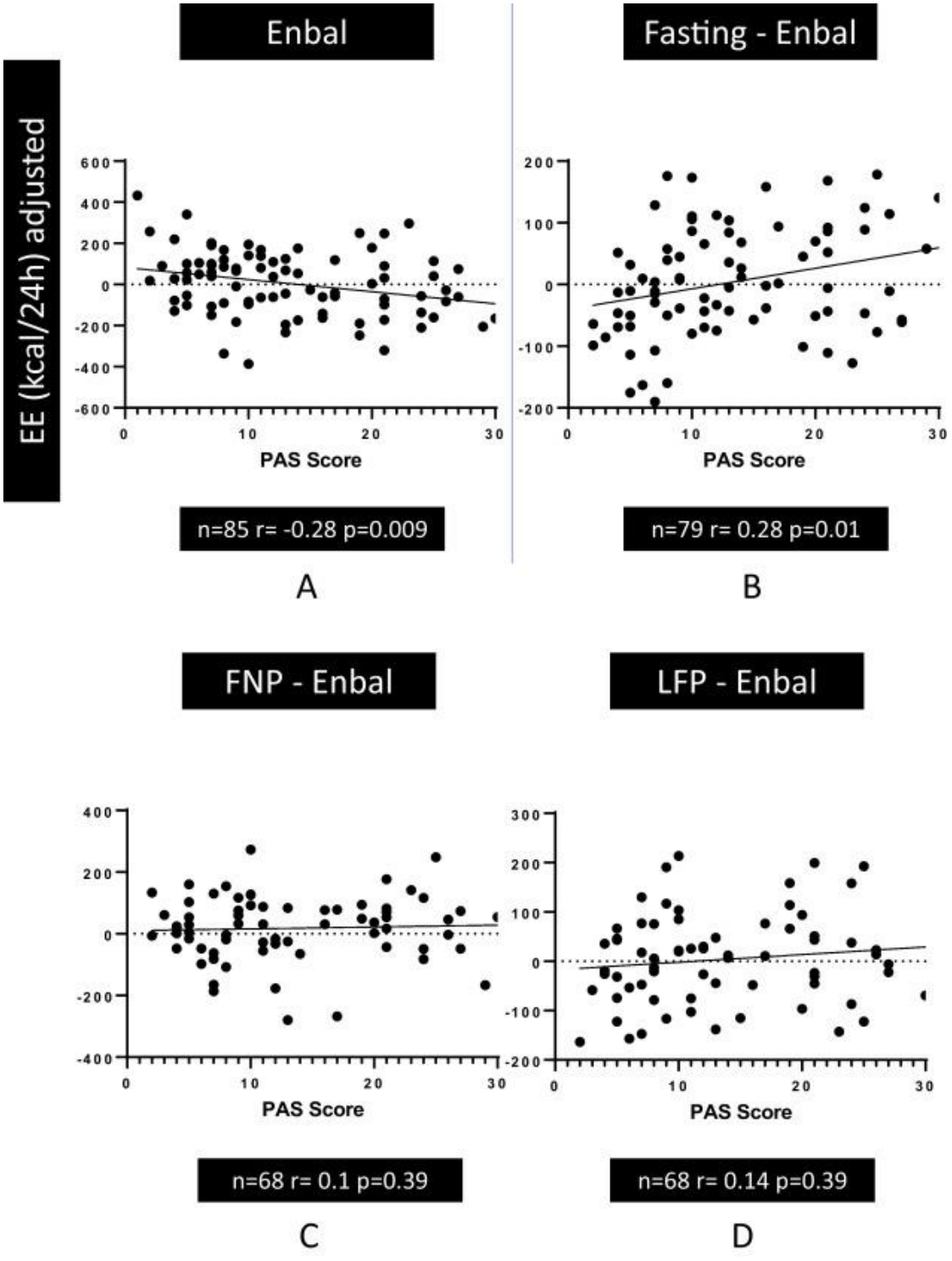
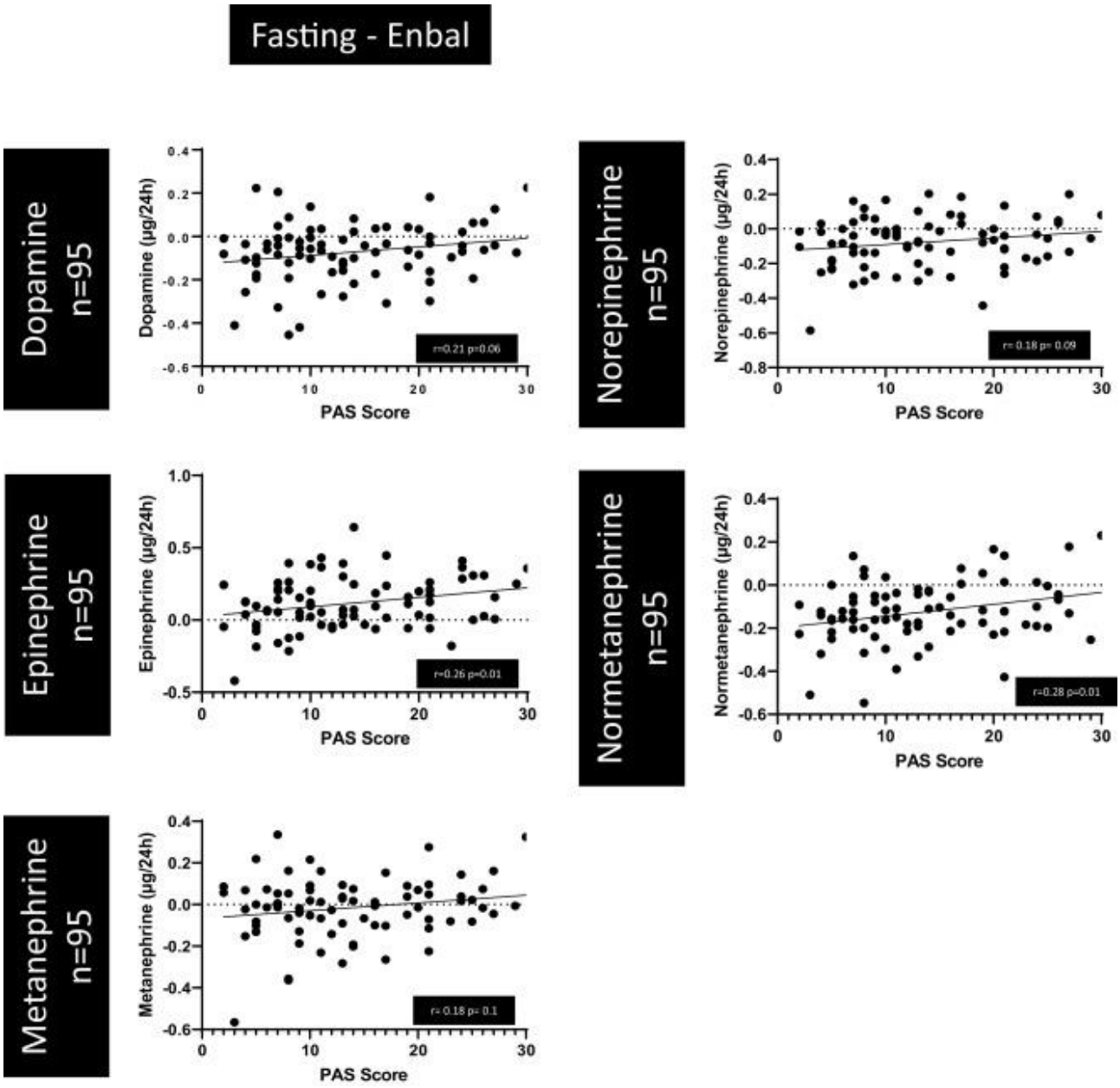


Figure 3. Correlations of Anhedonia and Catecholamine Responses during Fasting. Enbal, Energy Balance; PAS, Physical Anhedonia Scale. Catecholamine values on Y axis represent the difference from Fasting minus Energy Balance.



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