Comparison of Adiponectin Levels in Anorexia Nervosa, Bulimia Nervosa, Binge-Eating Disorder, Obesity, Constitutional Thinness, and Healthy Controls: A Network Meta-Analysis

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Abstract: Adiponectin is a protein hormone that is produced and secreted primarily by adipose tissue. The levels of adiponectin in those with eating disorders, obesity, and healthy controls have been extensively studied. However, the general picture of the differences in adiponectin levels across the mentioned conditions is still unclear and fragmented. In this study, we pooled previous studies and performed a network meta-analysis to gain a global picture of comparisons of adiponectin levels across eating disorders, obesity, constitutional thinness, and healthy controls. Electronic databases were searched for anorexia nervosa, avoidant restrictive food intake disorder, binge-eating disorder, bulimia nervosa, healthy controls, night eating syndrome, obesity, and constitutional thinness in studies where adiponectin levels were measured. A total of 4262 participants from 50 published studies were included in the network meta-analysis. Adiponectin levels were significantly higher in participants with anorexia nervosa than in healthy controls (Hedges' g = 0.701, $p < 0.001$). However, adiponectin levels in constitutionally thin participants were not significantly different from those of healthy controls (Hedges' g = 0.470, $p = 0.187$). Obesity and binge-eating disorder were associated with significantly lower adiponectin levels compared to those of healthy controls (Hedges' g = −0.852, $p < 0.001$ and Hedges' g = −0.756, $p = 0.024$, respectively). The disorders characterized by excessive increases or decreases in BMI were associated with significant changes in adiponectin levels. These results suggest that adiponectin may be an important marker of severely disequilibrated homeostasis, especially in fat, glucose, and bone metabolisms. Nonetheless, an increase in adiponectin may not simply be associated with a decrease in BMI, as constitutional thinness is not associated with a significant increase in adiponectin.

Keywords: adiponectin; anorexia nervosa; bulimia nervosa; binge-eating disorder; obesity; constitutional thinness; network meta-analysis

1. Introduction

Eating disorders such as anorexia nervosa (AN), bulimia nervosa (BN), and binge-eating disorder (BED) affect millions of people each year, as the current one-year prevalence rate is estimated to be 1.66%, and the rate for women is as high as 2.62% [1]. The Centers for Disease Control and Prevention (CDC) estimates that 41.9% of adults 20 and older in the United States are obese [2]. Despite the prevalence and associated health effects of both eating disorders and obesity, there is still much that is unknown about their biomarkers. A more comprehensive understanding of such biomarkers may improve the identification and treatment of eating disorders and of the physical complications associated with both eating disorders and obesity. Obesity is listed under "Other Conditions That May Be a Focus of Clinical Attention" in the DSM-5, but it is not included in the DSM-5 as a mental

disorder. However, there are robust associations between obesity and mental disorders (e.g., binge-eating disorder, depressive and bipolar disorders, and schizophrenia) as also stated in the DSM-5.

One such biomarker that is relevant to the clinical worsening of eating disorders is adiponectin, an amino-acid protein secreted primarily by adipose tissue and found abundantly in serum and plasma circulation [3]. This protein is thought to be largely involved in metabolic, cardiovascular, and inflammatory processes and is closely related to body mass index (BMI), making it especially relevant in the study of eating disorders and their effects on health [4–7].

Elevated levels of adiponectin have been shown to increase insulin sensitivity [8–10], reduce atherosclerosis [5], and regulate inflammation [6]. Insufficient levels of circulating adiponectin are closely related to obesity [3], insulin resistance [7], type II diabetes [5], and cardiovascular disorders [11,12].

Several studies have established a negative correlation between adiponectin levels and BMI [3,7]. In a study of thin, normal weight, overweight, and obese adolescents, mean levels of adiponectin were significantly lower in both the overweight and obese groups and significantly higher in the thin group as compared to the normal weight group [13].

Adiponectin levels can also be affected by the presence of eating disorders, especially AN. Two meta-analyses have confirmed significantly increased levels of adiponectin in AN compared to healthy controls [14,15]. However, it is not clear whether constitutional thinness (C.Thin) is associated with increased adiponectin levels compared to those of healthy controls [16–18].

Obese patients have decreased levels of mRNA and serum levels of adiponectin compared to those of healthy controls (HCs) [18–22]. An inverse relationship between adiponectin serum levels and BMI has been reported in cross-sectional studies repeatedly [23–26]. Notably, there may be an even stronger inverse relationship between adiponectin serum levels and body total fat mass [27–29].

Studies of adiponectin levels in BN patients show inconsistent findings, with BN patients having either higher [30,31], the same [32], or lower adiponectin levels as compared to HCs [18]. These results mimic the breadth of presentation of this disorder, consisting of heterogenous binge or purge habits.

Previous work has compared adiponectin levels between several of the aforementioned groups, but no global analysis has yet been conducted comparing those of AN, BN, obesity, and C.Thin patients to those of HCs. Network meta-analysis is a statistical technique for comparing multiple effect sizes simultaneously in a single analysis by combining direct and indirect evidence within a network of comparative trials [33]. This network meta-analysis seeks to pool and rank the comparisons of adiponectin levels in all these populations by their magnitude of effect sizes to create a global picture of adiponectin across disorders and give researchers a better understanding of the role and place of adiponectin across eating disorders, obesity, and constitutional thinness.

2. Methods

This research was conducted per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [34].

2.1. Data Sources and Search Strategy

The PubMed, EMBASE, and PsycNET search engines were examined with the Boolean processors *for "anorexia nervosa [Title/Abstract] OR bulimia nervosa [Title/Abstract] OR obesity [Title/Abstract] OR binge-eating disorder [Title/Abstract] OR thin [Title/Abstract] OR lean [Title/Abstract] OR healthy controls [Title/Abstract] OR normal [Title/Abstract] OR night eating syndrome [Title/Abstract] OR avoidant restrictive food intake [Title/Abstract] AND adiponectin [Title/Abstract]".* "Species" and "article type" filters of the search engines were activated to limit the results to "human" and "clinical trial" studies. The reference lists of the articles found were searched for additional reports.

2.2. Selection of Studies

To reduce methodological heterogeneity, only studies with diagnoses based on the Diagnostic and Statistical Manual Version III (DSM-III) or subsequent versions (DSM-III-R, DSM-IV, DSM-IV-TR, or DSM-5) were included. Case reports, case series, and review articles were excluded. Studies reporting adiponectin levels in severe disorders (such as diabetes mellitus, kidney disease, polycystic ovary disease, cardiac disorders, systemic sclerosis, and fatty liver disease) were excluded from the meta-analysis. The PRISMA flowchart of the article selection process is presented in Figure 1. The PRISMA checklist for meta-analysis is included in Supplement Table S1.
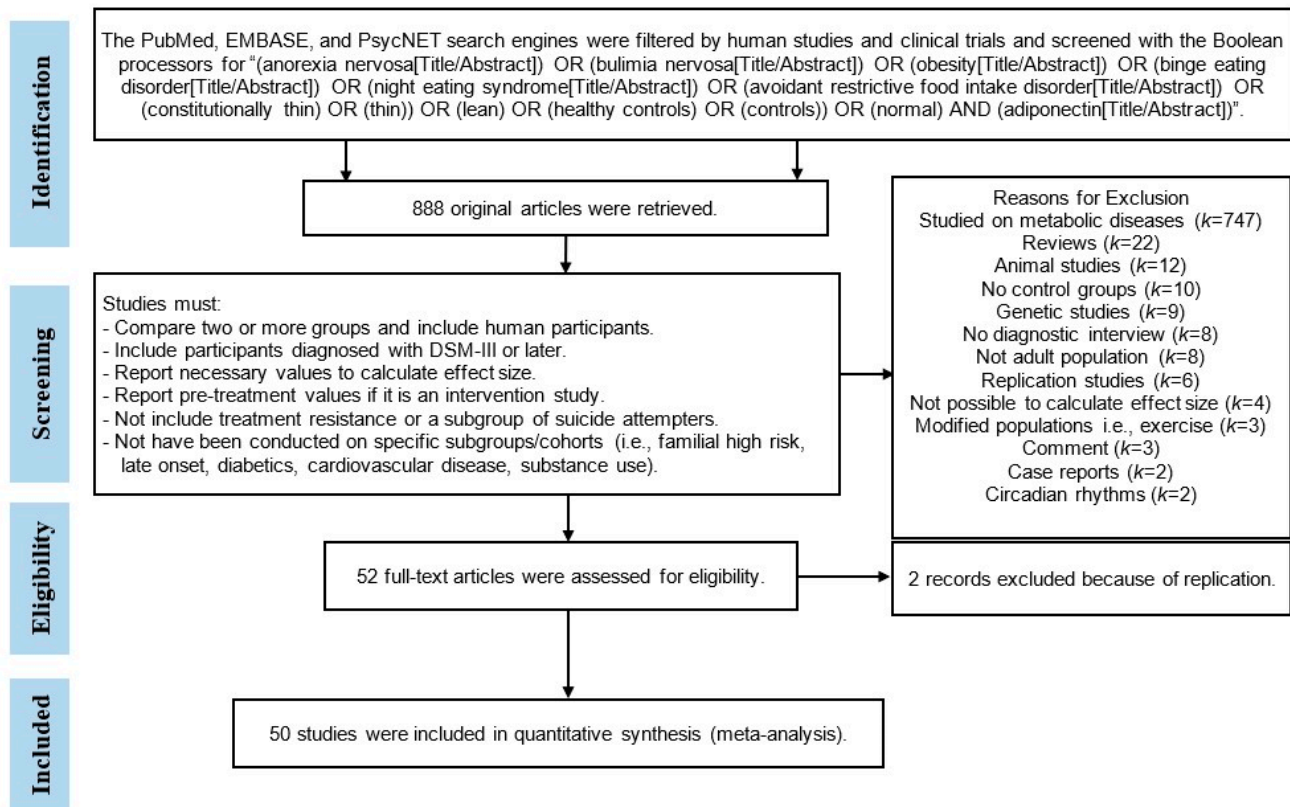
Identification

The PubMed, EMBASE, and PsycNET search engines were filtered by human studies and clinical trials and screened with the Boolean processors for "(anorexia nervosa[Title/Abstract]) OR (bulimia nervosa[Title/Abstract]) OR (obesity[Title/Abstract]) OR (binge eating disorder[Title/Abstract]) OR (night eating syndrome[Title/Abstract]) OR (avoidant restrictive food intake disorder[Title/Abstract]) OR (constitutionally thin) OR (thin)) OR (lean) OR (healthy controls) OR (controls)) OR (normal) AND (adiponectin[Title/Abstract])".

888 original articles were retrieved.

Screening

Studies must:
- Compare two or more groups and include human participants.
- Include participants diagnosed with DSM-III or later.
- Report necessary values to calculate effect size.
- Report pre-treatment values if it is an intervention study.
- Not include treatment resistance or a subgroup of suicide attempters.
- Not have been conducted on specific subgroups/cohorts (i.e., familial high risk, late onset, diabetics, cardiovascular disease, substance use).

Reasons for Exclusion
Studied on metabolic diseases (k=747)
Reviews (k=22)
Animal studies (k=12)
No control groups (k=10)
Genetic studies (k=9)
No diagnostic interview (k=8)
Not adult population (k=8)
Replication studies (k=6)
Not possible to calculate effect size (k=4)
Modified populations i.e., exercise (k=3)
Comment (k=3)
Case reports (k=2)
Circadian rhythms (k=2)

Eligibility

52 full-text articles were assessed for eligibility.

2 records excluded because of replication.

Included

50 studies were included in quantitative synthesis (meta-analysis).

Figure 1. PRISMA flowchart of the article-selection process.

2.3. Inclusion and Exclusion Criteria

Studies including at least 2 (or more) study groups with participants who were either inpatients or outpatients, written in English, available from the earliest date to February 2023, were included in this meta-analysis. After a review of the abstracts of retrieved articles, full texts of the articles that included thin or obese participants or subjects diagnosed with AN or BN or BED compared to each other, or to a healthy control group, were evaluated. Only articles that reported the necessary information related to participants' characteristics (especially N, SD, and mean of adiponectin level) or statistical test values to calculate effect sizes were included in this meta-analysis. If more than one subtype of AN (i.e., restrictive or bulimic/purgative) were included in a study, the subtypes' means and standard deviations were pooled in a single group (3 studies, see Appendix A Table A1). The meta-analysis included only pre-intervention (baseline) values for studies that involved repeated measurements in two or more study groups. Single-arm studies designed as before-after interventions in patients or healthy controls were excluded because they did not compare two groups head to head or because it was not possible to generate effect size from unpaired comparison groups.

2.4. Extraction of Data

A database file was prepared for the selected articles to record the first author's name(s), year, sample size, sex, body mass index (BMI), mean age, assay method (the enzyme-linked immunosorbent assay-ELISA or radioimmunoassay-RIA), source of each metabolite (plasma or serum), and mean levels and SD of adiponectin. Medians and IRs, which were reported in two included studies, were converted to mean and SD approximations [35]. Consistent with the open science framework, the extracted dataset used in this meta-analysis can be found in Appendix A.

2.5. Statistics and Meta-Analytic Strategy

A random network meta-analysis, with the residual (restricted) maximum likelihood (REML) algorithm to estimate tau2, combined direct and indirect evidence of bias-corrected effect sizes (Hedges' g) from multiple-arm studies. The consistency of direct and indirect evidence extracted from each study was checked. Heterogeneity between studies was tested by Cochrane's Q test, and the I2 value was inspected. Publication bias across the studies was explored with funnel plots and the Begg–Mazumdar and Egger tests. The SUCRA ranking score (Surface Under the Cumulative Ranking) was used to evaluate which diagnosis in the network was the most likely to be associated with the highest effect size in the network meta-analysis. All analyses were performed using the "network meta-analysis" [36] and "netmeta" [37] packages in the Stata (version 14.1) and R software (version 14.2), respectively [38,39].

3. Results

A pool of 4262 participants, 1265 AN (*k* = 39), 75 BN (*k* = 5), 57 BED (*k* = 3), 867 obese (*k* = 17), 426 C.Thin (*k* = 5), and 1572 healthy controls (*k* = 46), obtained from a total of 50 study articles, successfully generated a connected network (Figure 2).
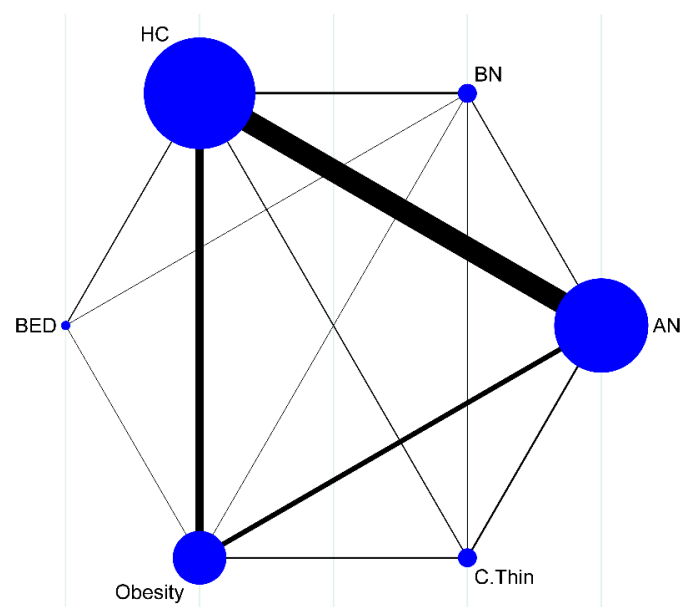

Figure 2. Successfully connected network map (circle size is associated with the number of studies, and line width is associated with the number of comparisons).

The electronic database search did not retrieve any results on night eating syndrome or avoidant restrictive food intake disorder, so they could not be included in the current network meta-analysis. Appendix A Table A1 presents the summarized study characteristics, design, and effect sizes. The Forest plot graph summarizes the pooled effect sizes in each diagnostic group vs. HCs that were extracted from the 50 studies (Figure 3).
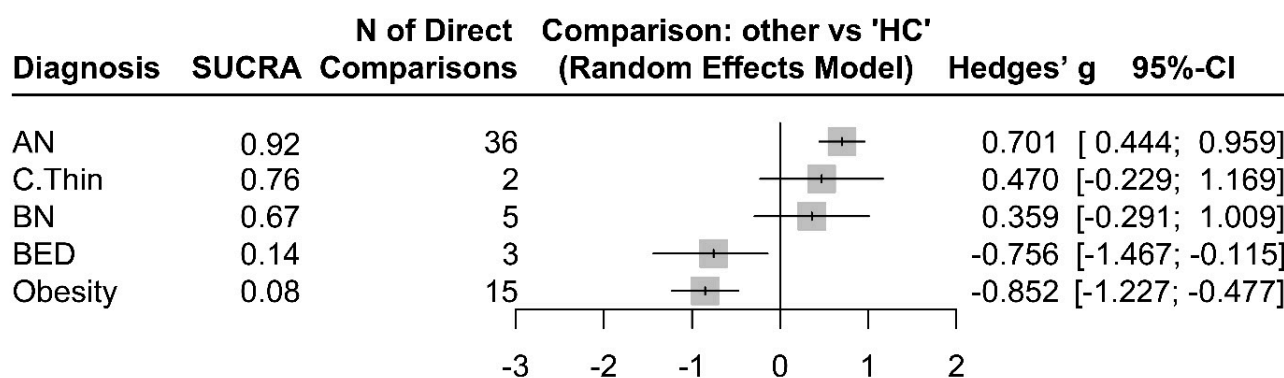
Diagnosis	SUCRA	N of Direct Comparisons	Comparison: other vs 'HC' (Random Effects Model)	Hedges' g	95%-CI
AN	0.92	36		0.701	[0.444; 0.959]
C.Thin	0.76	2		0.470	[-0.229; 1.169]
BN	0.67	5		0.359	[-0.291; 1.009]
BED	0.14	3		-0.756	[-1.467; -0.115]
Obesity	0.08	15		-0.852	[-1.227; -0.477]

Figure 3. Magnitudes of standardized adiponectin differences (Hedges' g) in AN, BED, BN, Obesity, and C.Thin compared to HC.

3.1. Comparisons of Study Groups vs. HCs

As seen in Figure 3, patients with AN had significantly increased adiponectin levels compared to those of HCs (Hedges' g = 0.701, z = 5.34, $p < 0.001$). The adiponectin levels were also significantly decreased in patients with BED (Hedges' g = −0.756, z = −2.25, $p = 0.024$) and obesity (Hedges' g = −0.852, z = −4.45, $p < 0.001$) compared to those of HCs. Although constitutionally thin subjects (Hedges' g = 0.4701, z = 1.32, $p = 0.1873$) and patients with BN (Hedges' g = 0.359, z = 1.08, $p = 0.279$) had numerically increased levels of adiponectin compared to those of HCs, the differences were not statistically significant. There was significant within-design (Q = 456.98, df = 42, $p < 0.001$) and between-design (Q = 201.74, df = 18, $p < 0.001$) heterogeneity (Total I^2 = 91%).

3.2. Consistency of Direct and Indirect Evidence

There was no overall inconsistency across the study arms between direct and indirect evidence ($\chi^2_{(18)}$ = 28.22, $p = 0.0588$). Although global inconsistency was not significant (Supplement Table S2), individual comparisons of direct and indirect evidence obtained from obese vs. HC (diff = −1.26, z = −2.56, $p = 0.011$) and from AN vs. BED (diff = −2.38, z = 2.50, $p = 0.012$) comparisons yielded significant differences. A split forest of direct and indirect evidence is summarized in Figure 4. The net heat plot, which can be found in Supplement Figure S1, is a matrix visualization that highlights hot spots of inconsistent contribution of the corresponding design (diagonally) and inconsistency between direct and indirect evidence in a network estimate (off-diagonal).

3.3. Risk of Bias in Included Studies

Bias assessment of the included papers was performed according to the *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0.* [40]. There was no noticeable evidence of bias in the studies included in the meta-analysis (Supplement Figure S2). More than 65% of the papers were assessed to have a low risk of bias.

3.4. Publication Bias and Small Study Effect

Adjusted funnel plot and publication bias statistics supported an unbiased distribution (Supplement Figure S3). There was no significant publication bias or small study effect in the meta-analysis (Begg–Mazumdar $p = 0.304$; Egger test $p = 0.110$, Thomson–Sharp $p = 0.760$).
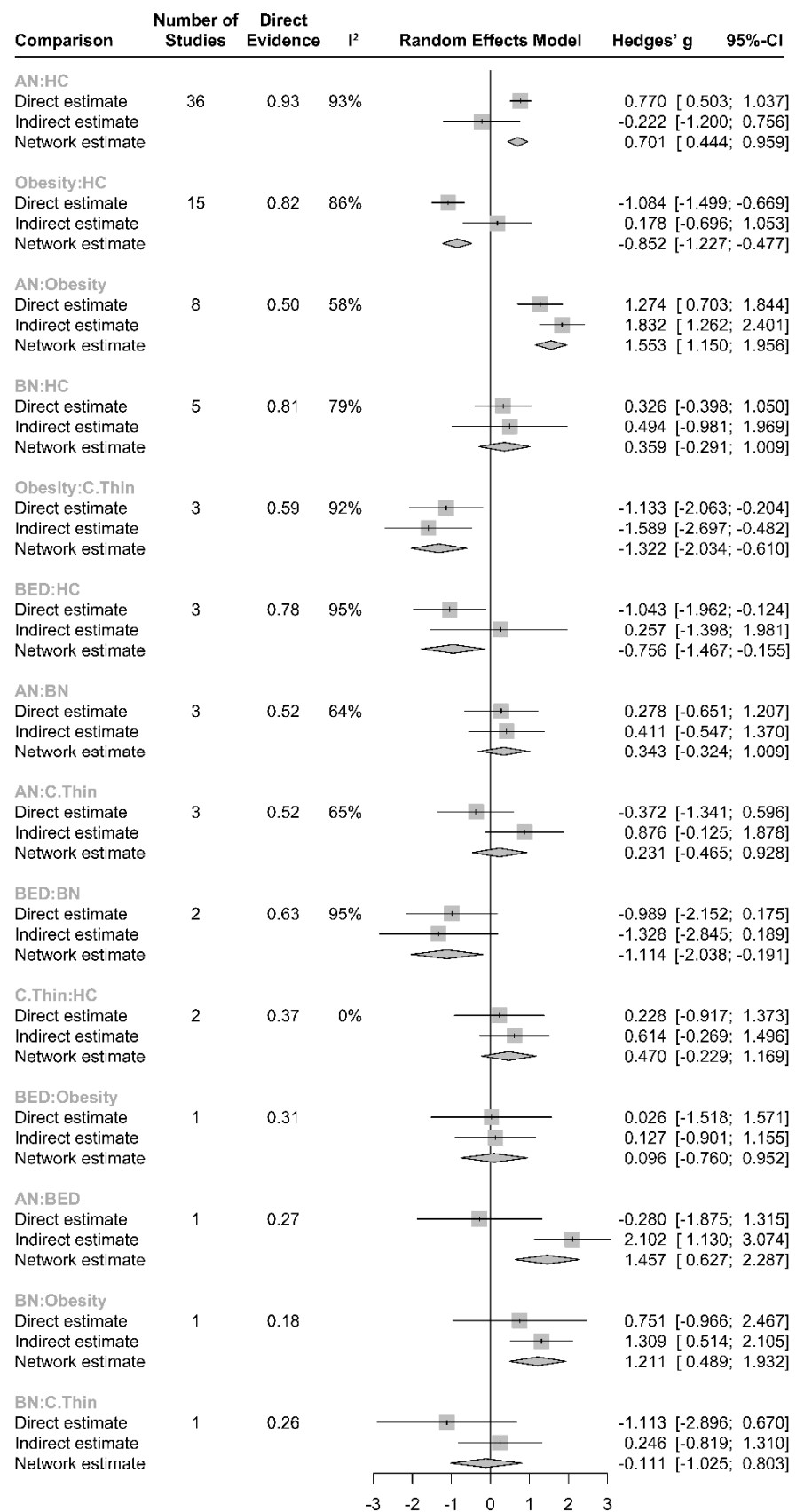
Comparison	Number of Studies	Direct Evidence	I²	Random Effects Model	Hedges' g	95%-CI
AN:HC						
Direct estimate	36	0.93	93%		0.770	[0.503; 1.037]
Indirect estimate					-0.222	[-1.200; 0.756]
Network estimate					0.701	[0.444; 0.959]
Obesity:HC						
Direct estimate	15	0.82	86%		-1.084	[-1.499; -0.669]
Indirect estimate					0.178	[-0.696; 1.053]
Network estimate					-0.852	[-1.227; -0.477]
AN:Obesity						
Direct estimate	8	0.50	58%		1.274	[0.703; 1.844]
Indirect estimate					1.832	[1.262; 2.401]
Network estimate					1.553	[1.150; 1.956]
BN:HC						
Direct estimate	5	0.81	79%		0.326	[-0.398; 1.050]
Indirect estimate					0.494	[-0.981; 1.969]
Network estimate					0.359	[-0.291; 1.009]
Obesity:C.Thin						
Direct estimate	3	0.59	92%		-1.133	[-2.063; -0.204]
Indirect estimate					-1.589	[-2.697; -0.482]
Network estimate					-1.322	[-2.034; -0.610]
BED:HC						
Direct estimate	3	0.78	95%		-1.043	[-1.962; -0.124]
Indirect estimate					0.257	[-1.398; 1.981]
Network estimate					-0.756	[-1.467; -0.155]
AN:BN						
Direct estimate	3	0.52	64%		0.278	[-0.651; 1.207]
Indirect estimate					0.411	[-0.547; 1.370]
Network estimate					0.343	[-0.324; 1.009]
AN:C.Thin						
Direct estimate	3	0.52	65%		-0.372	[-1.341; 0.596]
Indirect estimate					0.876	[-0.125; 1.878]
Network estimate					0.231	[-0.465; 0.928]
BED:BN						
Direct estimate	2	0.63	95%		-0.989	[-2.152; 0.175]
Indirect estimate					-1.328	[-2.845; 0.189]
Network estimate					-1.114	[-2.038; -0.191]
C.Thin:HC						
Direct estimate	2	0.37	0%		0.228	[-0.917; 1.373]
Indirect estimate					0.614	[-0.269; 1.496]
Network estimate					0.470	[-0.229; 1.169]
BED:Obesity						
Direct estimate	1	0.31			0.026	[-1.518; 1.571]
Indirect estimate					0.127	[-0.901; 1.155]
Network estimate					0.096	[-0.760; 0.952]
AN:BED						
Direct estimate	1	0.27			-0.280	[-1.875; 1.315]
Indirect estimate					2.102	[1.130; 3.074]
Network estimate					1.457	[0.627; 2.287]
BN:Obesity						
Direct estimate	1	0.18			0.751	[-0.966; 2.467]
Indirect estimate					1.309	[0.514; 2.105]
Network estimate					1.211	[0.489; 1.932]
BN:C.Thin						
Direct estimate	1	0.26			-1.113	[-2.896; 0.670]
Indirect estimate					0.246	[-0.819; 1.310]
Network estimate					-0.111	[-1.025; 0.803]

Figure 4. Split forest of direct evidence (%) vs. indirect evidence in effect size.

4. Discussion

We have compared the adiponectin levels across eating disorders, obesity, and constitutional thinness to those of healthy controls. The main finding of the meta-analysis was that adiponectin is significantly increased in AN patients compared to HCs; however, constitutionally thin people do not have significantly elevated adiponectin levels compared to those of HCs. This finding may suggest that the increases in adiponectin levels in AN cannot be explained simply by low BMI, as constitutional thinness is not associated with a significant increase in adiponectin compared to the levels in HCs. Thus, adiponectin increases in AN might be associated with heavily disequilibrated bodily physiological functions in many systems of the body rather than simply low BMI. Alternatively, adiponectin levels may be strongly associated with the clinical symptoms observed in AN such as amenorrhea and bone mineral loss, which again puts a significant stress on physiological systems [41–43]. These aforementioned symptoms are not observed in constitutionally thin people and may therefore constitute the line between health and disease. Previous studies have also shown significant relationships between various inflammatory factors and adiponectin [15,24,44]. The current findings further highlight the role of heavily disturbed general body functions in AN compared to constitutional thinness. Moreover, it is not yet clear whether adiponectin elevation in AN is permanent or if levels return to normal following re-feeding, since studies on re-feeding of AN patients have shown conflicting results [45,46]. Therefore, it can be hypothesized that the slightly increased adiponectin levels may play a protective role in maintaining energy levels during starvation, but sharply increased adiponectin levels may represent a compensatory mechanism during heavy disruption in metabolism as observed in AN. Furthermore, it can also be hypothesized that the increased adiponectin levels, which as noted may play a protective role in maintaining energy levels during starvation, are not needed in non-disordered weight loss. Rough calculations of means by groups can be found in Supplement Figure S4: the mean adiponectin levels in participants with AN are more than two times higher than in constitutionally thin people.

Obesity, which is known to be associated with disequilibrated physiological functions, has significantly decreased adiponectin levels as compared to those of HCs. It is thought that adipokine drop in obesity is one of the key events in promoting systemic metabolic dysfunction, cardiovascular disease, and colorectal cancers [47]. BED appears to be associated with weight gain in the long term, though it can also be seen in non-obese persons [48,49]. We have found significantly lower levels of adiponectin in BED patients compared to HCs; however, it should be noted that the number of the studies in the BED arm was limited ($k = 3$) in the current network meta-analysis. Of note, the National Comorbidity Survey has reported that BED is associated with a lifetime of increased BMI (OR = 4.9, 95%CI = 2.2–11.0) compared to those without an eating disorder even after controlling for age and sex [49]. Therefore, lowered adiponectin levels are reasonable given the expected increase in BMI in BED. The same study reported that the majority of patients with BN have a normal BMI with no significant BMI changes across their lifetimes [49]. Additionally, DSM-5 classification does not seek BMI change in the diagnosis of BN. These findings support our result of nonsignificant changes in adiponectin levels in BN patients compared to HCs. Symptoms of severe destruction in bodily functions are not expected in BN; thus, significant changes in adiponectin levels may not accompany BN.

As expected, the limitations of the current meta-analysis are related to the limitations of the studies we pooled. The most important shortcomings were missing sample characteristics (sex, age, race, and socioeconomic status) and insufficient data on moderators, such as duration of the disorder, severity measurements, number of episodes, the magnitude and speed of weight loss, familial predisposition, or comorbidity, which may influence adiponectin levels. For example, the duration of AN and magnitude of weight loss could have also been significant moderators of adiponectin, but insufficient information was presented in the included studies for this analysis. Another limitation was the lack of a clear definition of constitutional thinness. In the future, more robust information about adiponectin will require studies in which those mentioned variables will be controlled.

The presence of heterogeneity in the current network meta-analysis suggests that the variation in the study outcomes was significantly beyond expectations. Therefore, there may be other factors contributing to the extracted effect sizes from the studies other than the diagnosis. The aforementioned missing features of the pooled studies may have increased the heterogeneity. Single-arm studies (without comparisons) were excluded from the meta-analysis because it was not possible to extract a standardized mean difference between the groups. This exclusion procedure might have impacted the results. There was no publication bias in the pooled studies, which could contribute to reliable effect size estimations. Since the current network meta-analysis included a good number of studies, a low statistical power for detecting publication bias was not expected. There was no significant inconsistency between the direct and indirect evidence of the effect size. Therefore, our conclusions are valid even though only direct comparisons were considered.

However, the current network meta-analysis cannot clarify the cause of the increase or decrease in adiponectin levels in the studied populations. The current network analysis cannot tell us if BMI in healthy people sometimes drops to the levels of those of with AN. Nonetheless, these findings support that multiple physiological changes occur in AN, BED, and obesity, and significant changes in adiponectin may not be solely explained by BMI, as a similar change has not been found in constitutionally thin participants or in BN participants. Therefore, a significant change in adiponectin levels may represent heavily disturbed physiological equilibrium.

Appendix A

Table A1. General features of the studies included in the network meta-analysis.

Study	Group 1			Group 2			Design	Group 1	Group 2	Effect Size (Hedges' g)	Standard Error
	Mean Adiponectin (μg/mL)	SD	N	Mean Adiponectin (μg/mL)	SD	N					
[50]	18.16	14.35	21	6.10	15.71	59	AN Obesity	AN	Obesity	0.777	0.262
[51]	6.06	3.93	9	7.59	1.83	9	AN HC	AN	HC	−0.475	0.480
[24]	7.52	4.09	12	9.32	3.42	11	AN HC Obesity	AN	HC	−0.538	0.423
[24]	7.52	4.09	12	4.90	1.72	11	AN HC Obesity	AN	Obesity	0.783	0.430
[24]	9.32	3.42	11	4.90	1.72	11	AN HC Obesity	HC	Obesity	1.320	0.460
[52]	0.58	0.10	30	0.49	0.05	30	HC Obesity	HC	Obesity	1.124	0.279
[53]	6.89	2.62	20	5.39	1.91	27	AN HC	AN	HC	0.659	0.303
[54]	6.70	3.25	23	5.19	1.56	43	AN HC	AN	HC	0.653	0.265
[55]	12.24	5.54	20	10.10	4.90	25	AN HC	AN	HC	0.406	0.303
[56]	16.10	4.59	26	11.80	4.41	24	AN HC	AN	HC	0.940	0.299
[57]	38.23	18.43	12	24.94	12.39	18	AN HC	AN	HC	0.859	0.391
[58]	57.80	26.01	17	33.00	28.00	17	AN HC Obesity	AN	HC	1.260	0.357
[58]	57.80	26.01	17	18.70	12.50	51	AN HC Obesity	AN	Obesity	1.987	0.321
[58]	33.00	28.00	17	18.70	12.50	51	AN HC Obesity	HC	Obesity	0.727	0.286
[59]	46.40	15.81	10	28.00	10.05	12	AN HC	AN	HC	1.365	0.484
[60]	36.50	17.85	17	19.90	9.44	17	AN HC	AN	HC	1.135	0.373
[61] *	33.99	14.89	41	20.58	8.10	41	AN HC	AN	HC	1.108	0.238
[62]	7.77	7.66	23	23.48	8.88	45	BED HC Obesity	BED	HC	−2.460	0.300
[62]	7.77	7.66	23	7.60	2.16	60	BED HC Obesity	BED	Obesity	0.026	0.245
[62]	23.48	8.88	45	7.60	2.16	60	BED HC Obesity	HC	Obesity	2.486	0.253

Table A1. *Cont.*

Study	Group 1			Group 2			Design	Group 1	Group 2	Effect Size (Hedges' g)	Standard Error
	Mean Adiponectin (μg/mL)	SD	N	Mean Adiponectin (μg/mL)	SD	N					
[13]	2.30	0.90	133	1.10	0.50	19	HC Obesity C.Thin	HC	Obesity	1.348	0.255
[13]	2.30	0.90	133	2.50	1.00	31	HC Obesity C.Thin	HC	C.Thin	−0.225	0.200
[13]	1.10	0.50	19	2.50	1.00	31	HC Obesity C.Thin	Obesity	C.Thin	−1.573	0.303
[44]	10.72	2.60	26	10.34	3.77	24	AN HC	AN	HC	0.116	0.283
[63]	36.50	18.87	19	19.90	9.16	16	AN HC	AN	HC	1.064	0.365
[64]	19.60	10.44	10	11.20	1.32	7	AN HC	AN	HC	0.981	0.528
[32] *	46.63	22.13	26	29.95	13.79	15	AN BN HC	AN	BN	0.927	0.338
[32]	46.63	22.13	26	26.01	8.52	12	AN BN HC	AN	HC	1.146	0.368
[32]	29.95	13.79	15	26.01	8.52	12	AN BN HC	BN	HC	0.219	0.388
[25]	26.21	4.18	16	15.81	3.55	16	HC Obesity	HC	Obesity	2.612	0.496
[65]	12.20	4.20	21	10.00	3.60	19	AN HC	AN	HC	0.549	0.323
[21]	23.12	8.92	20	16.67	4.89	28	AN HC Obesity	AN	HC	0.995	0.304
[21]	23.12	8.92	20	14.23	5.60	28	AN HC Obesity	AN	Obesity	1.372	0.315
[19]	16.67	4.89	28	14.23	5.60	28	AN HC Obesity	HC	Obesity	0.376	0.269
[66]	11.95	4.91	34	13.30	5.58	14	AN BED BN HC	AN	BED	−0.280	0.318
[66]	11.95	4.91	34	12.08	3.3	14	AN BED BN HC	AN	BN	−0.027	0.318
[66]	11.95	4.91	34	11.37	4.8	41	AN BED BN HC	AN	HC	0.120	0.232
[66]	13.3	5.58	14	12.08	3.3	14	AN BED BN HC	BED	BN	0.253	0.378
[66]	13.3	5.58	14	11.37	4.8	41	AN BED BN HC	BED	HC	0.311	0.400
[66]	12.08	3.3	14	11.37	4.8	41	AN BED BN HC	BN	HC	0.147	0.310
[67]	58.44	37.94	28	33.24	27.19	38	AN HC Obesity	AN	HC	1.087	0.257

Table A1. *Cont.*

Study	Group 1			Group 2			Design	Group 1	Group 2	Effect Size (Hedges' g)	Standard Error
	Mean Adiponectin (µg/mL)	SD	N	Mean Adiponectin (µg/mL)	SD	N					
[67]	58.44	37.94	28	17.02	10.44	77	AN HC Obesity	AN	Obesity	1.786	0.245
[67]	33.24	27.19	38	17.02	10.44	77	AN HC Obesity	HC	Obesity	0.699	0.203
[68] $	11.77	5.74	17	8.1	3.36	50	HC Obesity	HC	Obesity	0.889	0.292
[20] $	16.78	13.12	49	8.33	4.85	27	HC Obesity	HC	Obesity	0.764	0.248
[69]	19.00	7.70	50	12.00	5.80	50	AN HC	AN	HC	1.019	0.213
[20]	6.39	1.70	27	4.82	1.30	26	AN HC Obesity	AN	HC	0.983	0.286
[20]	6.39	1.70	27	4.30	1.70	27	AN HC Obesity	AN	Obesity	1.309	0.292
[21]	4.82	1.30	26	4.30	1.70	27	AN HC Obesity	HC	Obesity	0.326	0.276
[17]	33.50	25.50	9	37.20	13.28	10	AN C.Thin	AN	C.Thin	−0.176	0.461
[70]	12.80	5.27	23	12.50	7.79	21	AN HC	AN	HC	0.045	0.302
[71]	13.30	6.10	17	11.90	7.10	19	AN HC	AN	HC	0.206	0.335
[45]	16.80	3.56	20	11.90	3.30	13	AN HC	AN	HC	1.381	0.399
[72]	4.91	2.37	20	12.91	4.27	20	BED BN HC	BED	BN	−2.234	0.381
[72]	4.91	2.37	20	8.69	3.69	20	BED BN HC	BED	HC	−1.057	0.332
[72]	12.91	4.27	20	8.69	3.69	20	BED BN HC	BN	HC	1.178	0.335
[22]	13.70	6.30	11	9.56	2.98	11	AN HC Obesity	AN	HC	0.954	0.446
[22]	13.70	6.30	11	7.57	1.90	10	AN HC Obesity	AN	Obesity	1.412	0.477
[22]	9.56	2.98	11	7.57	1.90	10	AN HC Obesity	HC	Obesity	0.459	0.441
[73]	7.80	5.80	156	6.20	5.70	164	HC Obesity	HC	Obesity	0.278	0.112
[74] *	11.22	6.65	24	11.09	4.86	14	AN HC	AN	HC	0.021	0.336
[75]	16.43	5.85	15	11.09	6.31	20	AN HC	AN	HC	0.853	0.358
[41]	43.67	48.32	86	24.35	11.55	21	AN HC	AN	HC	0.438	0.245

Table A1. *Cont.*

Study	Group 1			Group 2			Design	Group 1	Group 2	Effect Size (Hedges' g)	Standard Error
	Mean Adiponectin (µg/mL)	SD	N	Mean Adiponectin (µg/mL)	SD	N					
[76]	30.50	15.80	11	22.60	10.90	26	AN HC	AN	HC	0.618	0.368
[77]	16.53	6.41	51	12.67	4.48	106	AN HC	AN	HC	0.741	0.176
[16]	16.10	5.40	220	17.50	5.00	360	Obesity C.Thin	Obesity	C.Thin	−0.271	0.086
[78] *	13.84	4.98	27	9.70	3.90	24	AN HC	AN	HC	0.905	0.296
[31]	13.32	3.71	15	10.58	2.87	45	BN HC	BN	HC	0.874	0.309
[18]	11.00	7.80	31	11.50	6.20	11	AN BN HC Obesity C.Thin	AN	BN	−0.065	0.351
[18]	11.00	7.80	31	18.30	9.80	16	AN BN HC Obesity C.Thin	AN	HC	−0.945	0.319
[18]	11.00	7.80	31	5.70	2.00	9	AN BN HC Obesity C.Thin	AN	Obesity	0.686	0.383
[18]	11.00	7.80	31	20.10	7.60	6	AN BN HC Obesity C.Thin	AN	C.Thin	−1.178	0.458
[18]	11.50	6.20	11	18.30	9.80	16	AN BN HC Obesity C.Thin	BN	HC	−0.880	0.399
[18]	11.50	6.20	11	5.70	2.00	9	AN BN HC Obesity C.Thin	BN	Obesity	0.751	0.454
[18]	11.50	6.20	11	20.10	7.60	6	AN BN HC Obesity C.Thin	BN	C.Thin	−1.113	0.517
[18]	18.30	9.80	16	5.70	2.00	9	AN BN HC Obesity C.Thin	HC	Obesity	1.631	0.440
[18]	18.30	9.80	16	20.10	7.60	6	AN BN HC Obesity C.Thin	HC	C.Thin	−0.233	0.479
[18]	5.70	2.00	9	20.10	7.60	6	AN BN HC Obesity C.Thin	Obesity	C.Thin	−1.864	0.551
[79]	29.30	8.37	28	16.50	5.30	33	AN HC	AN	HC	1.837	0.309
[46]	14.97	6.74	76	11.65	4.58	30	AN HC	AN	HC	0.530	0.219
[80]	27.36	48.68	20	14.20	14.84	30	AN HC	AN	HC	0.396	0.292
[81]	31.30	13.50	19	29.60	6.90	19	AN C.Thin	AN	C.Thin	0.155	0.325
[26]	16.70	2.70	8	12.10	1.80	9	HC Obesity	HC	Obesity	1.927	0.613
[82]	40.24	6.76	308	15.02	5.87	164	AN HC	AN	HC	3.895	0.160

* Restrictive and bulimic/purgative subtypes of AN were pooled into a single group. $^{\$}$ Median and IR values were converted to means and SDs.

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