

Psychopharmacology of Obesity and Comorbid Eating Disorders

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Disclosures

Dr. Esther Dechant has no financial commercial interests to disclose.

Learning Objectives

- Review anorexia nervosa, bulimia nervosa and binge eating disorder including their association with obesity and metabolic syndrome
- Review overeating and OBE (objective binge eating)
- Review psychopharmacological treatment of binge eating disorder

Metabolic Syndrome

Glucose intolerance/insulin resistance (type 2 diabetes, impaired glucose tolerance, or impaired fasting glycemia)

Central obesity

Dyslipidemia (low HDL, elevated triglycerides)

Hypertension

Anorexia Nervosa – DSM V

Restriction of energy intake relative to requirements leading to **significantly low body weight**

Fear of weight gain or **behaviors** to avoid weight gain

Body image disturbance, denial of seriousness of illness, undue influence of body weight/shape on self-evaluation

Obesity/Metabolic Syndrome and AN

Lower rates of obesity and type II diabetes

No excess risk of metabolic syndrome

Dyslipidemia in acute ill – ***no evidence*** of increased risk of metabolic syndrome

However, there is ***cross over*** from AN to BN and widespread use of ***atypical antipsychotics*** in AN

Hudson, 2020

Bulimia Nervosa

Recurrent binge eating

Recurrent **compensatory behaviors** to prevent weight gain

On average **once** a week for three months

Self evaluation unduly influenced by body shape and weight

Does not occur exclusively during episodes of anorexia nervosa

Objective Binge Eating

BN: 3,000 to 4,000 Kcal

BED: 1,515 to 2,963 Kcal

Often energy dense, highly palatable food

Rapid consumption → Increased oxidative and inflammatory stress

Balantekin, 2024, Forney, 2015

Obesity and Metabolic Syndrome in BN

Some studies show associations with increased risk for metabolic syndrome components and some do not

The increased risk for metabolic syndrome is likely found in patients with increased obesity

Hudson, 2020

Binge Eating Disorder

Recurrent binge eating

No compensatory behaviors

On average **once** a week for three months

Rapid eating, eating without hunger, eating when uncomfortably full, eating alone due to embarrassment, feelings of disgust

Does not occur exclusively during episodes of anorexia nervosa or bulimia nervosa

Obesity and Metabolic Syndrome in BED

Overweight and weight gain

Increased risk of metabolic syndrome

Hudson, 2020

Overeating and Objective Binge Eating

Impacted by stress

Changes in sensitivity to reward and inhibitory control

Altered appetitive homeostatic processing

Metabolic/altered endocrine and inflammation

Volkow, 2013

BED and Metabolic Syndrome Components

Many studies have shown association between BED and obesity, especially severe obesity

Several studies have shown association between BED and type 2 diabetes

Four studies have shown an association between BED with hypertension

Three studies have shown association between BED and dyslipidemia

Hudson, 2020

Metabolic Syndrome and OBE: The Framingham Heart Study

Objective Binge Eating was found in 4.8% of women and 4.9% of men

Participants with OBE compared to non-binge eating odds ratios:

- 1.85 hypertension
- 1.42 hypertriglyceridemia
- 1.70 low HDL
- 3.18 insulin resistance
- 2.75 metabolic syndrome

Metabolic Syndrome and OBE: The Framingham Heart Study

OBE participants had 7.2 mg/dl higher fasting glucose

OBE participants had more visceral, subcutaneous and liver fat

Adjustment for BMI attenuated all except for fasting glucose

Abraham, 2014

Metabolic Syndrome and BED: A Community Sample

Five year longitudinal follow up of individuals with BED compared to BMI matched controls without BED had statistically significant increases:

2.2-fold for new dyslipidemia

1.7-fold for new diagnosis of any of hypertension, type 2 diabetes, or dyslipidemia

2.4-fold for new diagnosis of 2 or more metabolic syndrome components

Hudson, 2010

Psychopharmacology of BED

Therapies have evidence (e.g. CBT and IPT) with 50% durable remission rates

78.9% have at least one co-morbid condition

Lisdexamfetamine (FDA approved), topiramate, bupropion and naltrexone, SSRI

GLP-1 agonists

Hudson, 2007

Fluoxetine for BED – 16 week

	CBT and Placebo	Fluoxetine 60 mg daily	CBT plus Fluoxetine	Placebo
Remission of binge eating	73%	29%	55%	30%

Weight loss with remission was 7.4 lbs. vs 1.6 lbs. for no remission

Grilo, 2005

PRO-OPIOMELANOCORTIN NEURONS

→ **Anorectic effects** (decreased food intake and increased energy expenditure)

Bupropion – stimulates POMC
→ anorectic effects

Endogenous opioids – inhibit POMC
→ blocks anorectic effects

Naltrexone – block inhibition of endogenous opioids
→ anorectic effects

Naltrexone–Bupropion and BWL: 16 week RCT

	Behavioral Weight Loss and Placebo	Naltrexone- bupropion	BWL plus Naltrexone- bupropion	Placebo
Remission of binge eating	37.1%	31.3%	57.1%	17.7%
Greater or equal to 5% weight loss	31.4%	18.8%	37.1%	11.8%

Lisdexamfetamine

30 mg, 50 mg and 70 mg: 11 week RCT

	30 mg dose	50 mg	70 mg	Placebo
BE days per week	4.5 ± 1.0	4.5 ± 0.4	4.6 ± 0.5	4.3 ± 1.1
Weight loss in pounds	6.8	10.8	9.5	0.2

Lisdexamfetamine 50-70 mg: Two 12 week RCTs

	Trial 1 50-70 mg	Placebo	Trial 2 50-70 mg	Placebo
BE days per week (least mean squares)	-3.87	-2.51	-3.92	-2.26
Weight change in percentage	-6.3%	0.1	-5.6%	-0.2

Topiramate

(target dose 200 mg) added to CBT: 21week trial

	Topiramate (average dose 206 mg)	Placebo
Weight loss in pounds	15.0	2.0
Clinically significant weight loss >10%	33.3%	11.5%
Binge day frequency	4.2 ± 0	3.4 ± 0.3
Binge episodes per week	4.7 ± 0	3.8 ± 0.3

Topiramate (flexible dose): 14 week trial

	Topiramate	Placebo
Weight loss in pounds	13.0	2.6
Binge frequency per week	5.3 ± 0.3	6.3 ± 3.4
Binge day frequency	4.3 ± 0.3	4.8 ± 2.6

Trial	Weight loss
Topiramate – 14 weeks	13 lbs.
Topiramate – 21 weeks	15 lbs.
Lisdexamfetamine – 12 weeks	-6.3%
Lisdexamfetamine – 12 weeks	-5.6%
Lisdexamfetamine – 11 weeks	10.8#
Lisdexamfetamine – 11 weeks	9.5#
Naltrexone-bupropion – 16 weeks	-2.1%
Naltrexone-bupropion – 16 weeks	-3.4%

GLP-1 Agonists and BED

Pathophysiology of type 2 diabetes is hyperglycemia (combination of insulin resistance, inadequate insulin secretion and inappropriate secretion of glucagon)

GLP-1 agonists stimulate insulin secretion and suppress glucagon production

GLP-1 agonists slow gastric emptying and affect appetite-regulating neural pathways

GLP-1 Agonists and BED

Medications help with diabetes and weight loss (most patients regain weight once medications are stopped)

Weight loss clinically significant >10%

Loss of muscle mass with weight loss

Common GI side effects and less common, more serious side effects (e.g., pancreatitis)

GLP-1 Agonists and BED

Cons: could worsen pathological dietary restriction and prevent regular eating and thus maintain or worsen the eating disorder (especially once discontinued)

Pros: could also help with obesity/MetS along with overconsumption/binge eating urges

Bartell, 2023, Balantekin, 2024

Summary

BED and BN patients with obesity have increased rates of metabolic syndrome components

AN patients have lower rates of metabolic syndrome components but are often prescribed atypical antipsychotics – placing them at risk for binge eating/metabolic syndrome

Summary

Binge eating may cause oxidative and inflammatory stress

Binge eating is often driven by hunger, all or nothing thinking, emotional upset/stress, or substance disinhibition

Binge eating may also be affected by altered hedonic and appetitive control

Fairburn, 2008, Volkow, 2013

Summary

CBT, IPT, BWL, and many medications improve binge eating symptoms

GLP-1 agonists, topiramate, lisdexamfetamine, and naltrexone-bupropion are associated with weight loss

GLP-1 medications present exciting opportunities for patients with both BED and metabolic syndrome but should be used with caution

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