Supplementary Material for Peptide YY_{3-36} concentration in acute and long-term recovered anorexia nervosa

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SM 1 Supplemental Results

SM 1.1 Control analyses: Bayesian statistics

We employed Bayesian statistics conducted with JASP [1] to verify our results. One advantage of these tests is the possibility to test which hypothesis is best supported by the data and to specifically also test the evidence in favor of the null hypothesis (H_0).

From the results of prior studies on PYY and PYY_{3-36} in AN, it is possible to make an informed assumption about the pair-wise comparison between acAN and HC. To determine a likely effect size for the comparison between acAN and HC, we aimed to include all studies about total PYY or PYY_{3-36} in AN with a representative sample size of n>20 [2–6]. However, Germain et al. [5] was not included since the statistical parameters necessary to determine an effect size were not reported, and Misra et al., 2006 [6] was not included as Misra et al., 2008 [4] used data from the same subjects in their analyses. Thus, we used the results of the remaining three studies [2–4] to calculate the Cohen's *d* statistic for the pair-wise comparison between AN and HC participants according to the following formula:

$$d = \frac{M_1 - M_2}{SD_{pooled}}$$

where M_1 and M_2 are the means of the AN group and the HC group and SD_{pooled} is the pooled standard deviation, calculated according to the following formula (SD_1 and SD_2 are the standard deviations of the AN group and the HC group):

$$SD_{pooled} = \sqrt{\frac{(SD_1^2 + SD_2^2)}{2}}$$

The calculated effect sizes were d=10.98 for Eddy et al. [2] who measured PYY_{3-36} in 75 AN and 22 HC, d=0.33 for Fernández-Aranda et al. [3] who measured total PYY in 64 AN and 80 young HC, and d=1.60 for Misra et al. [4] who measured total PYY in 34 AN and 33 HC. The mean effect size for these three studies was d=4.30, which provides strong a priori evidence for the alternative hypothesis PYY: AN>HC.

Therefore, we conducted a Bayesian two-sample t test to test whether the data best supported the alternative hypothesis PYY_{3-36}: acAN>HC (H_+) or H_0. The Bayes factor BF_{0+} (H_0/H_+) suggested that the data were 11.6:1 in favor of the null hypothesis (strong evidence, Figure S1).

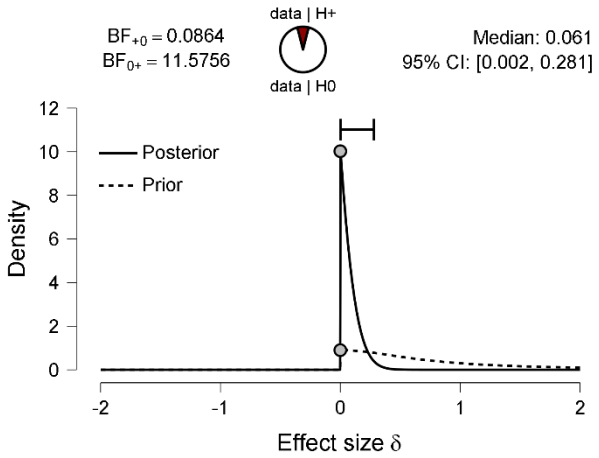

Figure S1. *Output of the Bayesian two-sample t-test performed with JASP* [1]. The probability wheel visualizes the evidence that the data provide for the null hypothesis H_0 and the one-sided alternative hypothesis H_+ ($PYY_{3\text{-}36}$: acAN > HC). The population effect size δ was assigned a Cauchy prior distribution with a prior width $r = \frac{1}{\sqrt{2}}$, truncated to allow only positive effect size values.

For the comparison between recAN and HC, there were no previous studies of PYY in blood. So there were two possible assumptions: the increase of PYY in acute AN observed in previous studies could a) (partially) persist or b) completely normalize with weight recovery. Therefore, we conducted a Bayesian two-sample t test to test whether the data best supported the alternative hypothesis $PYY_{3\text{-}36}$: recAN > HC (H_+) or H_0. The Bayes factor BF_{0+} (H_0/H_+) suggested that the data were 12.2:1 in favor of the null hypothesis (strong evidence, Figure S2).

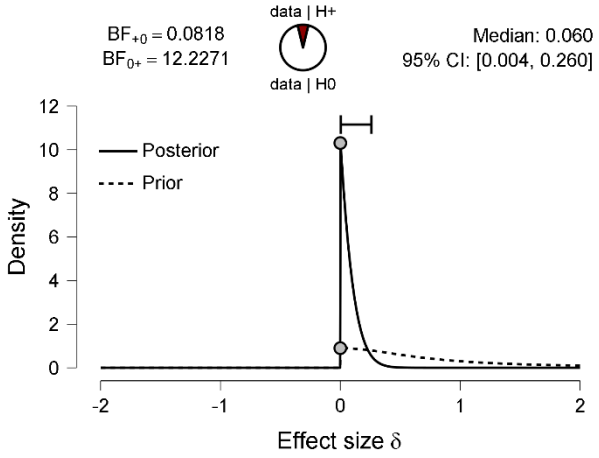

Figure S2. *Output of the Bayesian two-sample t-test performed with JASP* [1]. The probability wheel visualizes the evidence that the data provide for the null hypothesis H_0 and the one-sided alternative hypothesis H_+ ($PYY_{3\text{-}36}$: recAN > HC). The population effect size δ was assigned a Cauchy prior distribution with a prior width $r = \frac{1}{\sqrt{2}}$, truncated to allow only positive effect size values.

SM 1.2 Control analyses: Effects of duration of realimentation and BMI change

We conducted an exploratory analysis to test a possible influence of the duration of realimentation and BMI change from timepoint 1 (T1, admission to treatment) to timepoint 2 (T2, after short-term weight restoration) on PYY_{3-36} concentrations in the longitudinal AN study population (see Table S1 for statistical parameters). The median BMI change from T1 to T2 was 24.3% (interquartile range (*IQR*)=12.2, minimum=13.7%, maximum=47.9%). The median duration of realimentation from T1 to T2 was 84.5 days (*IQR*=27.8, minimum=51 days, maximum=256 days).

We divided the longitudinal study population into two subgroups: one subgroup with a duration of realimentation below the group median of 84.5 days and one subgroup with a duration of realimentation greater than or equal to the median. In the subgroup with shorter duration of realimentation, a Wilcoxon signed-rank test indicated no significant difference in PYY_{3-36} concentration between T1 and T2. Similarly, in the subgroup with longer duration of realimentation, there was no significant difference in PYY_{3-36} concentration between T1 and T2. Dividing the longitudinal study population into two subgroups on the basis of BMI change yielded a similar result. In the subgroup with a BMI change below the median of 24.3%, there was no significant difference in PYY_{3-36} concentration between T1 and T2. Similarly, in the subgroup with a BMI change greater or equal to 24.3%, there was no significant difference in PYY_{3-36} concentration between T1 and T2.

As an alternative approach, a repeated measures general linear model showed no significant difference between PYY_{3-36} concentrations at T1 and T2 after controlling for duration of realimentation and percentage of BMI change, $F(1,29)=0.26$, $p=0.616$.

Furthermore, we tested if the correlation between PYY_{3-36} concentration and BMI-SDS in the acAN group at T2 was influenced by duration of realimentation or BMI change from T1 to T2 (see Table S2 for statistical parameters). In the subgroup with shorter duration of realimentation, there was no significant relationship between PYY_{3-36} concentration at T2 and BMI-SDS at T2. Similarly, in the subgroup with longer duration of realimentation, there was no significant relationship between PYY_{3-36} concentration at T2 and BMI-SDS at T2. In the subgroup with a BMI change below the median of 24.3%, there was no significant relationship between PYY3-36 concentration at T2 and BMI-SDS at T2. Similarly, in the subgroup with a BMI change greater or equal to 24.3%, there was no significant relationship between PYY_{3-36} concentration at T2 and BMI-SDS at T2.

Table S1. *Wilcoxon signed-rank test comparing PYY_{3-36} concentrations in different subgroups between acAN-T1 and acAN-T2.*

	n	Median	IQR	T	z	p
PYY_{3-36} (pg/ml) Short duration of realimentation						
acAN-T1	16	82.8	26.4	59	-0.47	0.642
acAN-T2	16	75.5	28.4			
PYY_{3-36} (pg/ml) Long duration of realimentation						
acAN-T1	16	95.2	61.2	34	-1.48	0.140
acAN-T2	16	77.7	86.3			
PYY_{3-36} (pg/ml) Low BMI Change						
acAN-T1	16	79.5	25.0	54	-0.34	0.733
acAN-T2	16	76.9	33.7			
PYY_{3-36} (pg/ml) High BMI Change						
acAN-T1	16	97.6	42.4	40	-1.45	0.148
acAN-T2	16	78.4	37.6			

Abbreviatios: acAN-T1, acute anorexia nervosa participants at timepoint 1 (admission); acAN-T2, acute anorexia nervosa participants at timepoint 2 (after short-term weight rehabilitation); BMI, body mass index; IQR, interquartile range. Short duration of realimentation was defined as below the group median of 84.5 days, long duration of realimentation was defined as equal or greater than 84.5 days. Low BMI change was defined as below the group median of 24.3%, high BMI change was defined as equal or greater than 24.3%.

Table S2. *Correlations of PYY_{3-36} concentrations with BMI-SDS at acAN-T2 in different subgroups.*

	BMI-SDS
PYY_{3-36} (pg/ml) acAN-T2 Short duration of realimentation	*rs*=-0.194 *p*=0.471
PYY_{3-36} (pg/ml) acAN-T2 Long duration of realimentation	*rs*=0.153 *p*=0.572
PYY_{3-36} (pg/ml) acAN-T2 Low BMI Change	*rs*=-0.006 *p*=0.983
PYY_{3-36} (pg/ml) acAN-T2 High BMI Change	*rs*=-0.041 *p*=0.880

Spearmann correlation coefficients and p values were reported. There were no statistically significant correlations. Abbreviations: acAN-T1, acute anorexia nervosa participants at timepoint 1 (admission); acAN-T2, acute anorexia nervosa participants at timepoint 2 (after short-term weight rehabilitation); BMI-SDS, body mass index standard deviation score; IQR, interquartile range. Short duration of realimentation was defined as below the group median of 84.5 days, long duration of realimentation was defined as equal or greater than 84.5 days. Low BMI change was defined as below the group median of 24.3%, high BMI change was defined as equal or greater than 24.3%.

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