SICOM & AOCO 2024

SOMS International Conference on Obesity & Metabolism
in conjunction with Asia-Oceania Conference on Obesity

Hosted by

SOMS Society for Korean Obesity and Metabolism Studies

Co-Hosted by

aoaso Asia Oceania Association for the Study of Obesity

Empowering Health, Inspiring Change: Practical Solutions for Obesity

Date October 24 (Thu)~26 (Sat), 2024

Venue aT Center, Seoul, Republic of Korea
(3F Segyero Room & 4F Changjo Room)

Naltraxone/Bupropion (CONTRAVE®)

비만 환자 맞춤치료 최신 지견

Using a Phenotype-guided Approach for the Treatment of Obesity

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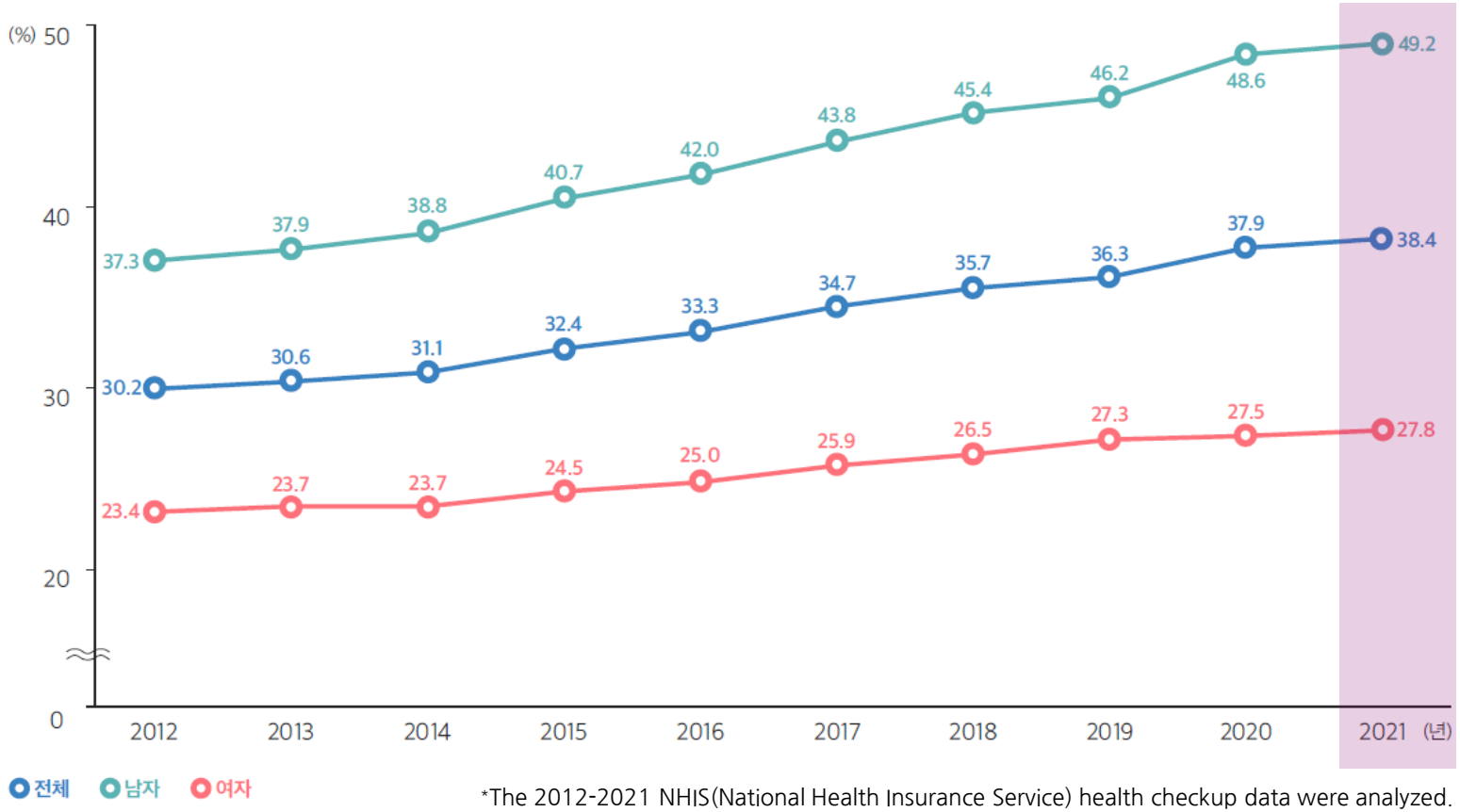
Contrave®
(naltrexone HCl/bupropion HCl)
8 mg/90 mg • Extended-Release Tablets

Kwangdong
광동제약

최근 10년간 비만 유병률[1]

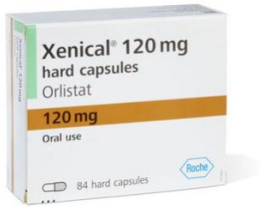
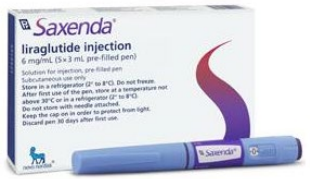
비만은 지난 10년간 꾸준히 증가해 왔고, 특히 남성의 경우 더욱 증가하였습니다. 2021년 기준으로 비만 유병률은 전체 인구의 38.4%로 관찰되었고, 남성의 경우 49.2% 및 여성의 경우 27.8%로 나타났습니다.[1]



*The 2012-2021 NHIS(National Health Insurance Service) health checkup data were analyzed.

1. KOREAN SOCIETY FOR THE STUDY OF OBESITY. 2023 OBESITY FACT SHEET (2023).

장기간 사용에 FDA 승인된 항비만제

Drug (trade name)	Orlistat (Xenical, Alli)	Phentermine/Topiramate (Qsymia)	Naltrexone/Bupropion (Contrave, Mysimba)	Liraglutide (Saxenda)	Semaglutide (Wegovy)	Tirzepatide (Zepbound)
Approval FDA/EMA (year)	FDA 1999 EMA 1998	FDA 2012	FDA 2014 EMA 2015	FDA 2014 EMA 2015	FDA 2021 EMA 2021	FDA 2023
Mechanism of action	Lipase inhibitor	Sympathomimetic amine anorectic/antiepileptic combination	Opioid antagonist /antidepressant combination	GLP-1 agonist	GLP-1 agonist	GLP-1/GIP dual agonist
Route of administration	Oral	Oral	Oral	Subcutaneous	Subcutaneous	Subcutaneous
Recommended dose	120 mg, three times a day	7.5 mg/46 mg, once a day	16 mg/180 mg, twice a day	3 mg, once a day	2.4 mg, once a week	15 mg, once a week
						

FDA, food and drug administration; EMA, european medicines agency; GLP-1, glucagon-like peptide-1; GIP, glucose-dependent insulinotropic polypeptide.

1. OT. Caklili et al., Diabetes, Metabolic Syndrome and Obesity. 2023;16:1767-1774. 2. M. Chakhtoura et al., EClinicalMedicine(Part of the lancet discovery science). 2023;58:101882.

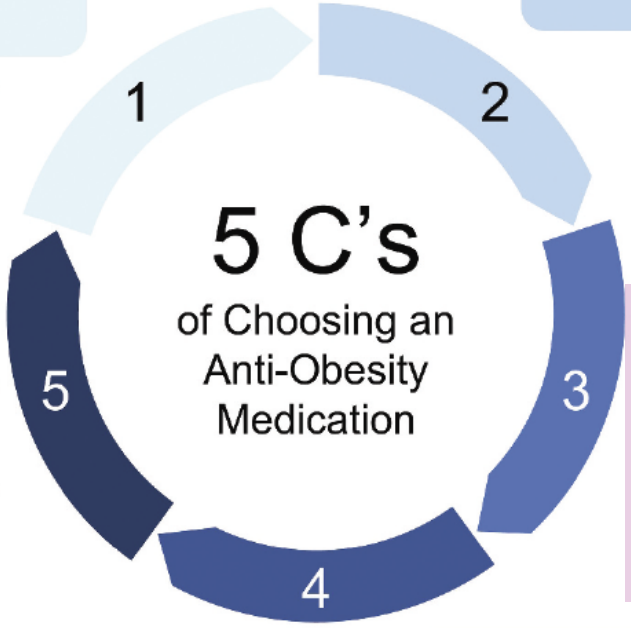
항 비만제를 선택하는 기준?

Contraindications and cautions

Assess the clinical history of the patient and assess the risk/benefit of each AOM

Comorbidities

When appropriate, select an AOM that can treat obesity and improve other comorbidities



Cues

Consider patient-described appetite control symptoms, side-effects and preference on mode of delivery

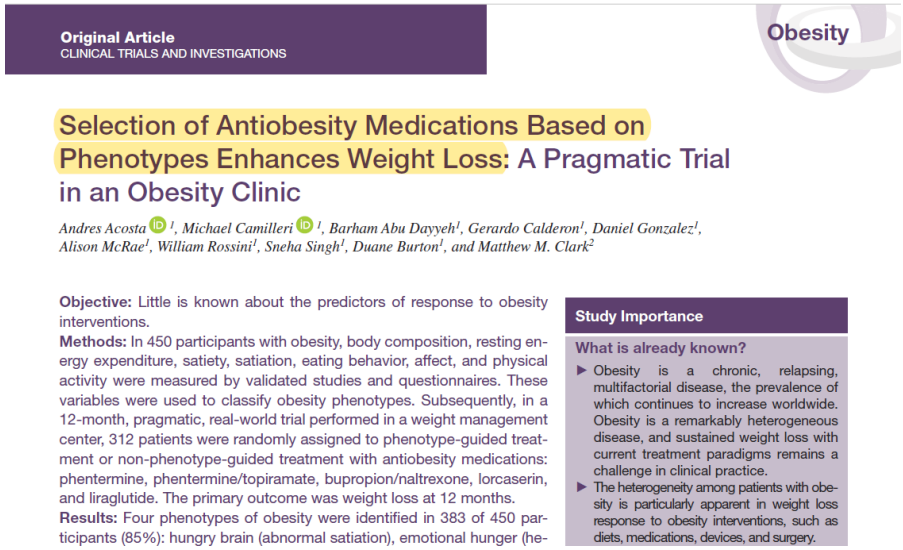
Cost/coverage

Consider the medication cost and the patient's insurance coverage

Combinations

Consider combination therapy with lifestyle interventions, other AOMs, and surgical procedures

Phenotype에 따른 항비만제의 선택[2]



Original Article
CLINICAL TRIALS AND INVESTIGATIONS

Obesity

Selection of Antiobesity Medications Based on Phenotypes Enhances Weight Loss: A Pragmatic Trial in an Obesity Clinic

Andres Acosta[1], Michael Camilleri[1], Barham Abu Dayyeh[1], Gerardo Calderon[1], Daniel Gonzalez[1], Alison McRae[1], William Rossini[1], Sneha Singh[1], Duane Burton[1], and Matthew M. Clark[2]

Objective: Little is known about the predictors of response to obesity interventions.
Methods: In 450 participants with obesity, body composition, resting energy expenditure, satiety, satiation, eating behavior, affect, and physical activity were measured by validated studies and questionnaires. These variables were used to classify obesity phenotypes. Subsequently, in a 12-month, pragmatic, real-world trial performed in a weight management center, 312 patients were randomly assigned to phenotype-guided treatment or non-phenotype-guided treatment with antiobesity medications: phentermine, phentermine/topiramate, bupropion/naltrexone, lorcaserin, and liraglutide. The primary outcome was weight loss at 12 months.
Results: Four phenotypes of obesity were identified in 383 of 450 participants (85%): hungry brain (abnormal satiation), emotional hunger (he-

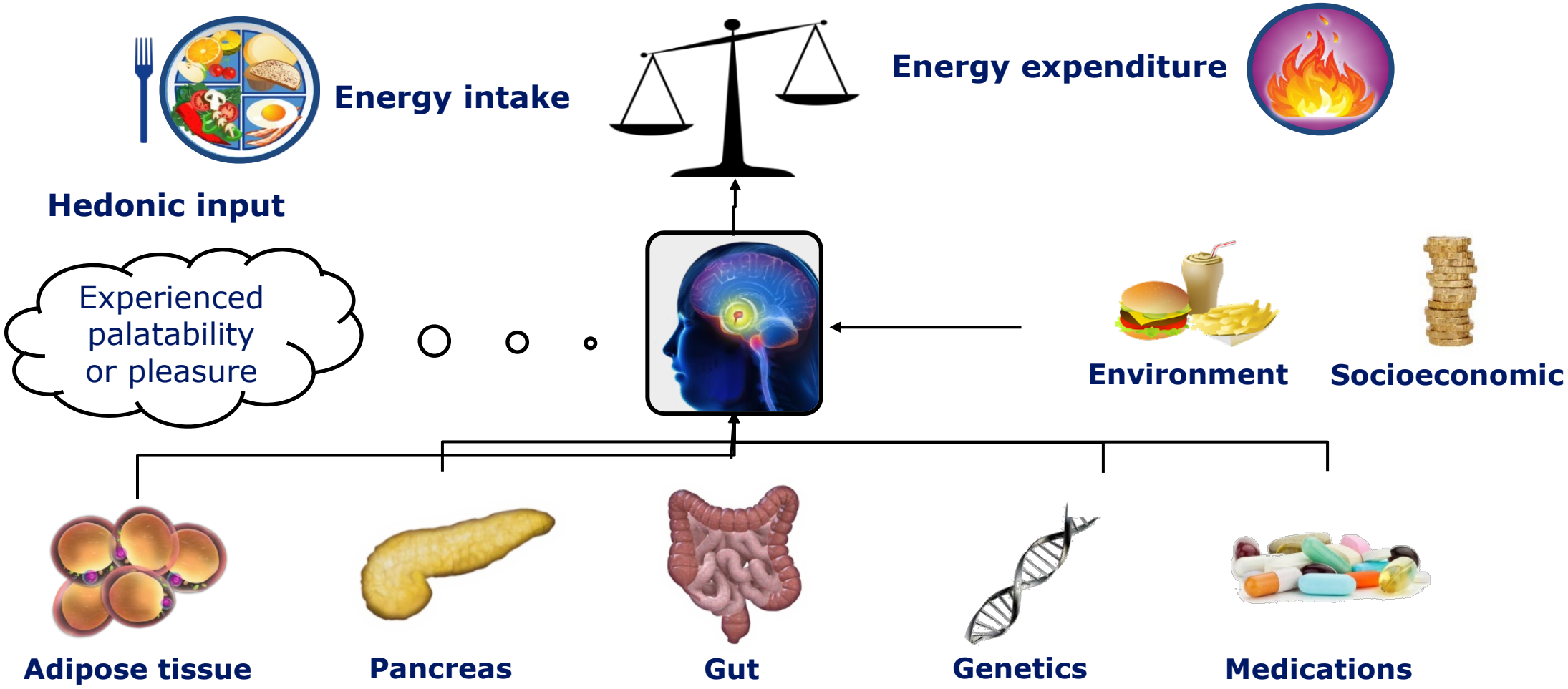
Study Importance

What is already known?

- Obesity is a chronic, relapsing, multifactorial disease, the prevalence of which continues to increase worldwide. Obesity is a remarkably heterogeneous disease, and sustained weight loss with current treatment paradigms remains a challenge in clinical practice.
- The heterogeneity among patients with obesity is particularly apparent in weight loss response to obesity interventions, such as diets, medications, devices, and surgery.

1. DB. Horn et al., POSTGRADUATE MEDICINE. 2022;134:359-375. 2. A. Acosta et al., Obesity. 2021;29(4):662-671.

에너지 균형에 영향을 주는 요인들



Woods SC, Seeley RJ. *Int J Obes Relat 7 Disord* 2002; 26:S8–10. **2.** Ludwig DS, Friedman MI. *JAMA* 2014; 311:2167–8.
Speliotes EK et al. *Nat Genet* 2010; 42:937–48. **4.** Garvey WT et al. *Endocr Pract* 2014; 20:977–89. **5.** Bray GA, Ryan DH. *Ann NY Acad Sci* 2014; 1311:1–13.
Guyenet SJ, Schwartz MW. *J Clin Endocrinol Metab* 2012; 97:745–55.

Obesity Phenotypes based on pathophysiology

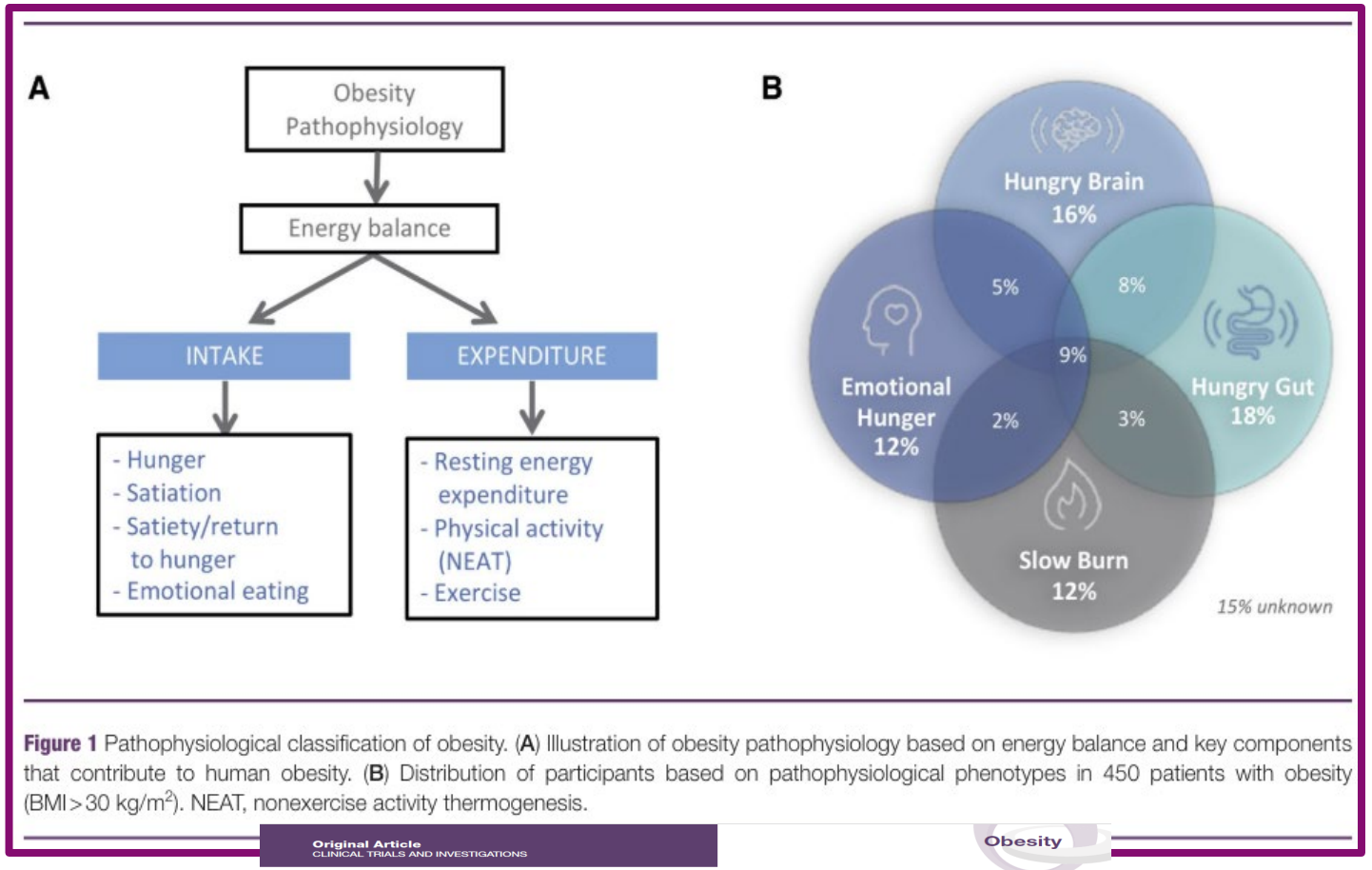


Figure 1 Pathophysiological classification of obesity. (**A**) Illustration of obesity pathophysiology based on energy balance and key components that contribute to human obesity. (**B**) Distribution of participants based on pathophysiological phenotypes in 450 patients with obesity (BMI > 30 kg/m^2). NEAT, nonexercise activity thermogenesis.

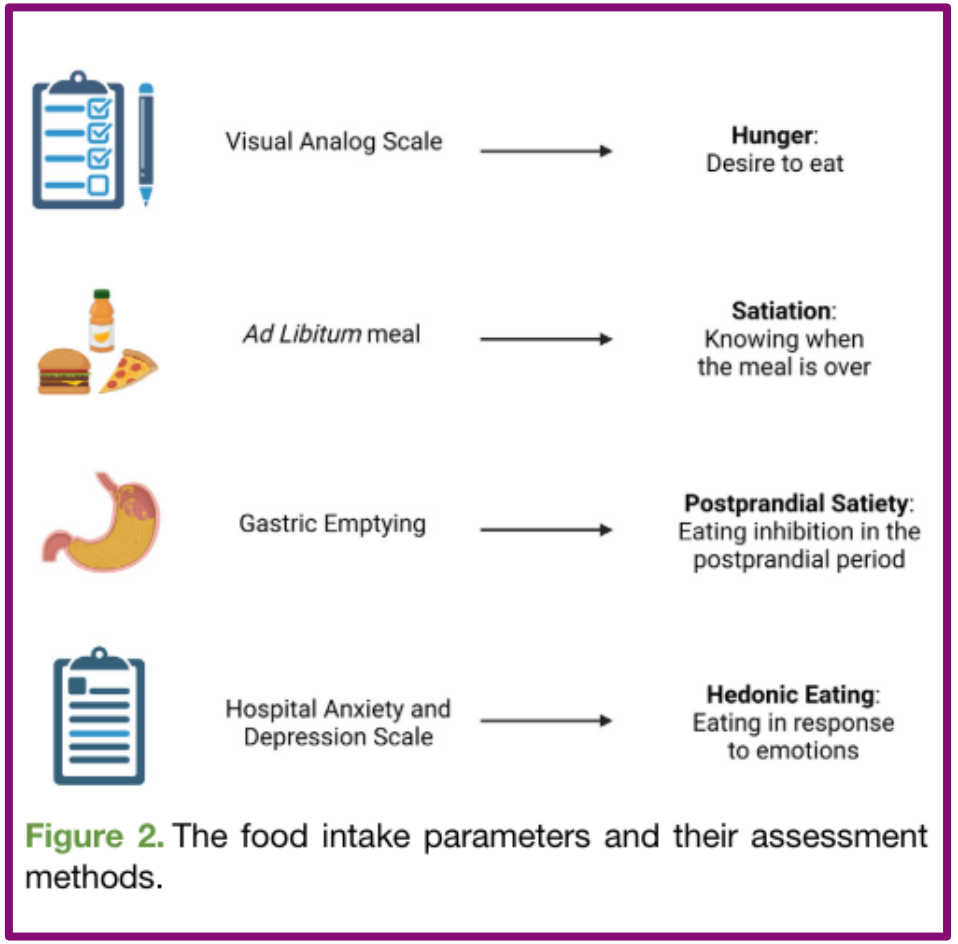


Figure 2. The food intake parameters and their assessment methods.

Original Article
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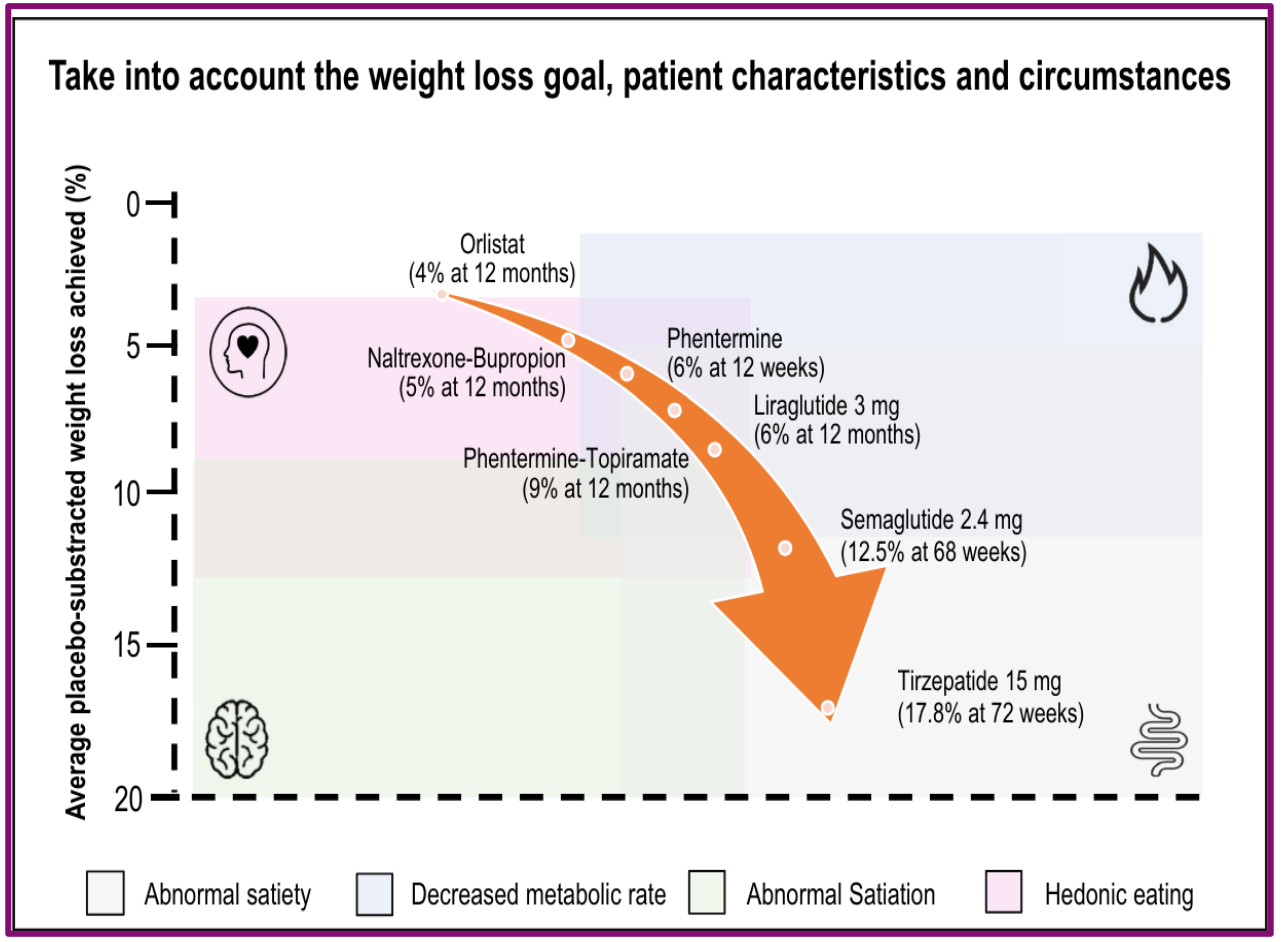
- The heterogeneity among patients with obesity is particularly apparent in weight loss response to obesity interventions, such as diets, medications, devices, and surgery.

Obesity (Silver Spring). 2021 Apr;29(4):662-671
Gastro Hep Adv. 2023;2(1):121-128.

Obesity Phenotypes based on pathophysiology

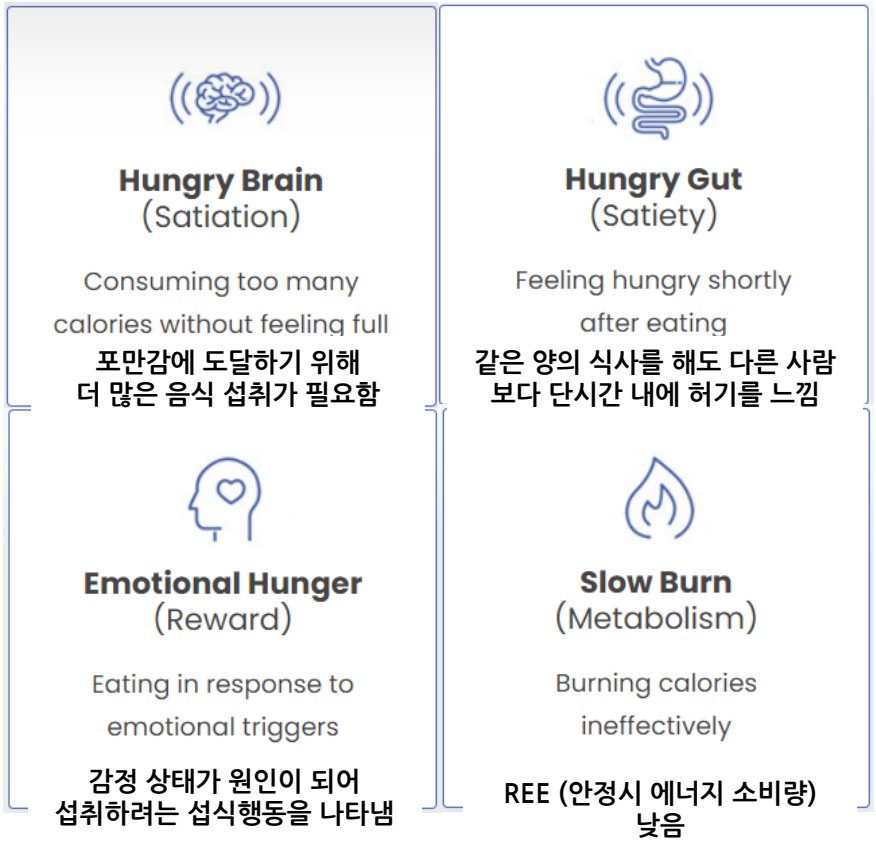
In a pragmatic clinical trial based on an approach guided by the phenotype, a more pronounced weight loss (1.75 fold) after 1 year was observed versus the non-phenotype guided group experimenting a 15.9% weight loss versus 9.0%; p<0.001 [138][139]. Interestingly, 79% of the patients reached >10% weight loss after 1 year versus 34% in the control group.

Phenotypes		Medication
Abnormal satiation	"Hungry brain", characterized by excessive calories consumption to terminate meal Measured by the kilocalories needed to reach maximal fullness	Phentermine-topiramate extended release
Hedonic eating	"Emotional hunger", characterized by the desire of eating to manage with emotions, cravings, and reward- seeking behaviors Measured by validated questionnaires	Bupropion-naltrexone
Abnormal satiety	"Hungry gut", characterized by rapid gastric emptying and reduced duration of fullness Measured by validated scales for hunger and gastric emptying by scintigraphy	Liraglutide
Decreased metabolic rate	"Slow burn", characterized by reduced resting energy expenditure and physical activity Measured by indirect calorimetry, reported exercise and physical activity	Low-dose phentermine plus resistance training



Reviews in Endocrine and Metabolic Disorders (2023) 24:795–807

비만 phenotype 분류



[Hungry Brain]

- Abnormal ad libitum buffet meal: 75th percentile for females >894 kcal and males >1,376 kcal

[Emotional Hunger]

- Abnormal behavioral questionnaire for anxiety: 75th percentile for both genders ≥7 points on HADS scale

[Hungry Gut]

- Accelerated gastric emptying of the radiolabeled solid 320-kcal, 30% fat meal: 25th percentile for females <101 minutes and males <86 minutes

[Slow Burn]

- Measured REE: 25th percentile for females <96% and males <94% of predicted REE based on Harris-Benedict equation

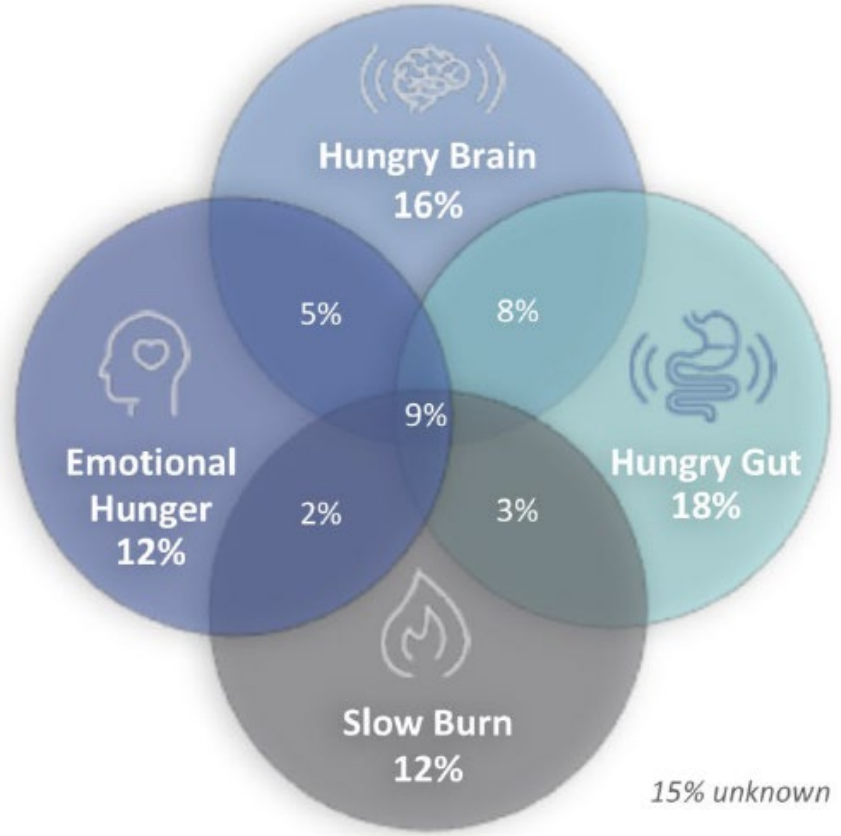
*Obesity phenotype classification was based on a cutoff of the 25th or 75th percentile of each measurement (applied separately for females and males) recorded in the first 100 participants who completed phenotype measurements. REE, resting energy expenditure.

1. A. Acosta et al., Obesity. 2021;29(4):662-671.

비만 phenotype 분류

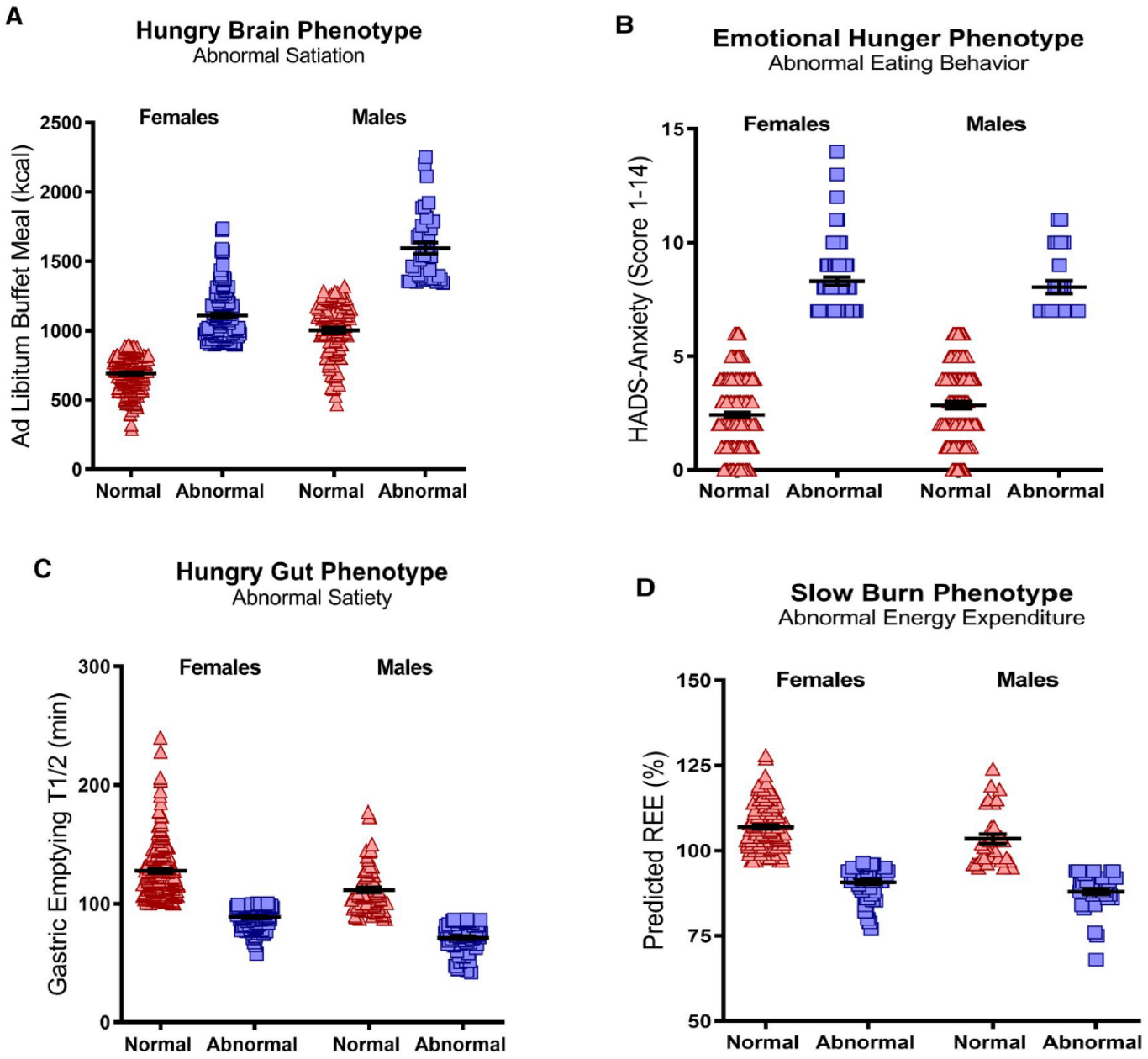
		Phenotype					
	All cohort	Hungry brain	Hungry gut	Emotional hunger	Slow burn	None	ANOVA *P*
Demographics							
Prevalence, *n* (%)	450 (100%)	143/450 (32%)	144/450 (32%)	96/450 (21%)	82/400 (21%)	68/450 (15%)	
Age, y	39 ± 0.5	37 ± 0.9	39 ± 0.9	37 ± 1.2	39 ± 1.2	40 ± 1.3	0.19
Gender (F), %	72	78	67	75	57	83	0.009#
Race (White), %	93	96	89	96	95	100	0.01#
Weight, kg	107 ± 1.0	108 ± 1.7	106 ± 1.7	111 ± 2.2	115 ± 3.2	106 ± 2.4	0.09
Height, cm	169 ± 0.4	170 ± 0.8	169 ± 0.8	169 ± 0.9	171 ± 1.1	168 ± 1.0	0.16
BMI, kg/m^2	37 ± 0.3	37 ± 0.5	36 ± 0.5	39 ± 0.7	39 ± 0.8	38 ± 0.8	0.07
Waist, cm	105 ± 0.1	106 ± 1.3	107 ± 1.1	108 ± 2.0	104 ± 2.3	105 ± 1.1	0.82
Hip, cm	120 ± 0.1	121 ± 1.1	121 ± 1.0	122 ± 1.9	117 ± 1.4	120 ± 1.3	0.80
Pulse, beats/min	74 ± 0.6	74 ± 1.0	73 ± 0.9	74 ± 1.3	75 ± 1.5	77 ± 2.0	0.25
SBP, mmHg	131 ± 0.7	132 ± 1.3	133 ± 1.3	130 ± 1.4	131 ± 2.0	131 ± 2.1	0.15
DBP, mmHg	82 ± 0.6	80 ± 0.9	81 ± 1.0	79 ± 1.1	81 ± 1.4	83 ± 1.4	0.45
Fasting glucose, mg/dL	103 ± 1.4	101 ± 2.8	103 ± 1.5	98 ± 1.8	97 ± 2.2	102 ± 1.9	0.55
Comorbidities^	1.1 ± 0.1	1.1 ± 0.1	1.0 ± 0.2	1.3 ± 0.3	1.3 ± 0.1	0.9 ± 0.4	0.19
Phenotyping tests							
Ad libitum buffet meal, kcal	929 ± 16	**1,224 ± 25**	996 ± 26	990 ± 34	918 ± 35	700 ± 21	<0.001
Gastric emptying T½, min	110 ± 1.4	107 ± 2.2	**83 ± 1.4**	111 ± 2.7	117 ± 3.3	133 ± 3.4	<0.001
HADS-Anxiety (0-21 scale)	4 ± 0.1	4 ± 0.3	3.7 ± 0.2	**8.1 ± 0.2**	3.9 ± 0.1	2.4 ± 0.2	<0.001
Predicted REE (HB), %	100 ± 0.6	102 ± 1.4	100 ± 1.4	103 ± 1.1	**89 ± 0.6**	106 ± 0.8	<0.001

비만환자(BMI >30 kg/m^2) 450명에서
병태생리학적 phenotype에 따른 분류 및 대상자 분포



1. A. Acosta et al., Obesity. 2021;29(4):662-671.

비만 phenotype에 따른 대상자의 병태생리학적 특성



1. A. Acosta et al., Obesity. 2021;29(4):662-671.

Phenotype에 따른 항비만제 선택

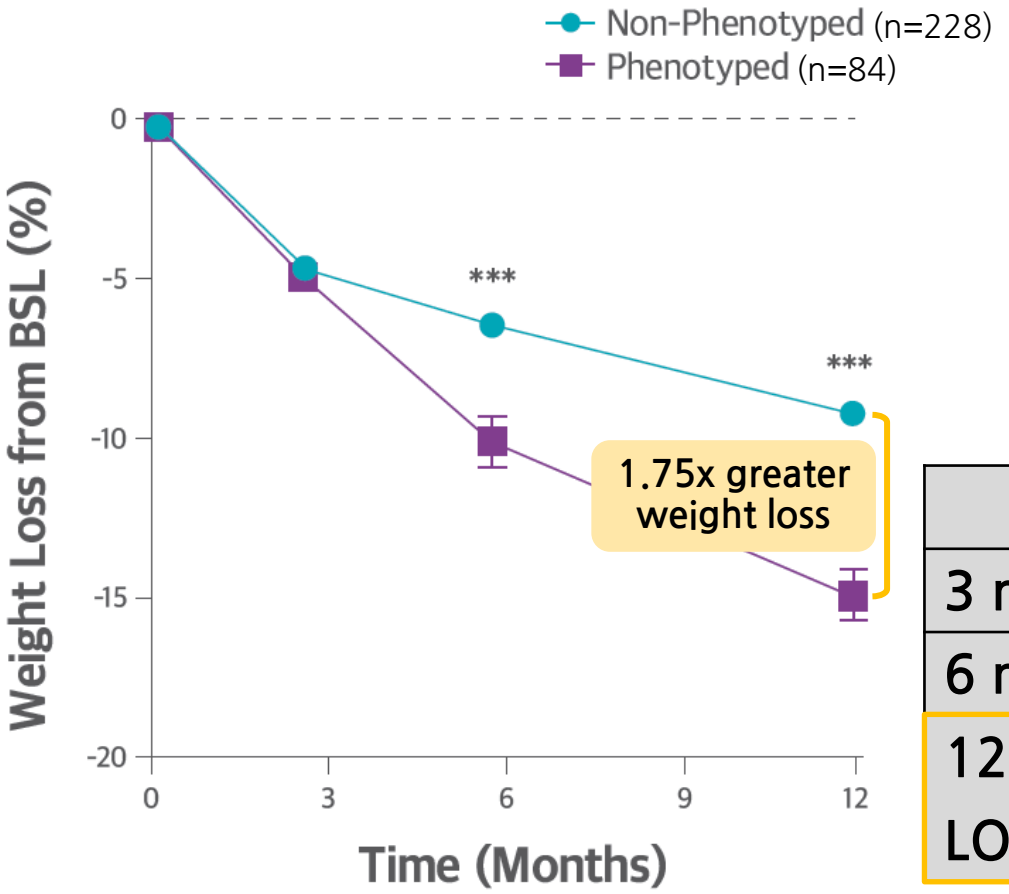
Phenotype	Drug	Dose
Hungry Brain	Phentermine-Topiramate extended release Lorcarserin	7.5/46 mg QD 20 mg QD
Emotional Hunger	**Naltrexone/Buproprion sustained release**	**16/180 mg BID**
Hungry Gut	Liraglutide	3 mg sc QD
Slow Burn	Phentermine + Increased physical activity	15 mg QD

*Treatment decisions in the phenotyped group were determined by an a priori management approach based on the medications' predominant mechanism of action.
Naltrexone/Bupropion sustained release was selected for the emotional hunger phenotype as bupropion is a dopamine/norepinephrine reuptake inhibitor and naltrexone is an opioid receptor agonist; **together they modulate appetite, mood, and cravings**.
*In the non-phenotyped group, medications were selected based on side effect profile, glycemic control, patient preference, cravings, insurance preference, previous successful attempts with same medication, abnormal satiation, and other/unknown reason.

1. A. Acosta et al., Obesity. 2021;29(4):662-671.

Phenotype에 따른 항비만제 투여 결과

Phenotype에 따라 항비만제를 투여한 경우, 1년 후 체중감량은 1.75배 높게 나타났습니다.[1]



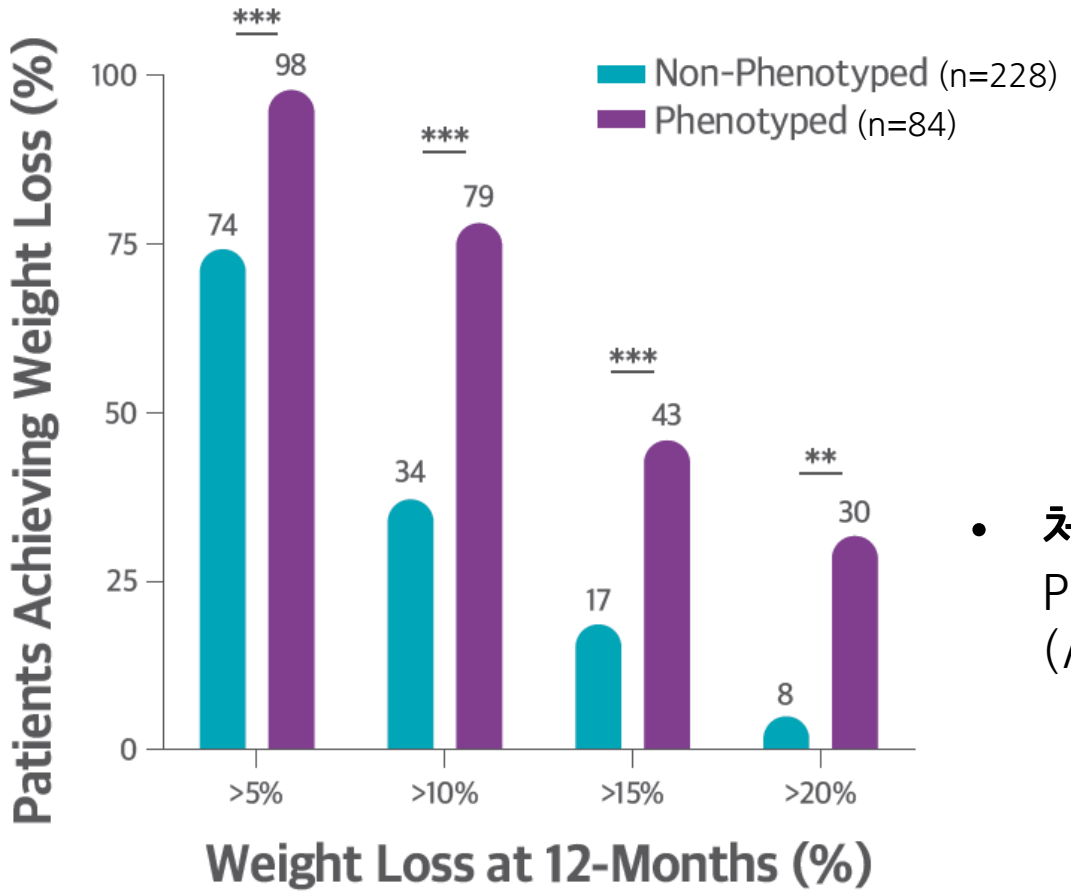
	Phenotyped	Non-Phenotyped	*P*
3 months	-5.4% (0.5%)	-5.1% (0.3%)	0.61
6 months	-10.5% (0.8%)	-6.3% (0.4%)	<0.001
12 months	-15.9% (1.1%)	-9.0% (0.6%)	<0.001
LOCF	-12.1% (0.9%)	-7.8% (0.5%)	<0.001

***P<0.001; BSL, baseline; LOCF, last observation carried forward.

1. A. Acosta et al., Obesity. 2021;29(4):662-671.

Phenotype에 따른 항비만제 투여 결과

Phenotype에 따른 항비만제 투여는 체중감량 효과를 보다 증가시킬 수 있습니다.[1]



- **체중감량 실패율 [TBWL 5% 이하]**
  Phenotyped(2%) VS Non-Phenotyped(26%)
  (P<0.001)[1]

**P<0.01, ***P<0.001; TBWL, total body weight loss.

1. A. Acosta et al., Obesity. 2021;29(4):662-671.

Why Naltrexone/Bupropion (CONTRAVE®)?

Emotional eating 환자에는 CONTRAVE®를 고려할 수 있습니다.

Contrave®
(naltrexone HCl/bupropion HCl)
8 mg/90 mg • Extended-Release Tablets

Kwangdong
광동제약

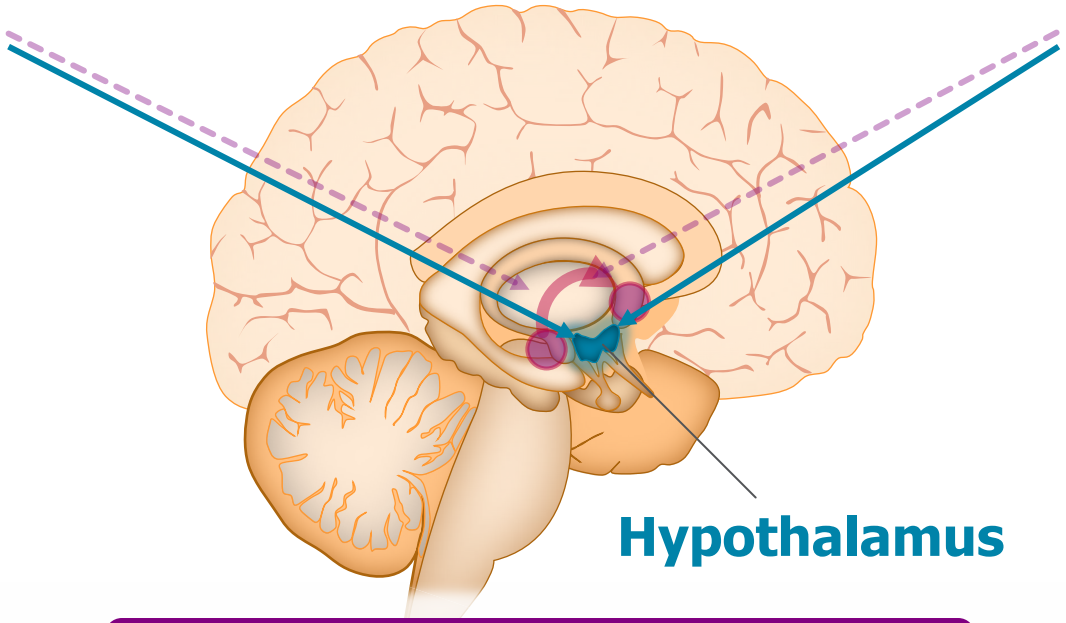
Naltraxone/Bupropion에 의한 Appetite 및 Craving 억제

CONTRAVE® 유효성분인 Naltrexone과 Bupropion은 또한 Hypothalamic Hunger System에도 작용하여 Appetite(Homeostatic eating)를 억제합니다.[1]

Bupropion HCl

Indicated for the treatment of **major depressive disorder** and as an aid to **smoking cessation**

Stimulates **POMC cells**, which suppresses appetite



Naltrexone HCl

Indicated for the treatment of **alcohol dependence** and for prevention of relapse to **opioid dependence**

Blocks **β-endorphin negative feedback loop** on POMC neurons, which further contributes to appetite suppression

Mesolimbic Reward System

+

Hypothalamic Hunger System

Homeostatic eating ↓

1. SK. Billes et al., Pharmacol Res. 2014;84:1-11.

Naltraxone/Bupropion에 의한 Appetite 및 Craving 억제

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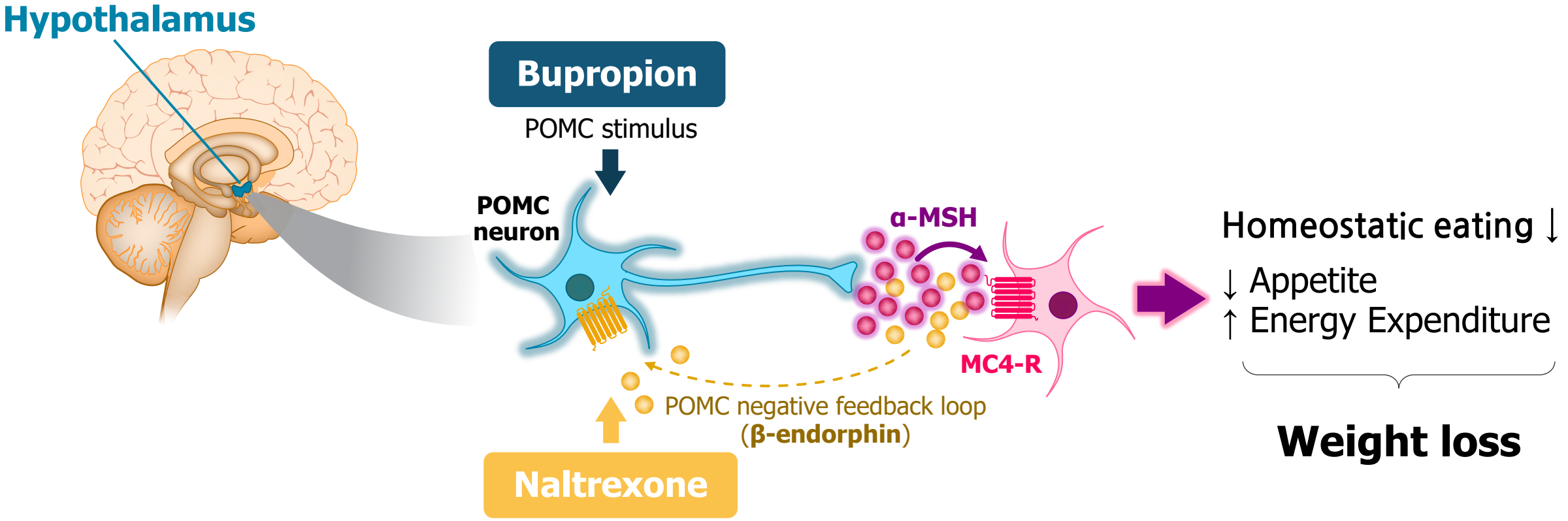


Binds at the μ-opioid receptor on POMC neurons,
thus blocking the β-endorphin negative feedback loop

MC4-R, melanocortin-4 receptor; MSH, melanocyte-stimulating hormone; POMC, pro-opiomelanocortin.

1. SK. Billes et al., Pharmacol Res. 2014;84:1-11.

Indication and contraindication of Contrave

금기 및 사용상의 주의사항	Contrave®[5]
항정신병약 병용 시	• 모노아민 산화효소 억제제 투여 후 14일 동안 금기 • 양극성 장애 환자 금기 • 향정신병약 병용시 발작 위험 증가 가능
자살 행동, 자살 충동	위험도가 높은 젊은 성인 환자들은 주의 깊은 관찰, 행동 변화 모니터링, 증상 발현 시 의사에게 연락
기분 및 수면 장애	1년간의 임상에서 위약군보다 관련 이상반응이 많은 것으로 보고 • 수면장애 (14.8% vs. 위약-8.4%) • 우울 (6.3% vs. 위약 5.9%) • 불안 (6.1% vs. 위약 4.4%)
인지기능	집중력 장애, 어지러움, 실신 등 위약군보다 빈번히 발생 (15.0% vs. 위약 5.5%), 집중력 장애 (2.5% vs. 0.6%) 가 가장 빈번
알코올 섭취	과도한 알코올 사용은 발작 위험을 높일 수 있음 음주를 최소화하거나, 금주하여야 한다.
운동 선수 경기 기간 중 사용[6]	허용 (부프로피온: 2020년 모니터링 프로그램 포함)

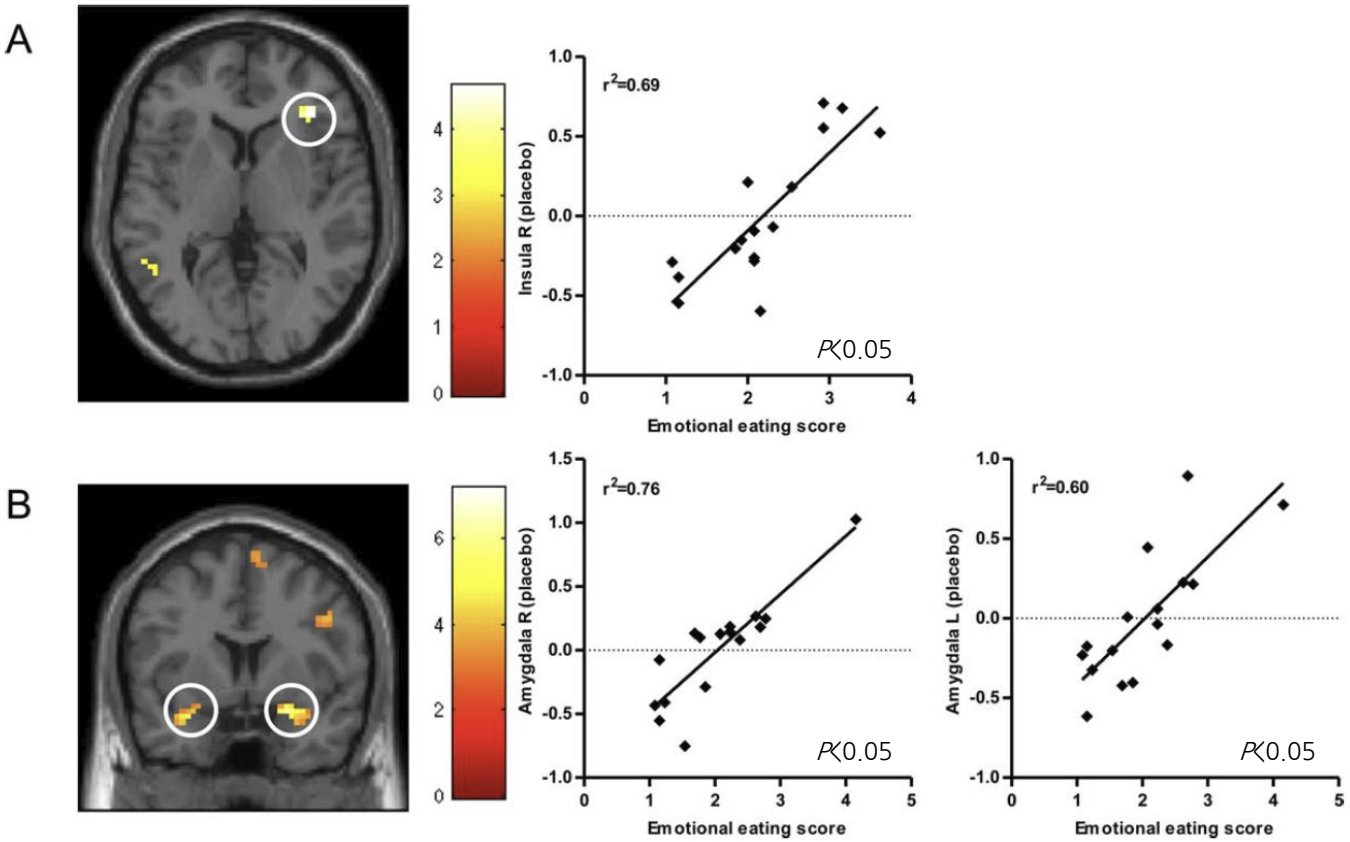
2. 다음 환자에는 투여하지 말 것
1) 이 약의 주성분 또는 다른 성분에 과민반응이 있는 환자
2) 조절되지 않는 고혈압 환자
3) 발작 장애 또는 발작 병력이 있는 환자
4) 중추신경계 종양이 있는 환자
5) 알코올 또는 벤조디아제핀계, 바르비탈류, 항간질약 등 약물복용을 갑자기 중단한 환자
6) 양극성 장애 환자
7) 부프로피온 또는 날트렉손을 함유하고 있는 다른 약을 투여 받고 있는 환자
8) 대식증 또는 신경성 식욕부진을 현재 또는 과거에 진단 받은 환자
9) 현재 아편성 또는 아편효능약(예, 메사돈) 의존성이 있는 환자 또는 급성 아편 금단증상을 지닌 환자
10) MAO 억제제를 투여중인 환자 (MAO 억제제 투여중지 후 최소 14일이 경과한 후 이 약을 투여할 수 있다.)
11) 급성 간염·간부전환자, 중증의 간장애 환자

12) 신장애 환자
13) 임부, 임신하고 있을 가능성이 있는 여성 또는 수유부
14) 이 약은 유당을 함유하고 있으므로, 갈락토오스 불내성(galactose intolerance), Lapp 유당분해효소 결핍증(Lapp lactase deficiency) 또는 포도당-갈락토오스 흡수장애(glucose-glactose malabosorption) 등의 유전적인 문제가 있는 환자에게는 투여하면 안된다.
15) 75세 이상의 고령자

3. 다음 환자에는 신중히 투여할 것
1) 발작의 위험이 있는 환자(이 약의 발작 발생률은 약 1/1,000으로 나타났다. 발작의 위험을 증가시킬 수 있는 요인은 5. 일반적 주의를 참고)
2) 고혈압 환자
3) 치료되지 않는 관상동맥질환자(예. 협심증, 심근경색증)
4) 뇌혈관질환 또는 뇌혈관질환 병력이 있는 환자
5) 조증 병력이 있는 환자
6) 65세 이상 고령자(75세 이상의 고령자는 투여가 권장되지 않는다.)

Emotional eating과 뇌 반응성 관련성

Emotional eating 점수는 음식 자극에 대한 뇌 반응성과 양의 상관관계를 나타내었습니다.[1]
[마른군과 비만군에서 Insula / T2DM군에서 Insula, Amygdala, Inferior OFC]



Emotional eating과 음식 사진에 대한 뇌 반응성 간의 상관관계

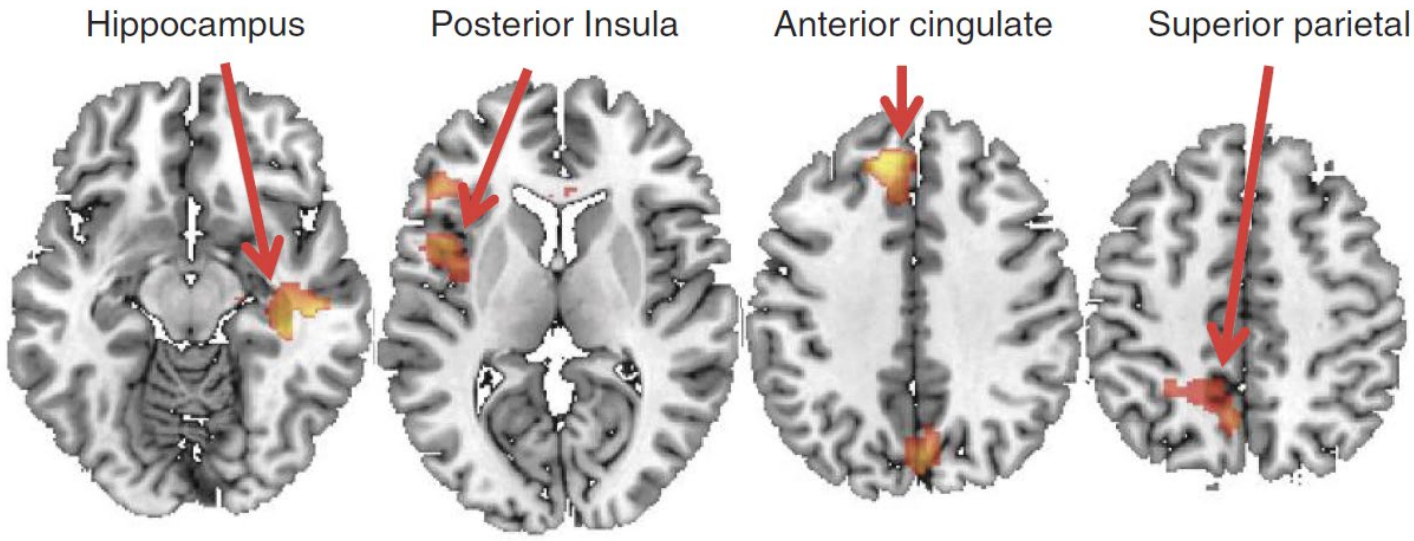
(A) Axial brain slice showing positive correlation in subjects with obesity (n=16) in right insula between emotional eating and brain responses to food VS non-food pictures.
(B) Coronal brain slice showing positive correlation in T2DM patients with obesity (n=16) in left and right amygdala between emotional eating and brain responses to food VS non-food pictures.

- **Anterior insula**: 시각적 음식 자극, 맛을 보거나 냄새를 맡는 과정, 음식을 갈망하는 과정에서 나타나는 미각 인지에 관여
- **Amygdala**: 부정적/긍정적 감정 처리와 자극-보상 학습과정에 관여
- **Inferior OFC(orbitofrontal cortex)**: 보상 과정과 의사 결정에 관여

1. L. van Bloemendaal et al., Obesity. 2015;23(10):2075-2082.

CONTRAVE®가 식품 신호(food cues)에 대한 뇌 반응성에 미치는 영향

위약군 대비 CONTRAVE®군에서 식품 신호에 반응하는 시상하부의 활성화는 유의적으로 감소한 반면, 억제조절 (Anterior cingulate), 내적인식 (Superior frontal, Insula, Superior parietal), 기억 (Hippocampus) 관련된 뇌 영역의 활성화는 유의적으로 증가함을 관찰하였습니다.[1] (whole-brain analysis; $P<0.05$)



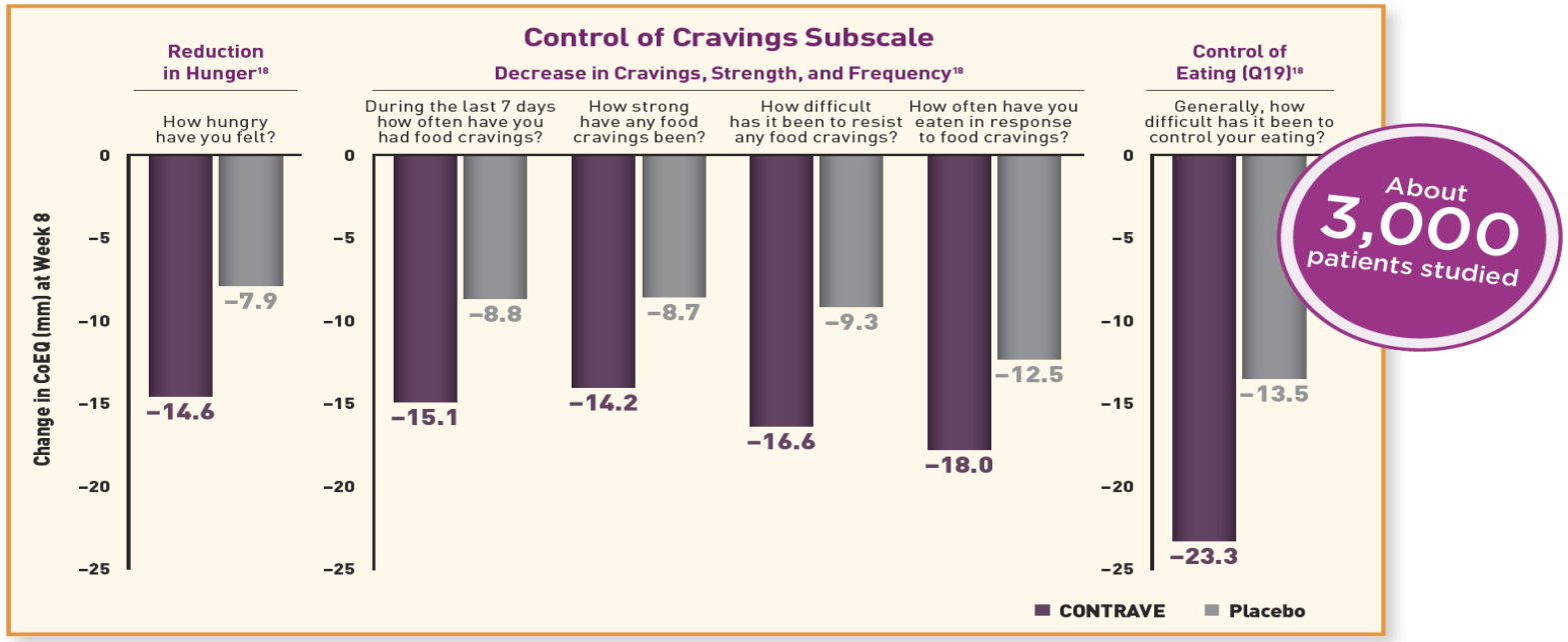
The greater effect of NB32 (n=20) as compared with placebo (n=20) in response to visual food cues

1. G-J Wang et al., International Journal of Obesity. 2014;38:682-688.

CONTRAVE®에 의한 Hunger/Craving 감소, 섭식 통제의 개선

Early improvement in food cravings are associated with long-term weight loss success in a large clinical sample, Int J Obes (Lond). 2017 Aug;41(8):1232-1236

Conclusions: These findings highlight the importance of the experience of food cravings in the treatment of obesity.

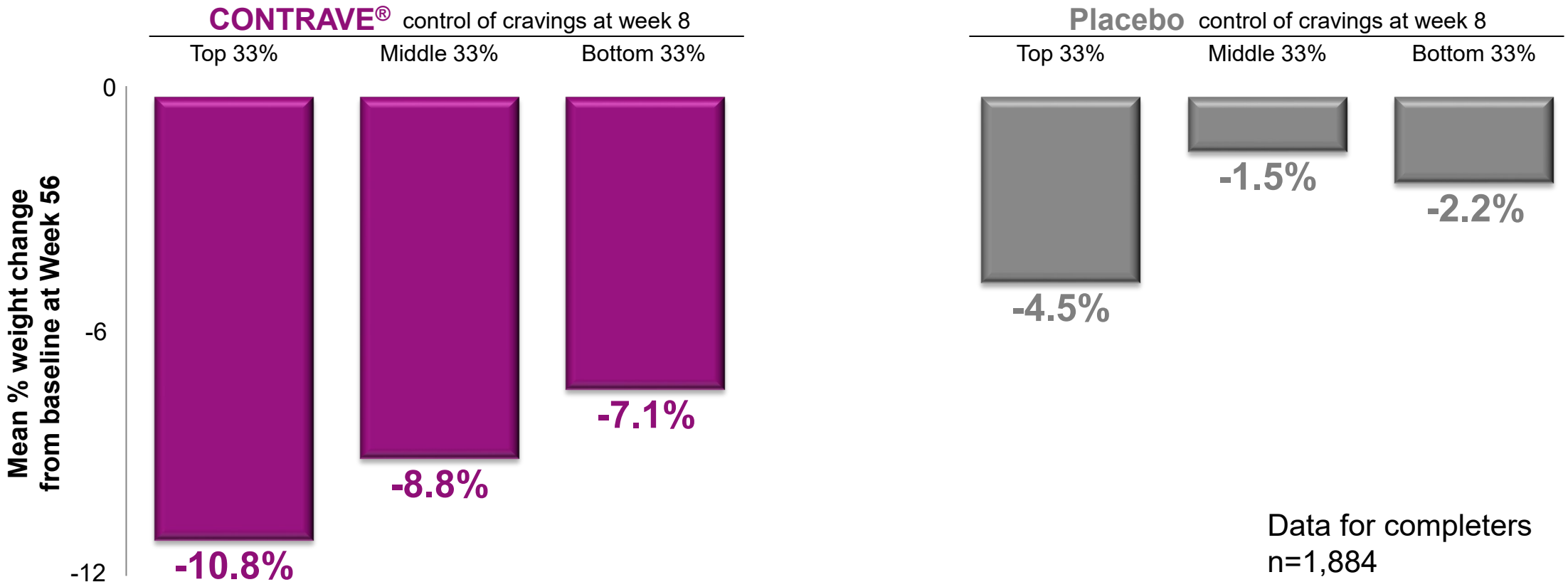


*First time point measured at week 8. Patients were administered the CoEQ(Control of Eating Questionnaire), which consists of 20 questions assessing hunger, cravings, and overall control of eating using a visual analogue scale. CoEQ Question 19 ("Generally, how difficult has it been to control your eating?") was a secondary efficacy endpoint in the studies. In validation work performed by the developers of the CoEQ, 6 of the 20 questions were found to represent the Control of Cravings Subscale.

1. Data on file, Currax Pharmaceuticals LLC.

CONTRAVE®에 의한 초기 Craving 감소와 장기간 체중감량 간 관련성

CONTRAVE®에 의한 Craving의 초기 개선은 장기간 더 많은 체중감량을 유도하였습니다.[1]

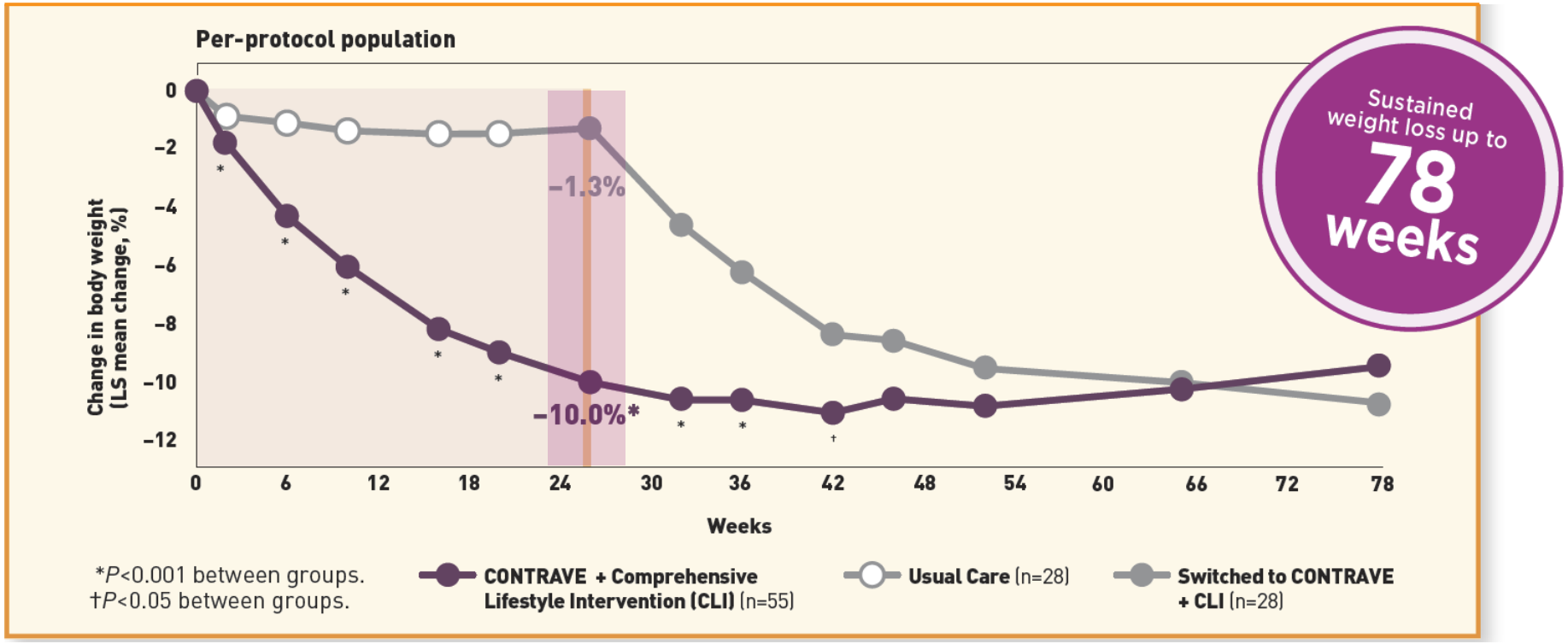


Patients were administered the CoEQ(Control of Eating Questionnaire), which consists of 20 questions assessing hunger, cravings, and overall control of eating using a visual analogue scale. In validation work performed by the developers of the CoEQ, 6 of the 20 questions were found to represent the Control of Cravings Subscale. Post hoc analyses of the CoEQ data across 4 studies explored the relationship between changes in CoEQ responses and changes in body weight.

1. Data on file, Currax Pharmaceuticals LLC. 2. M. Dalton et al., International Journal of Obesity. 2017;41(8):1232-1236.

CONTRAVE® 장기간 투여 연구: Open-label IGNITE study

26주 시, Usual Care군 대비 CONTRAVE®+CLI군에서 유의적인 체중감량이 관찰되었습니다. CONTRAVE® 78주 투여군에서는 유의적인 체중감량과 함께 감량의 최대치가 끝까지 유지되는 것을 확인하였습니다.[1]



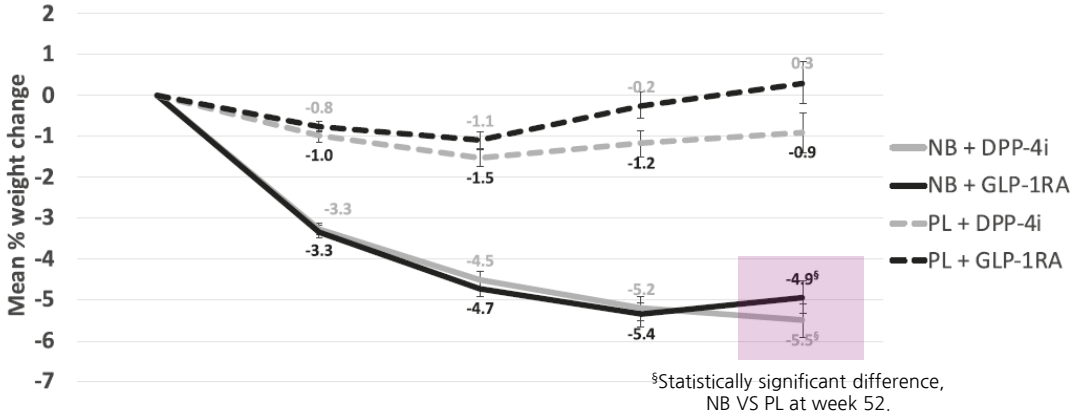
Per-protocol population was defined as modified intent-to-treat (mITT) subjects in compliance with the protocol in the controlled treatment period.
Patients who did not achieve 5% weight loss after 16 weeks of taking CONTRAVE® discontinued treatment and were not included in the per-protocol analysis. This determination occurred at week 16 for the CONTRAVE®+CLI group and week 42 for the Usual Care switched to CONTRAVE®+CLI group.

1. A. Halseth et al., Obesity. 2017;25:338-345.

Extended-release naltrexone/bupropion is safe and effective among subjects with type 2 diabetes already taking incretin agents: a post-hoc analysis of the LIGHT trial; Int J Obes (Lond). 2021 Aug;45(8):1687-1695

Conclusion: NB appears to be effective in reducing weight in patients with T2DM and obesity/overweight who are taking DPP-4ihibitors or GLP-1RA. The SAE rates in all arms of this analysis were lower than have been reported in other cardiovascular outcome trials in type 2 diabetes.

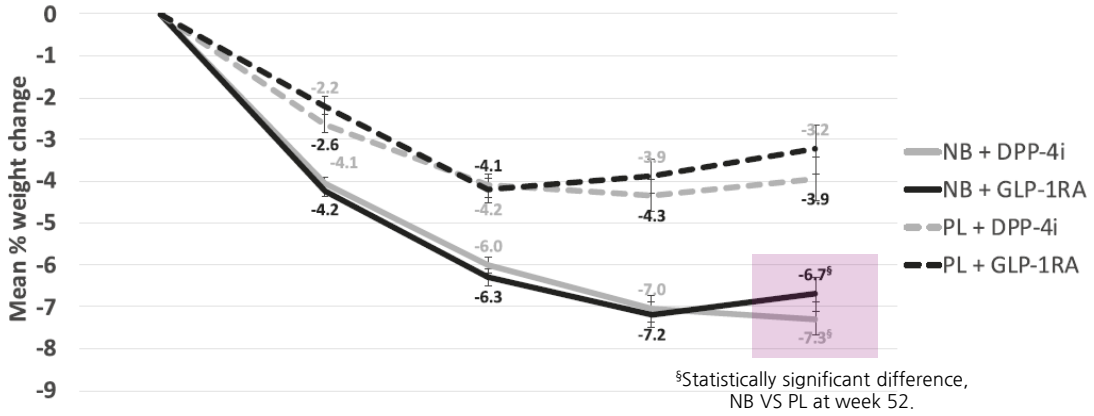
총 대상자 분석 [n=1,317; NB(n=684) VS PL(n=633)][1]



	Baseline	Week 8	Week 16	Week 26	Week 52
Number of patients in the model					
NB + DPP-4i	313	313	291	199	165
NB + GLP-1RA	300	300	270	200	170
PL + DPP-4i	305	304	285	124	96
PL + GLP-1RA	307	307	284	104	85

[DPP-4is 복용자] NB -5.5% VS PL -0.9%
Treatment Difference -4.6% (95% CI: -5.84 to -3.37, *P*<0.0001)
[GLP-1RAs 복용자] NB -4.9% VS PL +0.3%
Treatment Difference -5.2% (95% CI: -6.51 to -3.97, *P*<0.0001)

52주 완료자 분석 [n=548; NB(n=353) VS PL(n=195)][1]



	Baseline	Week 8	Week 16	Week 26	Week 52
Number of patients in the model					
NB + DPP-4i	174	174	174	173	165
NB + GLP-1RA	179	179	179	179	170
PL + DPP-4i	105	105	105	105	96
PL + GLP-1RA	90	90	90	89	85

[DPP-4is 복용자] NB -7.3% VS PL -3.9%
Absolute Difference -3.3% (95% CI: -4.67 to -2.03, *P*=0.0001)
[GLP-1RAs 복용자] NB -6.7% VS PL -3.2%
Absolute Difference -3.5% (95% CI: -4.85 to -2.10, *P*<0.0001)

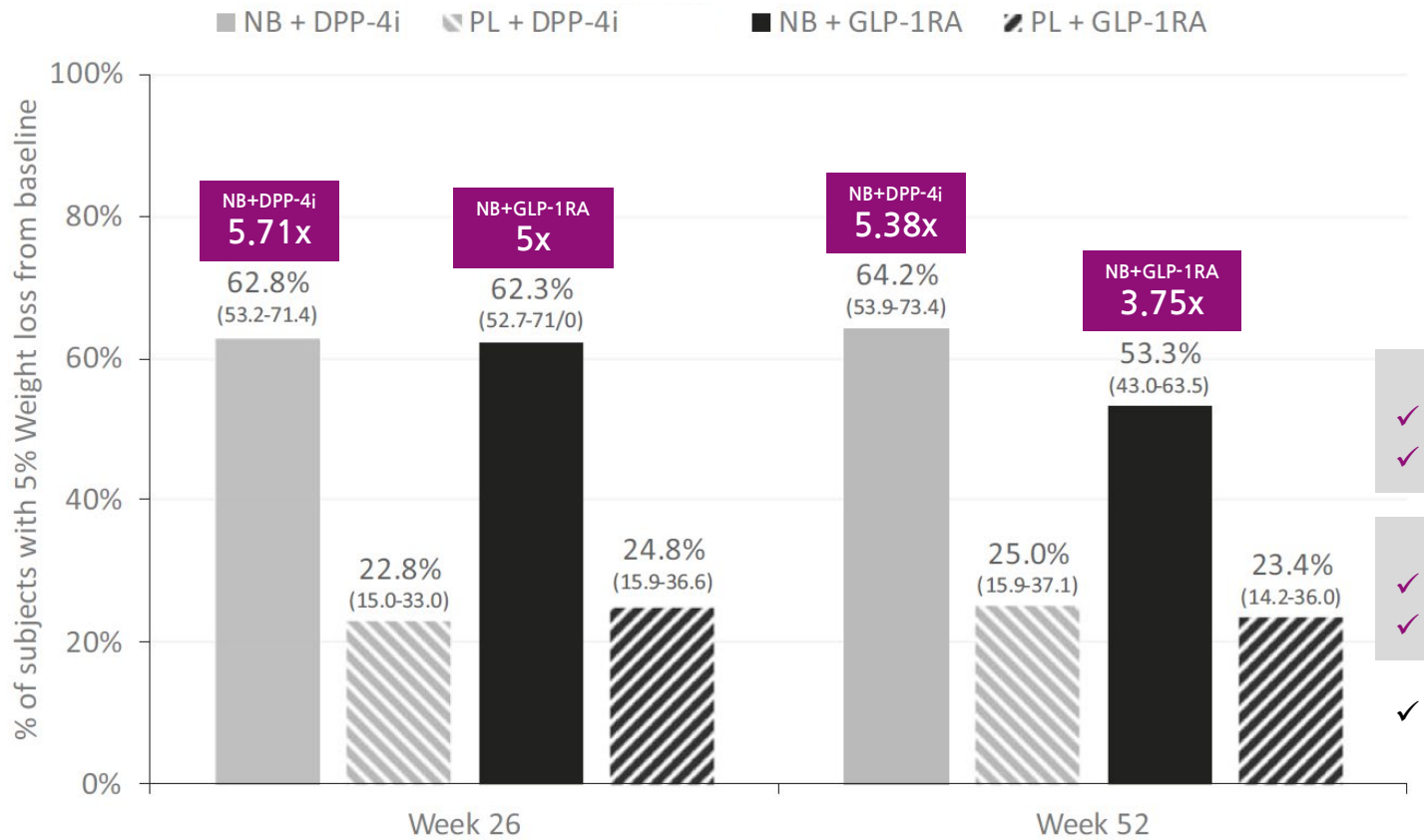
NB, naltrexone ER/bupropion ER; PL, placebo; DPP-4is, dipeptidyl peptidase 4 inhibitors; GLP-1RAs, glucagon-like peptide-1 receptor agonists.

1. S. Wharton et al., International Journal of Obesity. 2021;45:1687-1695.

Extended-release naltrexone/bupropion is safe and effective among subjects with type 2 diabetes already taking incretin agents: a post-hoc analysis of the LIGHT trial; Int J Obes (Lond). 2021 Aug;45(8):1687-1695

DPP-4is나 GLP-1RAs를 복용하는 비만한 제2형 당뇨환자에서 CONTRAVE® 병용투여 시, 위약군 대비 5% 이상 체중감량 달성이 유의적으로 더 많았고, 내약성도 좋았습니다.[1]

26주와 52주 시, 5% 이상 체중감량 달성자(%) (95% Confidence Interval)[1]



[26주 시, 5% 이상 체중감량 달성 가능성비]

- ✓ **NB+DPP-4i** VS PL+DPP-4i (**OR 5.71**, 95% CI 3.00-10.90, *P*<0.0001)
- ✓ **NB+GLP-1RA** VS PL+GLP-1RA (**OR 5.00**, 95% CI 2.52-9.90, *P*<0.0001)

[52주 시, 5% 이상 체중감량 달성 가능성비]

- ✓ **NB+DPP-4i** VS PL+DPP-4i (**OR 5.38**, 95% CI 2.63-11.00, *P*<0.0001)
- ✓ **NB+GLP-1RA** VS PL+GLP-1RA (**OR 3.75**, 95% CI 1.78-7.87, *P*=0.0005)

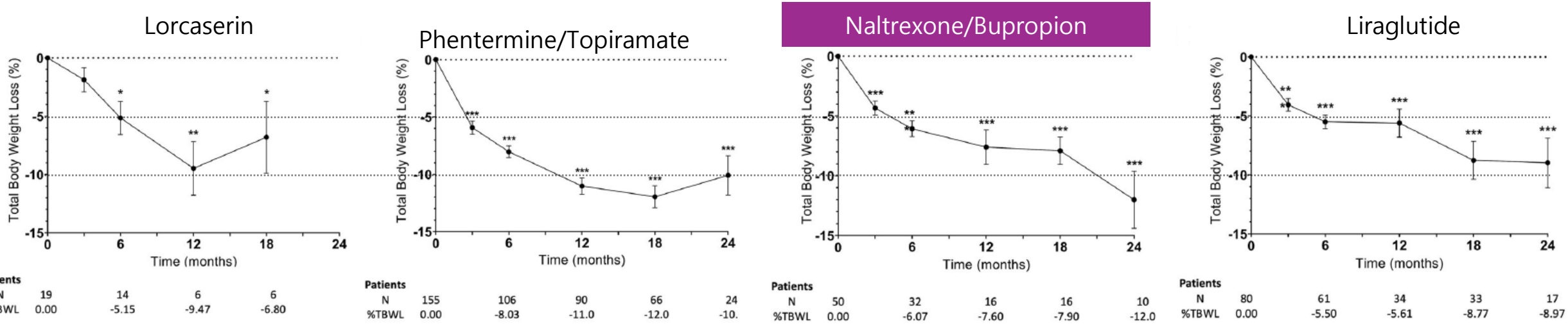
- ✓ **심각한 이상반응 발생률**(SAE, serious adverse events): 모든 군에서 **낮게** 관찰됨 [9.1-13.0%][1]

NB, naltrexone ER/bupropion ER; PL, placebo; DPP-4is, dipeptidyl peptidase 4 inhibitors; GLP-1RAs, glucagon-like peptide-1 receptor agonists.

1. S. Wharton et al., International Journal of Obesity. 2021;45:1687-1695.

항비만제별 체중감량 효과 [2년, Real-World Data][1]

2년간 장기적으로 복용 시, 가장 효과적인 체중감량을 보인 약물은 CONTRAVE® 였습니다.[1]



항비만제별 체중감량 결과 (최대 24개월)

투여 3/6/12/18/24개월 시, 항비만제별 총 체중감량 비율 (%TBWL, total body weight loss)

- **12개월** 추적조사 결과 **Phentermine/Topiramate ER**이 **총 체중감량 12%**로 **가장 높은 체중감량**을 나타냄
- **24개월** 추적조사 결과 **Naltrexone/Bupropion SR**이 **총 체중감량 12%**로 **가장 높은 체중감량**을 나타냄

- **목적:** 장기간 사용에 대해 FDA 허가된 항비만제(AOMs, anti-obesity medications)의 효과가 실제 임상 현장에서도 재현이 되는지의 유효성과 더불어 안전성을 평가
- **대상:** 비만환자 304명 [39-58세, 여성 76%] → Phentermine/Topiramate ER(n=155), Liraglutide(n=80), Naltrexone/Bupropion SR(n=50), Lorcaserin(n=19) → 24개월 완료자(n=52)
- **방법:** Retrospective, multi-site study → 장기간 사용에 대해 FDA 허가된 항비만제를 일정기간(2016.01.01~2020.01.31) 내에 처방받은 대상자들의 전자의무기록(EMR, electronic medical records)을 검토

1. G. Calderon et al., Effectiveness of anti-obesity medications approved for long-term use in a multidisciplinary weight management program: a multi-center clinical experience. International Journal of Obesity. 2022;46(3):555-563.

Efficacy and safety of the naltrexone and bupropion combination in obese population: post-marketing surveillance of the naltrexone and bupropion combination[1]

CONTRAVE®는 국내 비만환자에서 체중감량 효과와 안전성이 확인되었습니다[1]
[1일 유지용량 2~3정으로 12주 투여 시, 6.8% 체중감량 관찰]

콘트라브® 국내 PMS 결과와 3상 임상시험 비교[1-3]

	국내 PMS 결과[1] 유효성 평가(n=277), 안전성 평가(n=613)	3상 임상시험(COR-I)[3]
평가시점	**유지용량 이후 12주 시점**	유지용량 이후 52주 시점
투여(유지)용량	**평균 2.38정/일**	4정/일
기저치 대비 평균 체중변화(%)	**-6.8%**	-8.1% [Placebo: -1.8%]
5% 이상 체중감량 달성자(%)	**62.1%**	62.0% [Placebo: 23.0%]
안전성 결과	✓ 대표적으로 **구역, 두통, 어지럼증, 변비, 구토** 등이 관찰됨 ✓ 약물 관련 **중대한 이상반응은 없었음**	✓ 콘트라브® 투여로 구역, 두통, 변비, 어지럼증, 구토, 구갈 등이 위약 대비 더 많이 관찰됨

- **목적:** 국내 비만환자 또는 다른 위험인자가 있는 과체중 환자에서 CONTRAVE®의 유효성·안전성을 평가
- **대상:** 국내 비만환자 또는 다른 위험인자가 있는 과체중 환자 765명 [BMI 30 kg/m^2 이상 또는 다른 위험인자가 있는 BMI 27 kg/m^2 이상, 평균 44.52세, 여성 70.64%, 평균 체중 86.25 kg, 평균 BMI 32.14 kg/m^2]
- **방법:** 국내 54기관 참여, 총 6년간 진행 → 용량적정기간 4주 이후 유지용량 설정 [용량 증가가 어려운 경우, 마지막 용량을 유지용량으로 설정] → CONTRAVE® 유지용량으로 12주간 투여 또는 장기투여 대상자는 24주간 투여

1. YS. Lyu, SM. Hong, CY. Park. Efficacy and safety of the naltrexone and bupropion combination in obese population: post-marketing surveillance of the naltrexone and bupropion combination. KOREAN SOCIETY FOR THE STUDY OF OBESITY. 2024. [대한비만학회 춘계학술대회 초록집 게재]. 2. 콘트라브서방정®_재심사_시판 후 조사의 결과 [Internal data]. 3. FL. Greenway et al., Lancet. 2010;376:595-605.

CASE 1: 우울과 불안증상이 동반된 환자

F/27

For: 우울과 불안증상으로 치료중인 분으로 비만 치료 위해 협진의뢰 드립니다 From PSY

Body composition: Height 166.5 cm, Body weight: 67.6 kg, BMI= 24.3

Vital sigh SBP/DBP: 103/65mmHg

정신과 HADS_불안지수:21, 우울점수 20

탄수화물 중독이 있는 것 같다.

식습관: 불규칙, 아.점으로 햇반 에 반찬, 저녁에는 배달음식, 음료수 자주 먹음

Drug hx: 코팩사엑스알서방정, 트락손정 , 토피라메이트

#Treatment

Contrave qd-> bid-> 1t-2t-> 2t bid

Progress

BW 67.5kg ->64.9KG->62.7kg ->58.0kg->55.8kg

CASE 2: 타 항비만약제에 부작용이 있는 환자

F/27

For: 체중감량을 위해 내원

Body composition: Height 162.8 cm, Body weight: 90.7 kg, BMI=34.2

Vital sigh SBP/DBP: 141/89mmHg

최근 시행한 검진에서 고지혈증 높았음, 간수치도 높았다고 들음

잠은 잘잔다. 생리전 기분변화는 있음. 가끔 폭식이 있음.

삭센다. 효과가 없었음. 큐시미아: 두근거림에 민감하고 부작용이 있었음. 약값에 부담도 된다.

#Treatment

Contrave qd-> bid-> 1t-2t-> 2t bid

Progress

BW: 94kg-> 93.2kg ->91.5kg-> 89kg->87.7kg

CASE 3: 지방간에 동반된 환자

F/42

For: 지방간이 있는 환자로 비만치료 위해 의뢰 됨. From: GI

Body composition: Height 155.9 cm, Body weight: 75 kg, BMI=30.8

Vital sigh SBP/DBP: 147/98mmHg

자주 먹는다. 군것질 등, 끊이지 않고 먹는 편임.

이전 다이어트 경험: 삭센다는 울렁거림, Orlistat는 설사, 큐시미아는 얼굴 저림이 심함.

#Treatment

Contrave qd-> bid (군것질도 안하고, 운동도 시작하고 잠도 잘 자고 괜찮은 것 같다)

Progress

BW: 75kg -> 74.4kg-> 72.2kg

CASE 4: 위 풍선수술 과거력이 있는 환자

M/48

For: 체중조절위해 내원

Body composition: Height 171.7 cm, Body weight: 98.9 kg, BMI=33.5

Vital sigh SBP/DBP: 147/98mmHg

흡연, 저녁에 폭식장애, 자다가 일어나서 안 먹으면 잠이 안 온다.

이전 다이어트 경험: 위 풍선 수술 후 체중이 15kg 정도 빠졌다가 다시 요요가 옴.

#Treatment

Contrave 1t qd-> 1t bid->1t -2t

BW: 98.9kg-> 97kg-> 95.1kg

CASE 5: 스트레스가 심한 비만 환자

M/39

For: 체중조절위해 내원

Body composition: Height 170.8 cm, Body weight: 83 kg, BMI=28.4

Vital sigh SBP/DBP: 138/86mmHg

스트레스를 많이 받고 있는 상태, 폭식이 있음.

이전 다이어트 경험: 삭센다 구역감, 효과 없었음. 큐시미아: 우울감

#Treatment

Contrave 1t qd-> 1t bid->1t -2t

BW: 83kg-> 82kg-> 79.1kg-> 77.7kg -> 76.4kg

Thank you for your attention

Contrave®
(naltrexone HCl/bupropion HCl)
8 mg/90 mg • Extended-Release Tablets

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