

왜 체중감량의 유지가 어려운가?

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한건희

Case

- 20220628
- M/46
- C/C 체중감량 원해요
- Wt/Ht 179.3/127.7
- BMI 39.6
- BP 132/74
- Hx: total thyroidectomy(thyroid Ca. 10yra), HTN, DM

- 6개월 전 105kg
- 105-110정도에서 왔다갔다 하다가 최근 급격히 증가함
- exercise: 운동못함.
- sleep: 6~7시간, 새벽 2시~
- mood: D/A -/- 수술 후 기분 변화 심해짐
- appe: +> 단것을 먹으면 멈추지못함
- guilty: -
- adolescent obesity +
- diet 다양한 방법으로 많이 해보심
- - 40kg까지 감량해본적 있으나 항상 1년이내에 요요
- supplement: -
- 목표: 100kg 이하

검사항목	금회결과		과거결과	
	결과	기준범위	결과	검진일자
체지방률	42.4	10.0 ~ 20.0 (%)	43.2	18.11.13
체지방량	52.7		53.5	18.11.13
근육량	67.7		66.2	18.11.13
체성분/영양상담	결과지 참조			

- 202206 종합검진 : 특이소견 없음

검사항목	금회결과		과거결과	
	결과	기준범위	결과	검진일자
AST(SGOT)	28	0 ~ 33 (IU/L)	24	18.11.13
ALT(SGPT)	43	0 ~ 38 (IU/L)	32	18.11.13
알칼리포스파타제_ALP	172	104 ~ 338 (U/L)	215	18.11.13
총빌리루빈	0.83	0.20 ~ 1.57 (mg/dL)	0.87	18.11.13
γ-GTP	24	0 ~ 56 (IU/L)	58	18.11.13
총단백	7.3	6.4 ~ 8.4 (g/dL)	7.7	18.11.13
알부민	4.6	3.8 ~ 5.0 (g/dL)	5.2	18.11.13
알부민/글로불린 비율	1.7	0.9 ~ 2.2 (%)	2.1	18.11.13
M2BPGi	Negative(0.70)			

검사항목	금회결과		과거결과	
	결과	기준범위	결과	검진일자
혈당검사(정량)[식전]	103	70 ~ 99 (mg/dL)	123	18.11.13
헤모글로빈A1C-NGSP	5.9	4.0 ~ 5.6 (%)	6.1	18.11.13
헤모글로빈A1C-IFCC	41	20 ~ 38 (mmol/mol)		
헤모글로빈A1C-eAG	123	0 ~ 114 (mg/dL)		

갑상선질환 검사

검사항목	금회결과		과거결과	
	결과	기준범위	결과	검진일자
갑상선자극호르몬_TSH	0.781	0.270 ~ 4.200 (μIU/mL)	1.621	18.11.13
트리요도타이로닌_T3	1.28	0.80 ~ 2.00 (ng/mL)	1.32	18.11.13
유리싸이록신_Free T4	1.49	0.93 ~ 1.70 (ng/dL)	1.42	18.11.13

신장기능 검사

검사항목	금회결과		과거결과	
	결과	기준범위	결과	검진일자
요소질소(NPN포함)	10.8	6.2 ~ 23.3 (mg/dL)	11.0	18.11.13
크레아티닌	0.8	0.6 ~ 1.2 (mg/dL)	0.9	18.11.13
요소질소/크레아티닌 비율	13.5	6.0 ~ 27.0	12.2	18.11.13
시스타틴 씨	0.91	0.5 ~ 1.0 (mg/L)	0.82	18.11.13
신사구체여과율(e-GFR)	111	60 ~ 182 (mL/min/1.73m ²)	98	18.11.13

검사항목	금회결과		과거결과	
	결과	기준범위	결과	검진일자
고감도C-반응성단백	0.1	0 ~ 0.3 (mg/dL)	0.1	18.11.13
총콜레스테롤	147	98 ~ 199 (mg/dL)	114	18.11.13
지질-트리글리세리이드	138	10 ~ 149 (mg/dL)	143	18.11.13
HDL 콜레스테롤	49	40 ~ 99 (mg/dL)	46	18.11.13
LDL 콜레스테롤[계산식]	70	0 ~ 129 (mg/dL)	39	18.11.13
호모시스테인	9.0	5.0 ~ 15.0 (μmol/L)	8.1	18.11.13

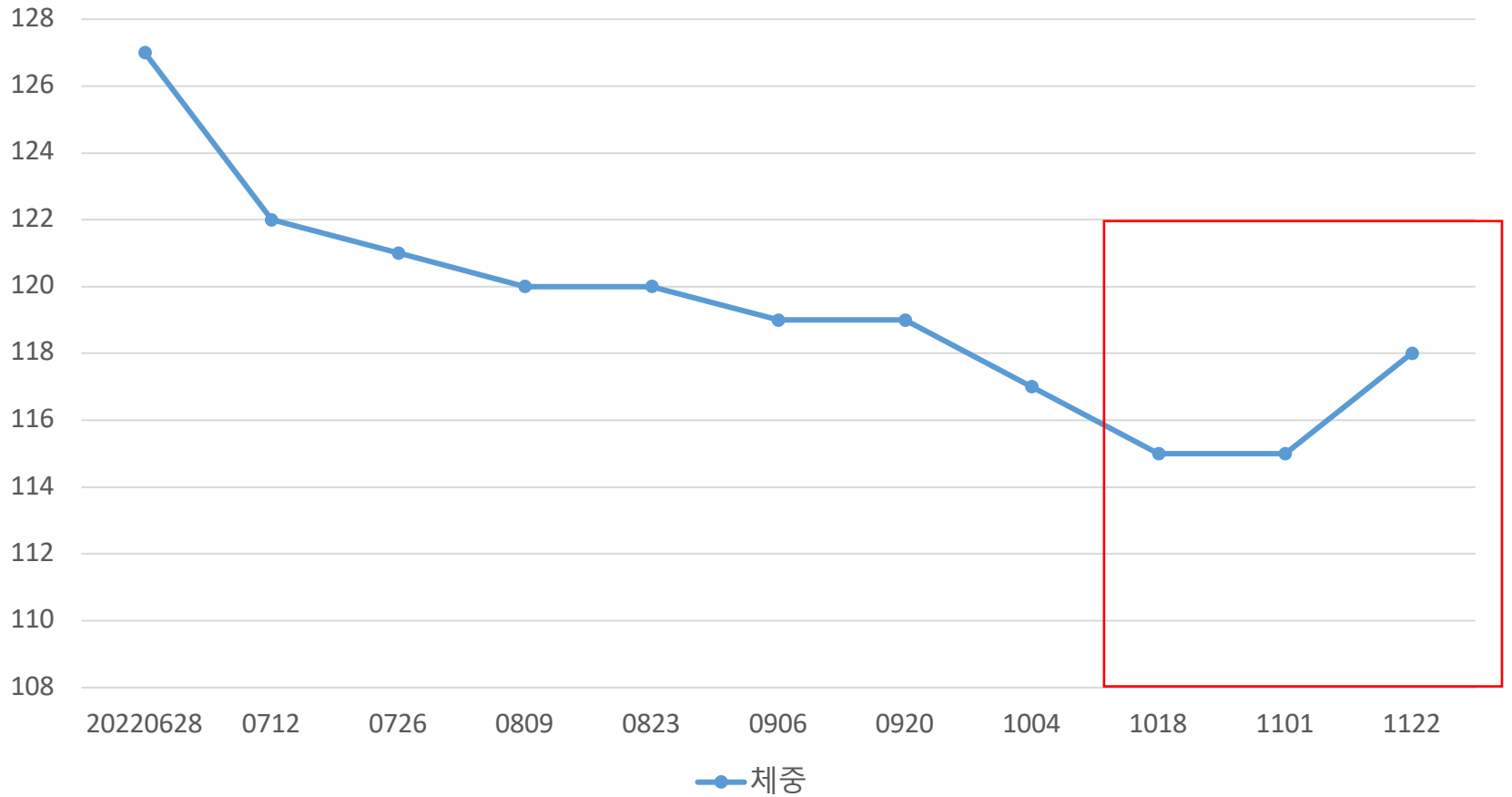
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DDTR25	Dilatrend 25mg/tab	정규	내복약	*	1 T
DTWS40/5	Twynsta tab.40/5mg (한국베링거			*	1 T
DBRST	Berast tab. 0.02mg (녹십자)			*	1 T
DQSYA3.75	QSYMIA CAP 3.75mg/23mg			*	1 C
DLTVZDW2	LITORVAZET TAB 10/20mg			*	1 T
WCCT	Vitamin D3 B.O.N inj. 1ml/Amp	정규	INJ.	*	1 AM

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DTEG0PC	K-cap tab. 50mg (씨제이헬스케어)	정규	내복약	*	1 T
DQSYA11.25	QSYMIA CAP 11.25mg/69mg			*	1 C

체중변화



Weight cycling

- Yo-yo effect
- repeated loss and gain of weight
- 많은 다이어터들이 처음 체중감량에 성공하나
- diet 이후 빠르게 체중이 증가하는 증상



비만환자를 바라보는 잘못된 시각

- 체중은 자율적인 조절의 통제하에 있고
- 체중 감량은 자가 조절이 가장 중요하다
- 체중감량후 다시 증가하는 것은 환자의 동기부족과 환자의 자가 조절의 실패 때문이다
- 그러므로 비만환자는 게으르고 신뢰하지 못할만하다
- 다 틀린말

Obesity stigma

- 자율적인 생활습관 변화(다이어트와 운동)를 오랫동안 유지하면 심지어 심각한 비만상태 에서도 완전히 정상체중으로 되돌릴 수 있다
- 생물학적 반응(compensatory)을 완전히 무시하는 가정이며
- 많은 과학적 근거들이 이를 뒷받침 하고있음
- 근거들은 보상과정이 장기적으로 weight regain을 일으킨다는 것을 제시함

Partner organizations

- American Association of Clinical Endocrinologists (AACE)
- American Association for Metabolic and Bariatric Surgery (ASMBS)
- American Diabetes Association (ADA)
- Diabetes UK
- European Association for the Study of Obesity (EASO)
- International Federation for the Surgery of Obesity and metabolic Disorders (IFSO)
- Obesity Action Coalition (OAC)
- Obesity Canada
- The Obesity Society (TOS), USA
- World Obesity Federation (WOF)

Other scientific and patient societies

- American Academy of Sleep Medicine (AASM)
- American Society for Nutrition (ASN)
- Association of British Clinical Diabetologists (ABCD)

- The Lithuanian Society of Bariatric Surgery
- Mexican Society of Obesity
- National Lipid Association (USA)
- Norwegian Society for the Surgery of Obesity
- Obesity Australia
- Obesity Care Advocacy Network (OCAN)
- Obesity Collective
- Obesity Medicine Association (USA)
- Obesity Society of Nigeria
- The Obesity Surgery Society India (OSSI)
- Obesity UK
- Romanian Federation of Diabetes, Nutrition, Metabolic diseases
- The Royal College of Physicians -RCP- (UK)
- Russian Society of Bariatric Surgeons
- Sociedad Argentina de Cirugía de la Obesidad Enfermedad Metabólica y Otras Relacionados con la Obesidad
- Sociedad Argentina de Obesidad y Trastornos Alimentarios



OPEN

Joint international consensus statement for ending stigma of obesity

2020년 statement

tion Canadienne des ergothérapeutes)

- The Canadian Society of Endocrinology and Metabolism (CSEM)
- CIHR-SPOR Chair in Innovative, Patient-Oriented, Behavioural Clinical Trials
- Chilean Society for Bariatric and Metabolic Surgery
- Colegio Mexicano de Cirugía Para la Obesidad y Enfermedades Metabólicas
- Croatian Society of Obesity
- Dietitians of Canada
- Dutch Society for Metabolic and Bariatric Surgery (DSMBS)
- The Endocrine Society (USA)
- European Coalition for People Living with Obesity (ECPO)
- French Clinical Research Network in Obesity (FORCE)
- French Society for Research and Care of Obesity (AFERO)
- French Society of Bariatric and Metabolic Surgery (SOFFCO-MM)
- Hellenic Medical Association for Obesity (HMAO)
- Hellenic Society for Bariatric and Metabolic Surgery

- *The Annals of Surgery*
- *Cell Metabolism* (Cell Press)
- *Cell Reports Medicine* (Cell Press)
- *Clinical Obesity*
- *The Lancet Diabetes & Endocrinology*
- *Med* (Cell Press)
- Nature Research (all journals)
- *Obesity*
- *Obesity Reviews*
- *Obesity Science and Practice*
- *Obesity Surgery*
- *Pediatric Obesity*
- *Surgery for Obesity and Related Diseases* (SOARD)
- *Trends in Endocrinology and Metabolism* (Cell Press)
- *Trends in Molecular Medicine* (Cell Press)

Academic institutions and hospitals

- Baker Heart and Diabetes Institute, Melbourne, Australia

Weight loss maintenance

- 전세계적으로 통일된 정도, 기간에 대한 단일 정의는 없는 상황
- everyday fluctuation과 가장 의미있는 체중변화 관점에서
- → 체중감량 달성 후 $\pm 3\%$
- 건강과 관련된 risk factor를 고려할 경우
- → 10% 체중 감량 후 이를 1년이상 유지
- → 또는 5% 체중 감량 후 1년이상 유지
- 1년이라는 기간은 일반적인 체중감량 프로그램으로 끌고갈 수 있는 기간으로 받아들여지고 있음

Weight loss maintenance

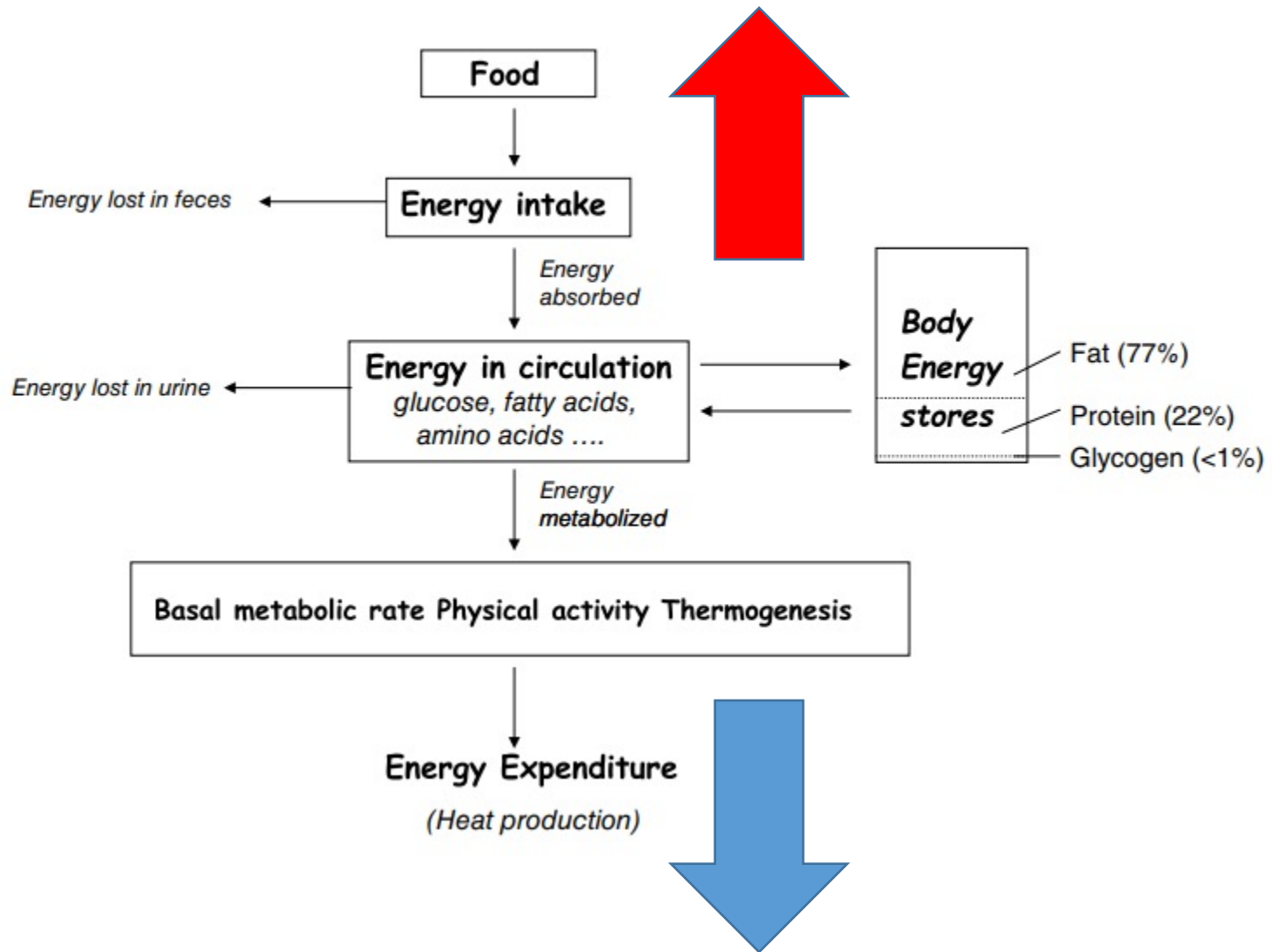
- Look Ahead study
- 4yr f/u
- T2DM and obesity
- 기저 체중대비 25%이상 감량한 군을 기준으로
- 긴 기간동안 체중 감량 상태가 유지될수록 3년뒤 CV risk 낮음

Definition	Weight change	Duration
Stevens et al. [4]	3% body weight	NA ND
Berger et al. [6]	25% of weight lost	3 years
Manore [8]	5% or 1 unit of BMI	1 year

Weight loss maintenance difficulty

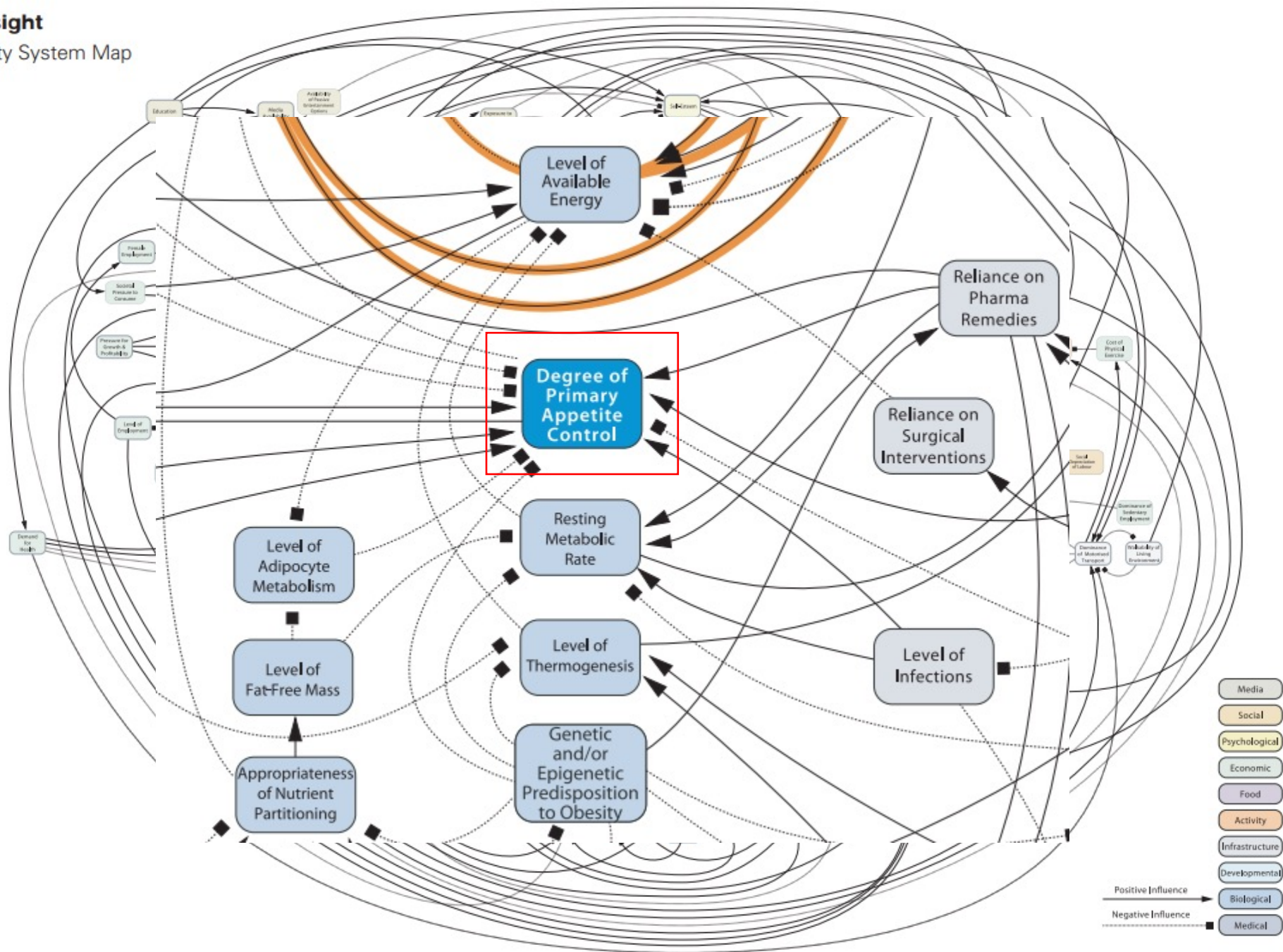
- 1년간 체중감량 프로그램후 4-5년뒤 f/u 시행시, 100%체중감량한 군 → 3%
- 초기 10%이상 체중 감량한 군에서 4년뒤 f/u시 유지 비율 → 28%
- 초기 체중감량 후 1년간 10%이상 체중감량을 유지한 비율 → 10%

Energy balance



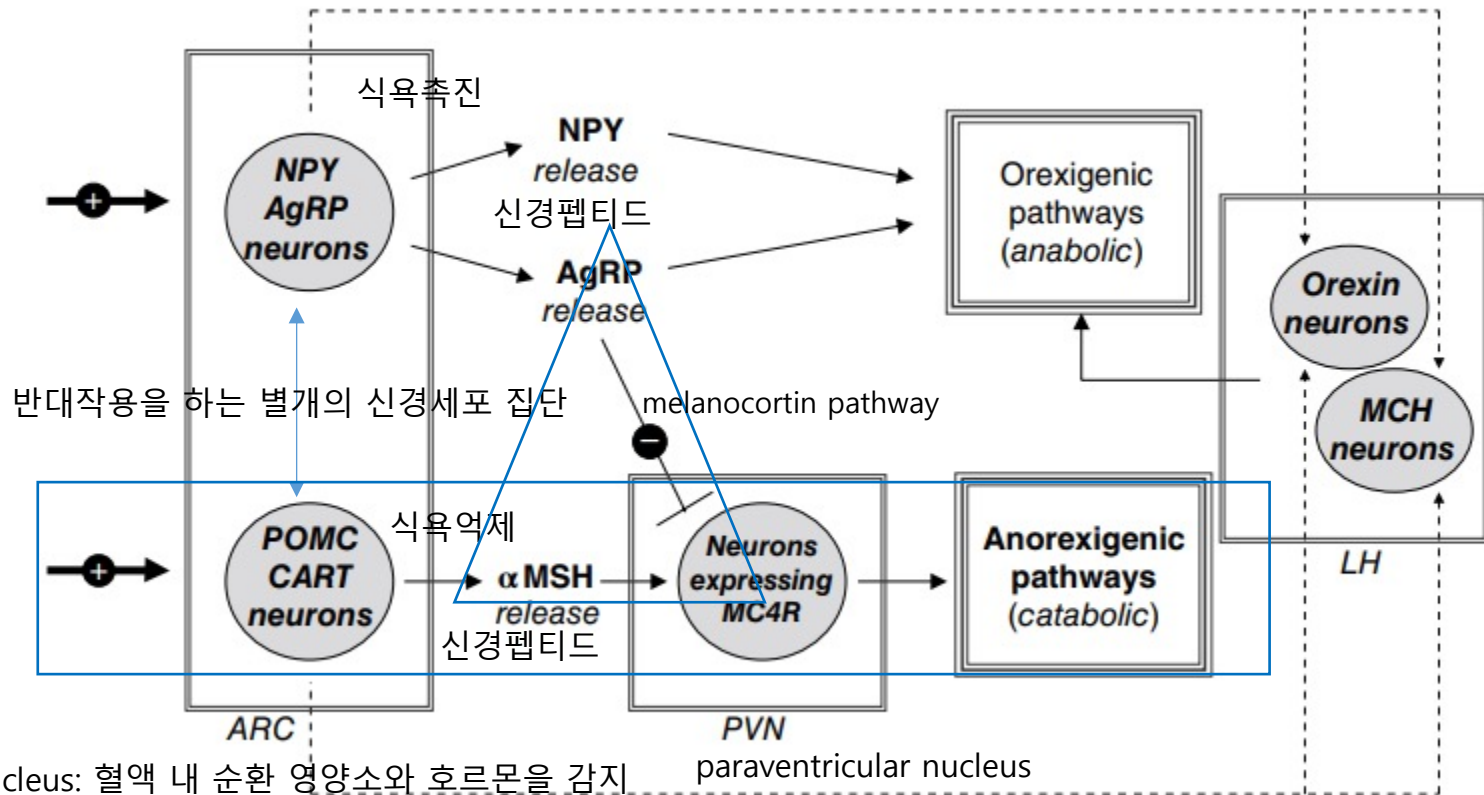
Foresight

Obesity System Map



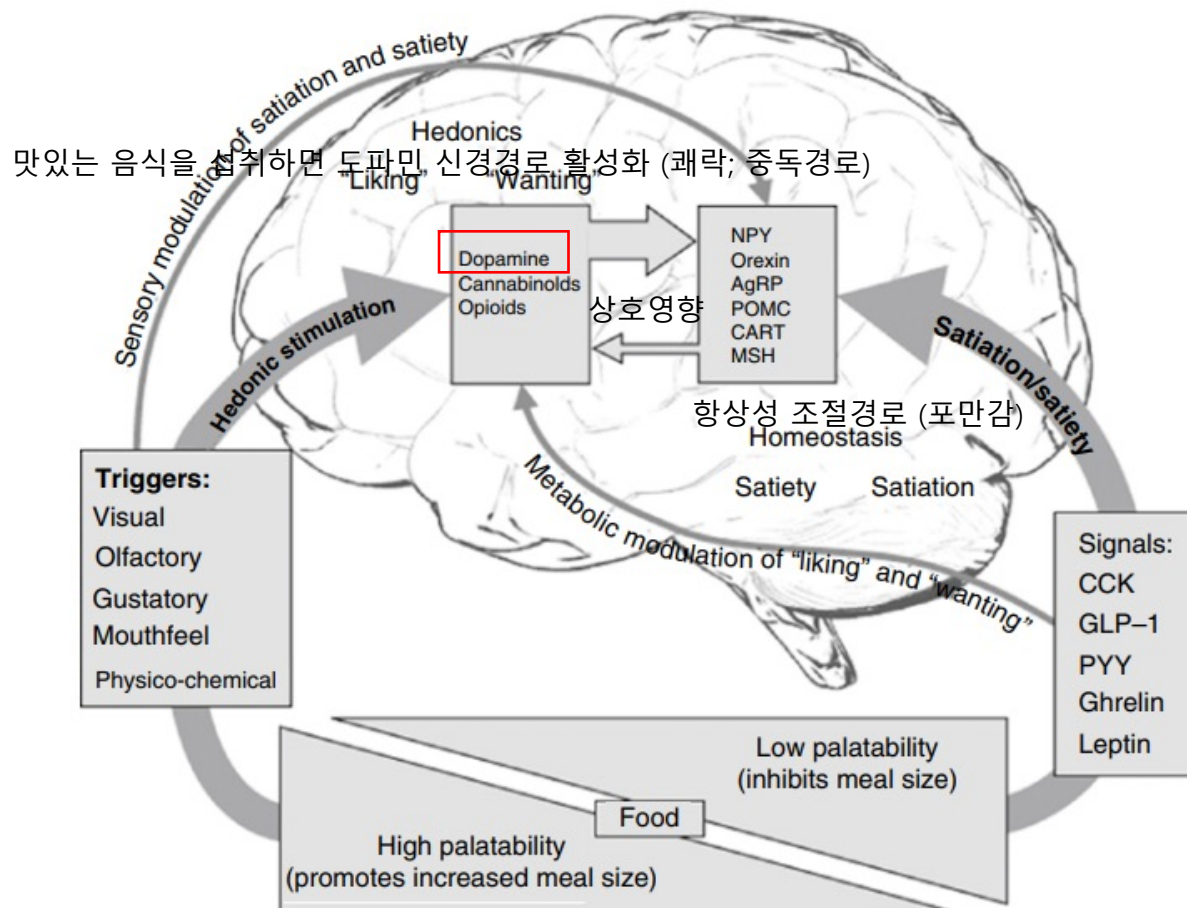
Hunger-satiety control centers in the brain

- hypothalamic circuits
 - 영양소와 호르몬감지를 통한 항상성 유지하는 가장 중요부위

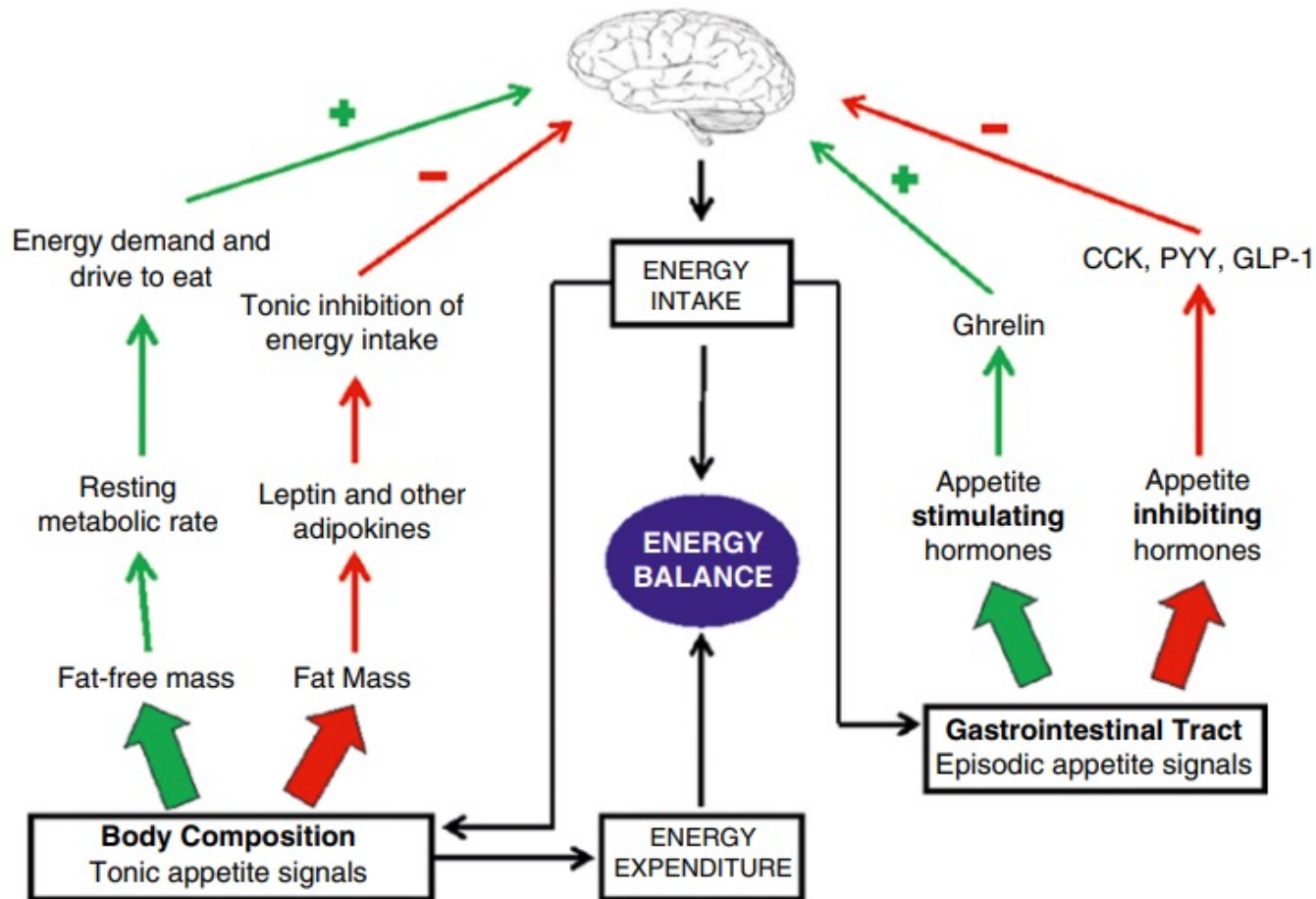


Hunger-satiety control centers in the brain

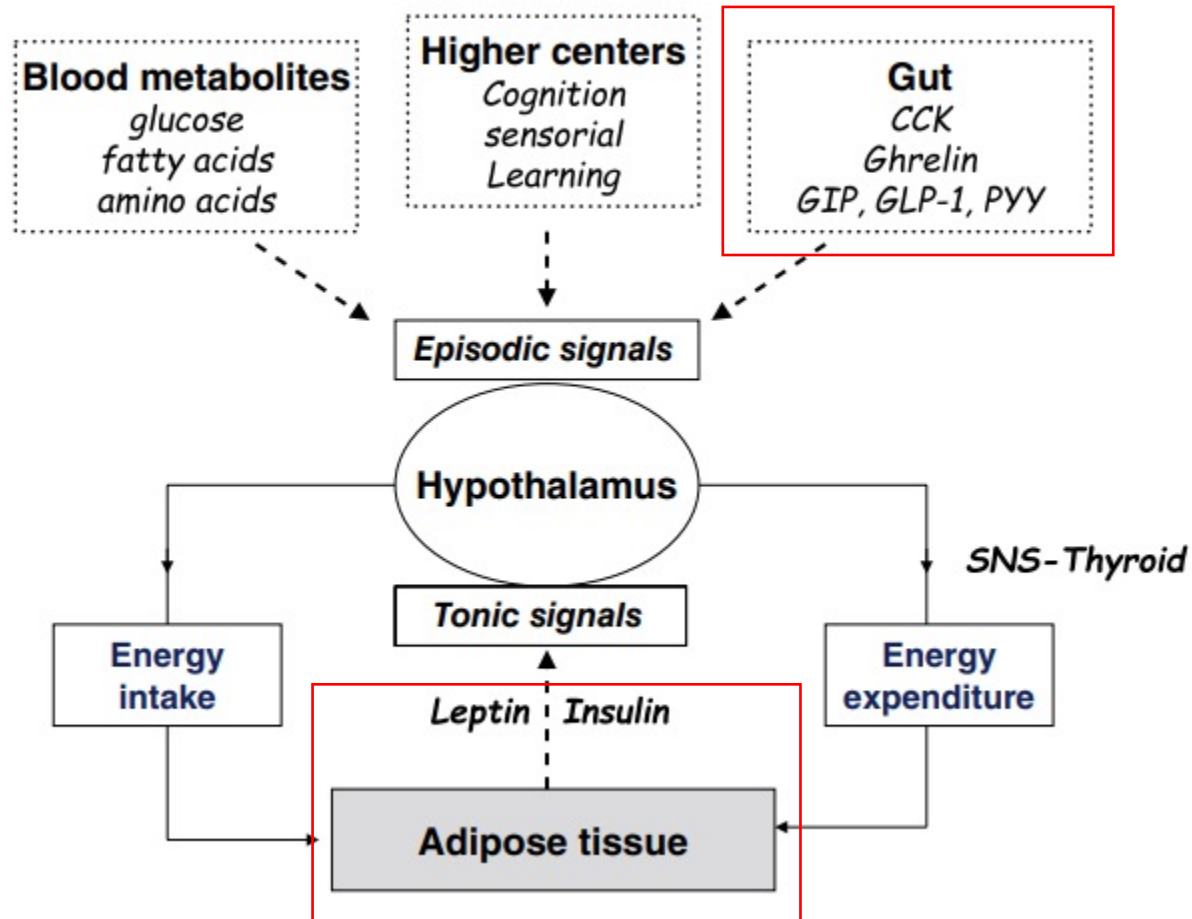
- Reward system



Hunger-satiety signals from the periphery



Hunger-satiety signals from the periphery



Hunger-satiety signals from the periphery – GI tract

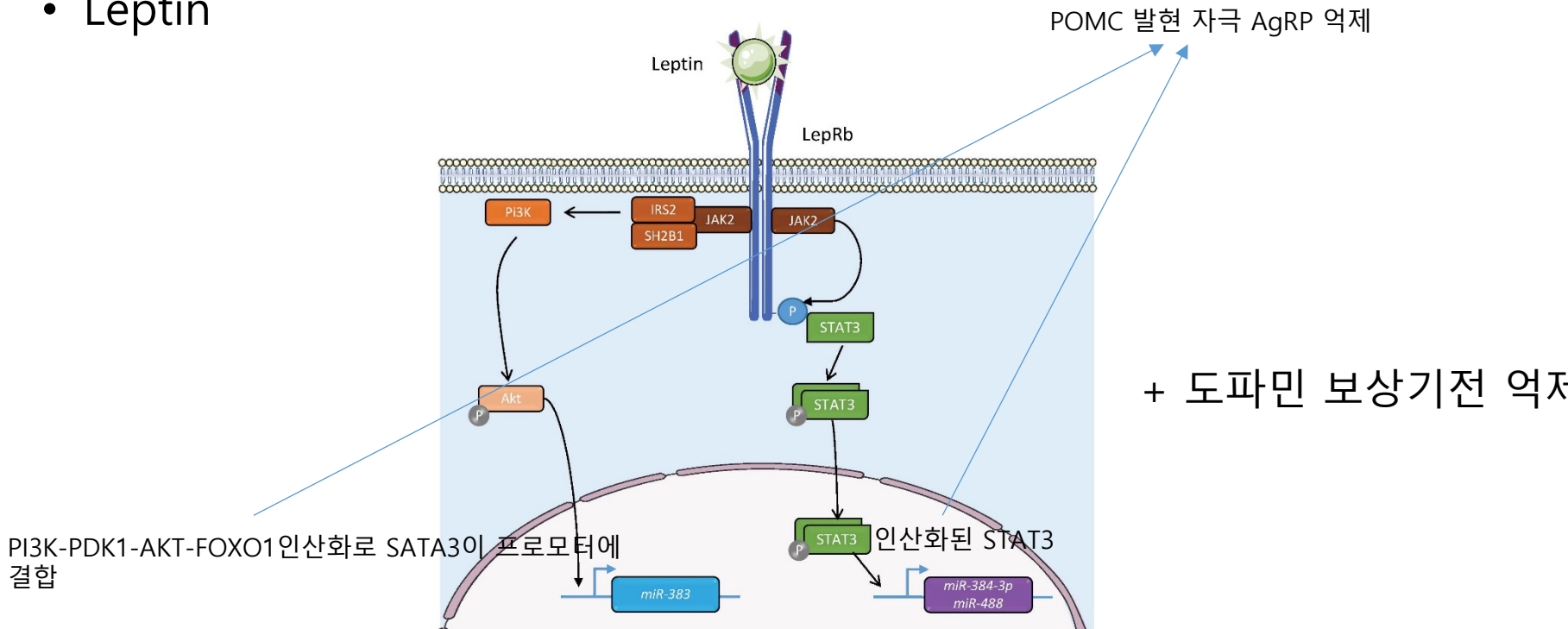
- Gut hormone: 음식섭취의 단기조절자
- Ghrelin
 - 식욕촉진
 - 위저부의 P/DI세포
 - median eminence를 통해 시상하부에 도달
 - NPY/AgRP 신경세포 활성화
 - VTA 도파민 뉴런활성화

Hunger-satiety signals from the periphery – GI tract

- CCK (cholecystokinin)
 - 장관내 I세포
 - CCK1수용체에 결합하여 식사량을 줄임
- PYY (peptide YY)
 - 장관 내 L세포
 - GLP-1과 함께 분비
 - NPY/AgRP neuron Y2수용체 억제, POMC뉴런 활성화
- GLP-1
 - 장관 내 L세포에서 분비되는 Incretin
 - 수용체는 시상하부 ARC, PVN, 뇌간의 NTS, area postrema등 여러영역에 발현
 - POMC 신경세포를 직접적으로 활성화
 - GABA를 통해 NPY/AgRP neuron간접 억제
 - 도파민 신경세포의 흥분성 시냅스 강도 약화

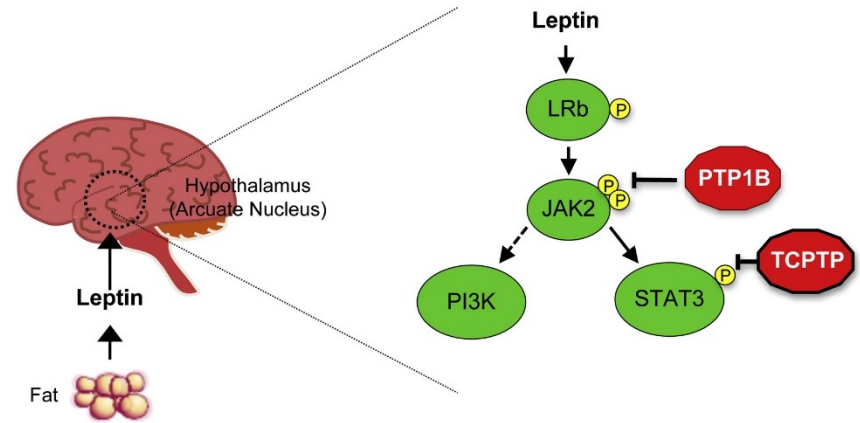
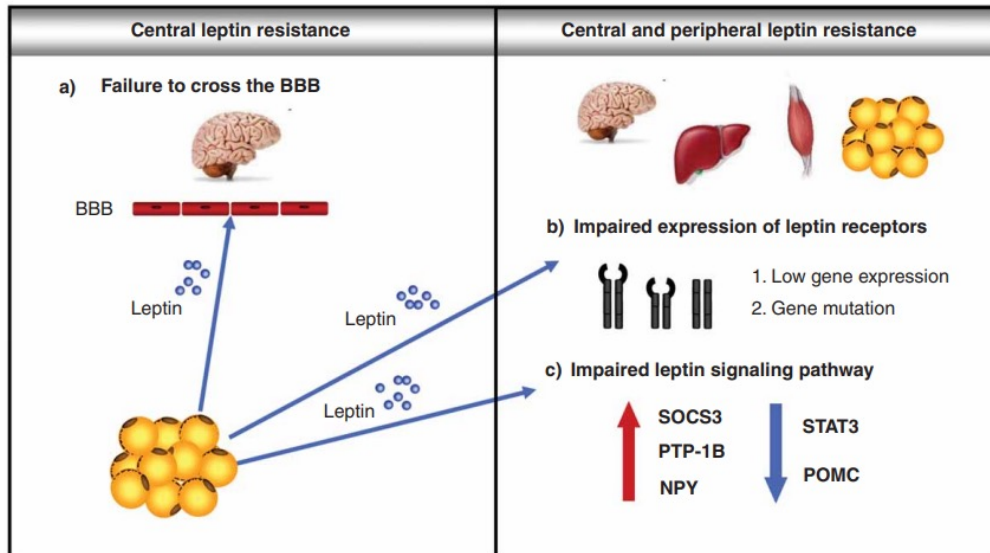
Hunger-satiety signals from the periphery – Adiposity signal

- Adiposity signal
- 음식섭취의 장기 조절자
- 저장된 지방의 총량에 비례해서 순환
- Leptin



Hunger-satiety signals from the periphery – Adiposity signal

- Leptin resistance
- hyperleptinemia + lack of response to hormone
- 비만은 시상하부의 PTP1B, TCPTP의 발현 증가

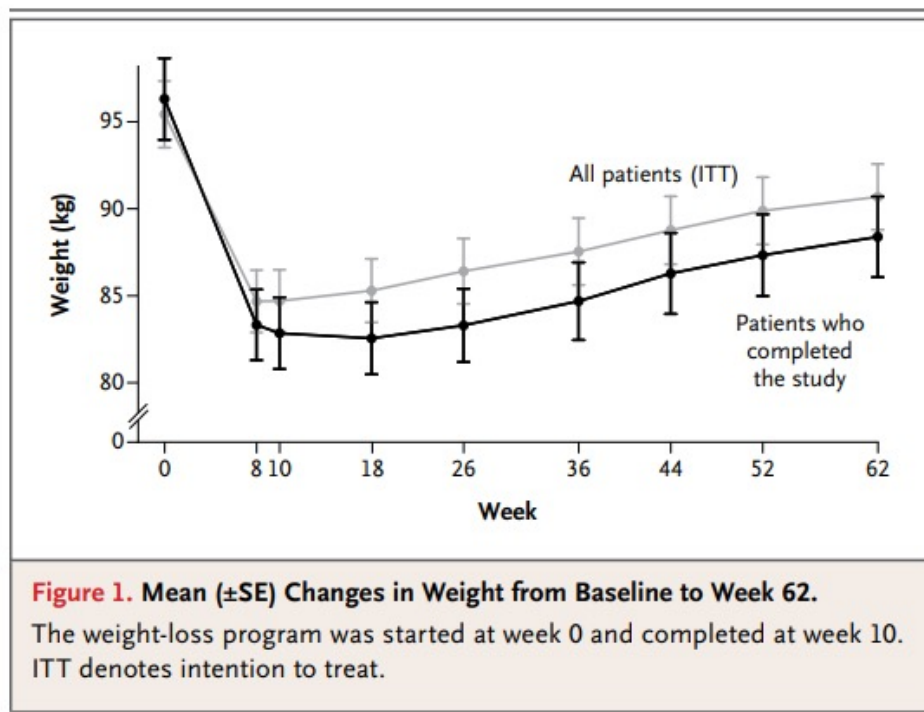


Gut hormone

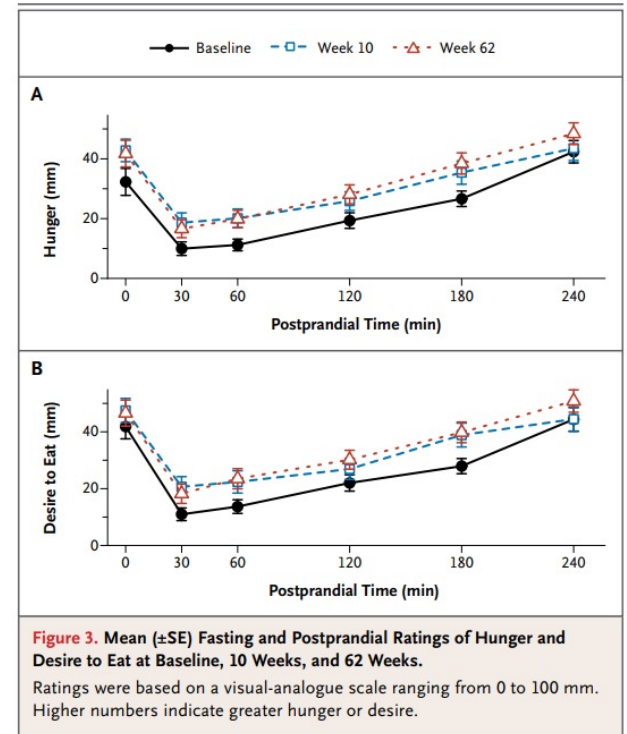
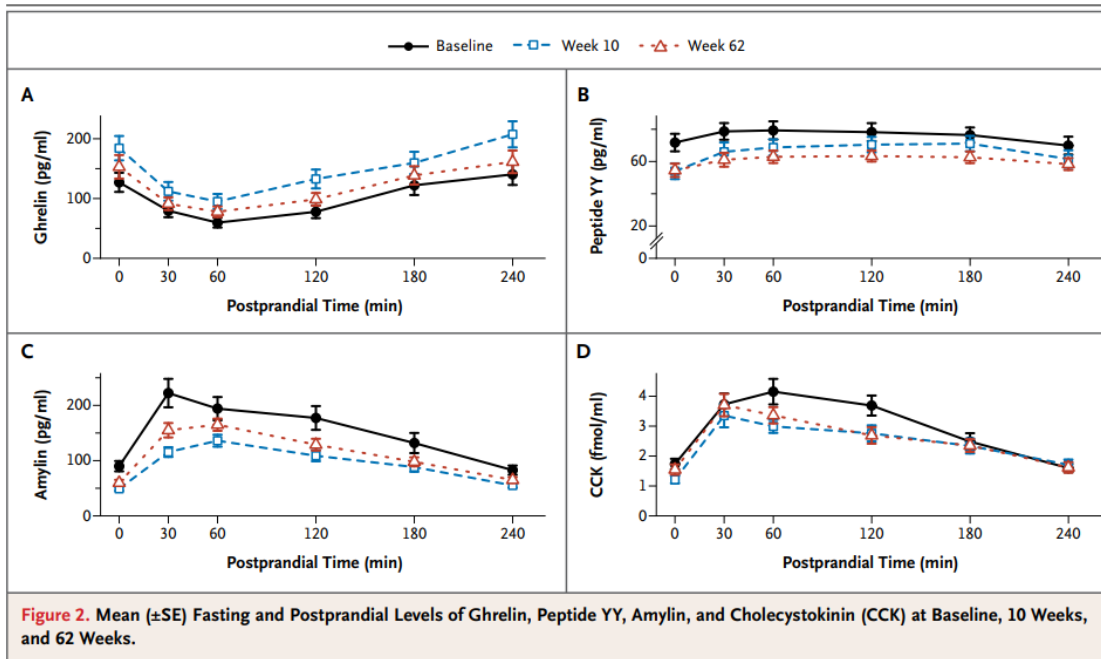
- key regulators of energy homeostasis
- 이 과정은 에너지 사용이 어려워질때 더 강화됨
- Energy restriction은 체중감소에 저항하는 강력한 보상기전을 활성화 시킴
- Gut hormone 분비의 변화는 체중감량에 따르는 에너지 저장과 weight regain을 drive

Gut hormone

- 50 participants c severe obesity
- After 10 weeks very low energy diet (VLED)
- 52 weeks f/u
- Mean w/t loss 13.5 ± 0.5 kg at 10wks
- 7.9 ± 1.1 kg at 52wks



Gut hormone

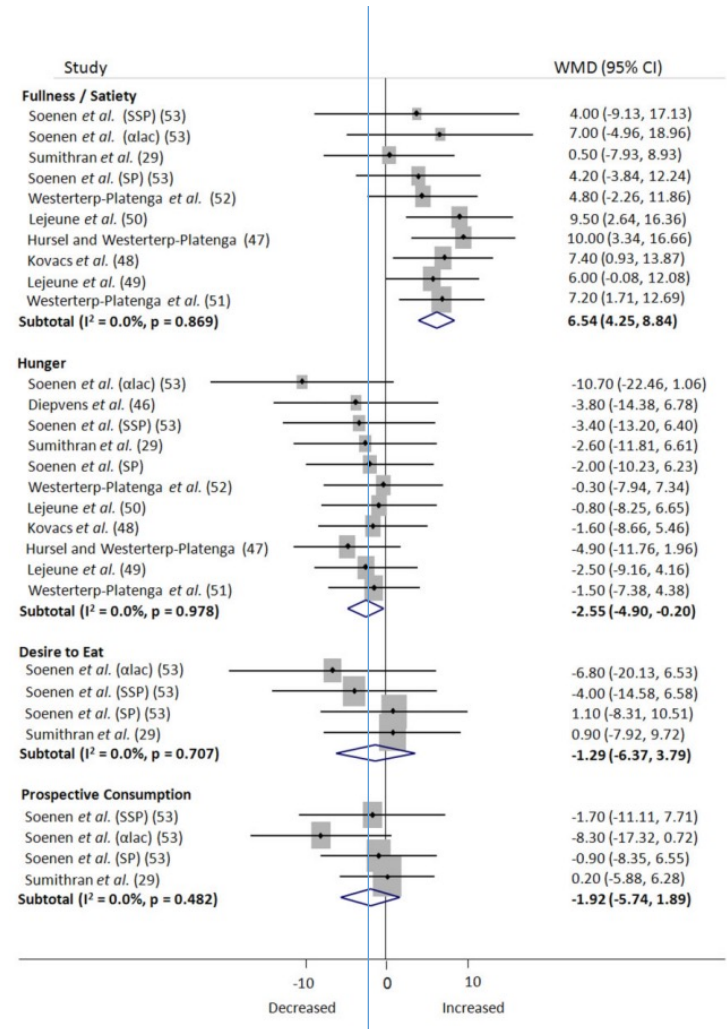
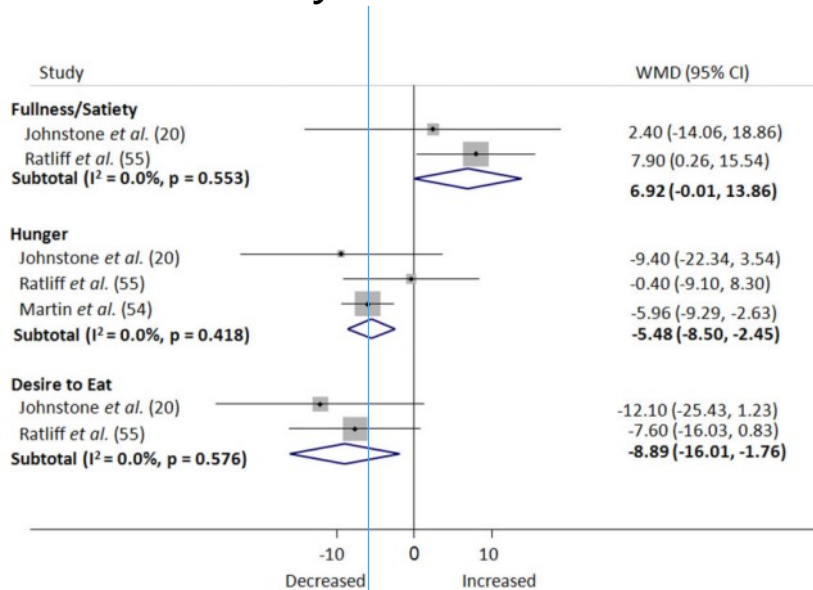


Gut hormone

Hormone	Overall effect of energy restriction on circulating levels [6]	Specific diets/circumstances
Ghrelin	↑	↔/↓ during ketosis [10]
GIP	↑	
PP	↑	
GLP-1	↓	↔ in low carbohydrate diet [13]
PYY	↓/↔	
CCK	↓	
Neurotensin	↓	
Amylin	↓	

Gut hormone

- 다이어트 방법에 따라 gut hormone 분비에 영향을 미칠 것으로 예상
- Ketogenic diet (Low carbohydrate)
- Meta-analysis

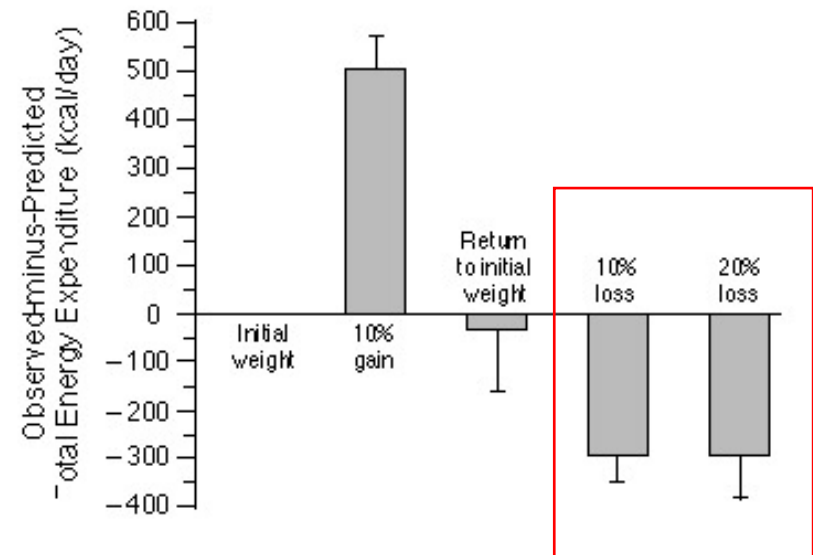
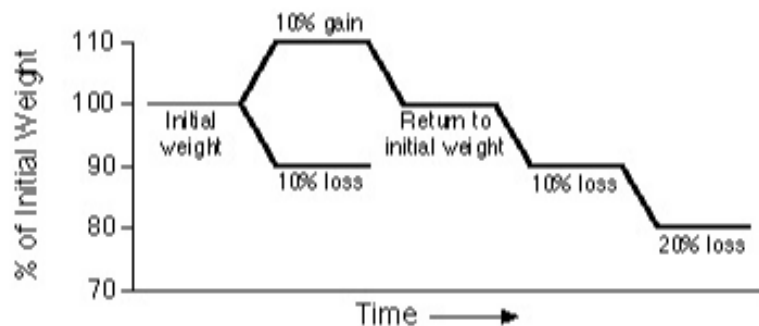


Metabolic adaptation

- Resting energy expenditure(REE)는 하루 에너지 소비의 약 60-70%를 차지
- REE는 체성분과 밀접한 상관성이 있음
- 특히 fat-free mass(FFM)로부터 REE를 유추해볼수 있음
- 따라서
- 다이어트로 인한 FFM의 감소는 일정한 비율의 REE의 감소를 가져올 것으로 예상되나
- 실제 연구에서 체성분의 변화가 REE의 감소에 미치는 영향은 계산식에 의한 기대보다 크며
- REE 감소가 예측된것보다 관찰된것에서 더 크다
- energy expenditure을 더 줄이기 위한 적응

Metabolic adaptation

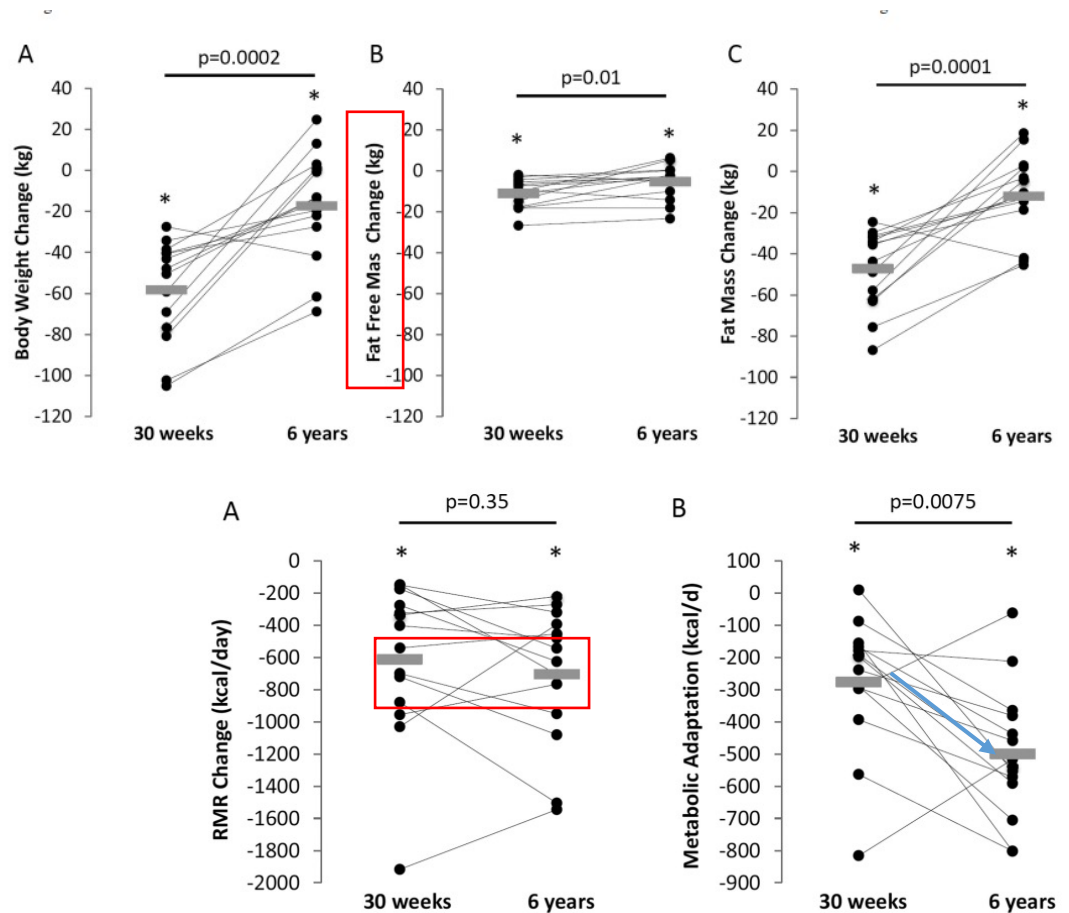
- = 체중 감소보다 더 많이 에너지 소비가 감소하는 현상
- Weight cycling시 metabolic adaptation





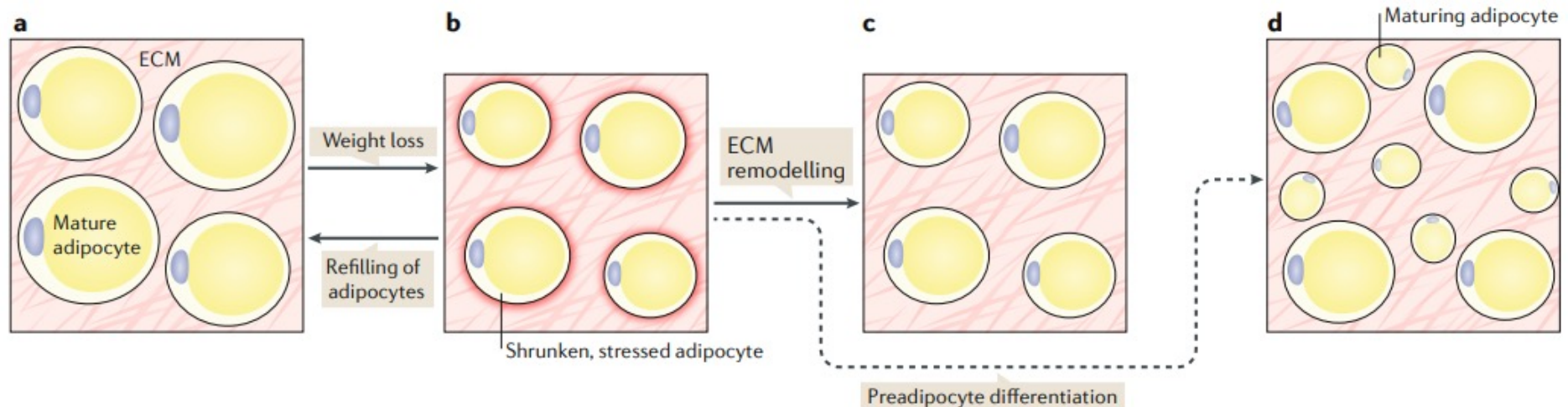
Metabolic adaptation

- Persistent metabolic adaptation
- 30wks
 - w/t loss 58.3 ± 24.9
 - REE 610 ± 483 kcal/day
- 6yrs
 - w/t loss 41.0 ± 31.3
 - REE 704 ± 427 kcal/day

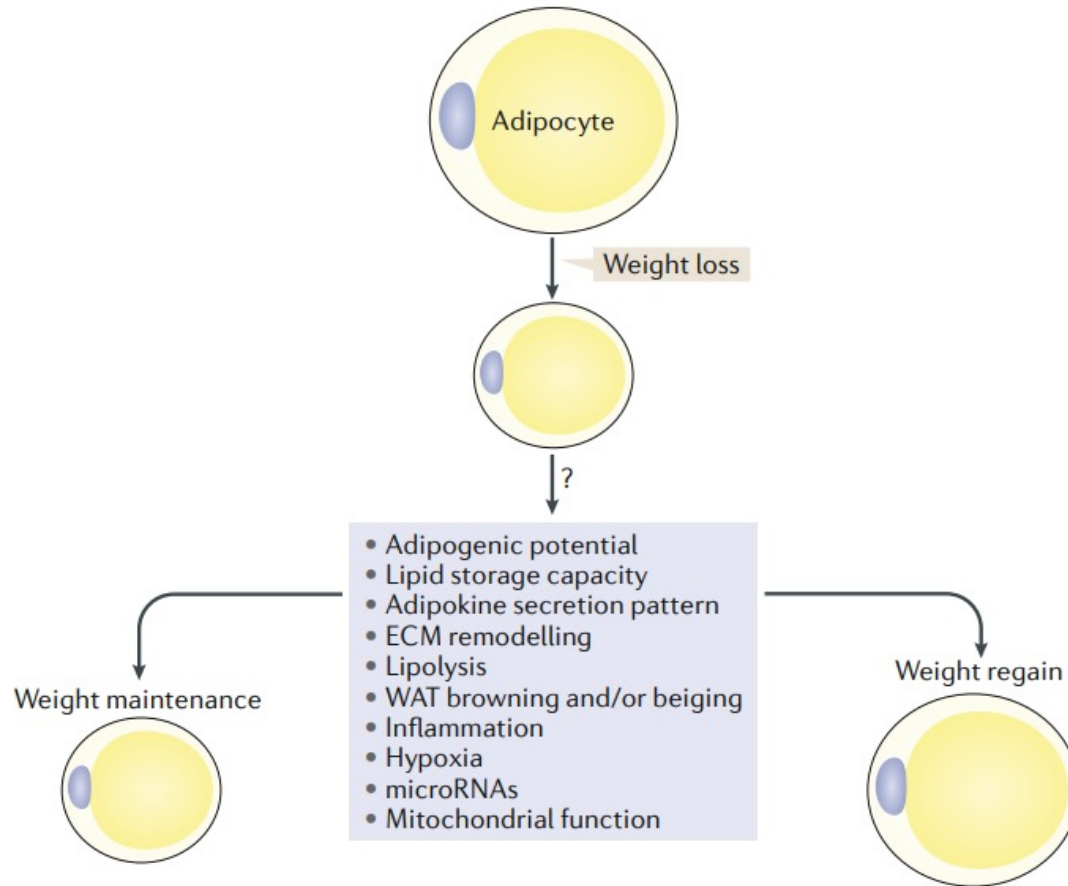


Adipose tissue

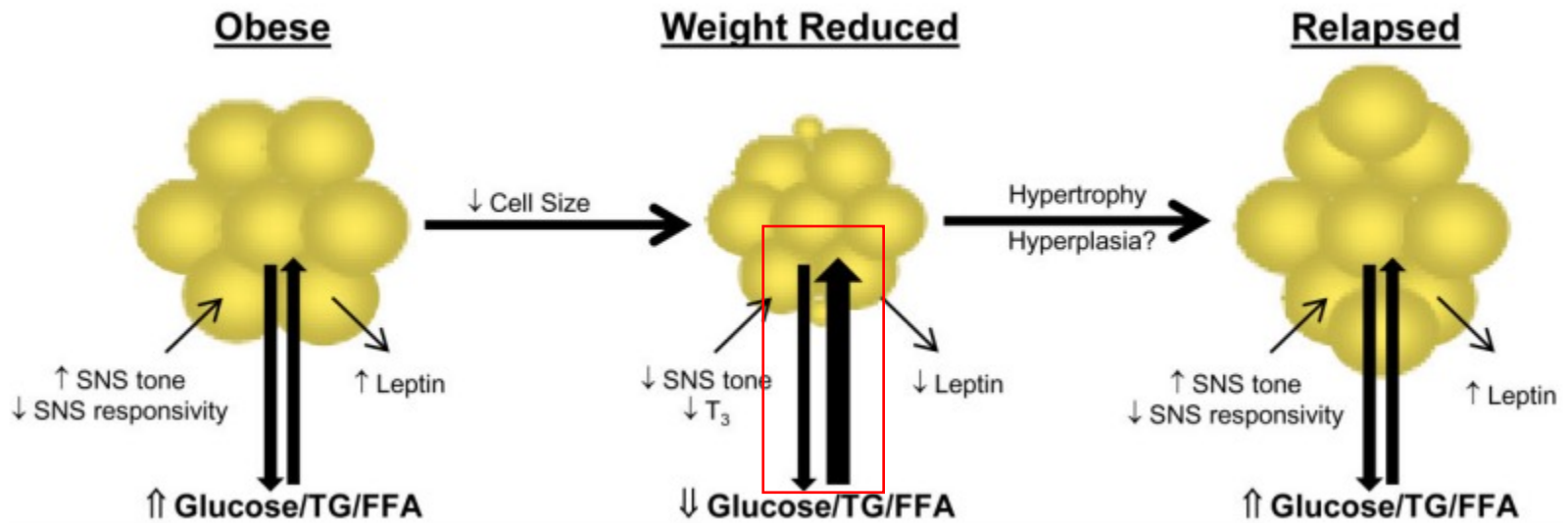
- 건강한 성인에서 성인기의 지방세포 수는 비교적 일정하게 유지
- 과다한 칼로리 섭취와 비만은 지방세포의 크기와 숫자를 증가
- 체중을 감량하는 다이어트는 크기를 줄일 뿐 세포의 수를 줄일 수는 없음
- 체중감량은 adipocyte에 기계적인 스트레스를 주고 이는 세포의 지질저장을 늘리는 등 weight regain시에 악영향을 줄 수 있음



Adipose tissue



Adipose tissue

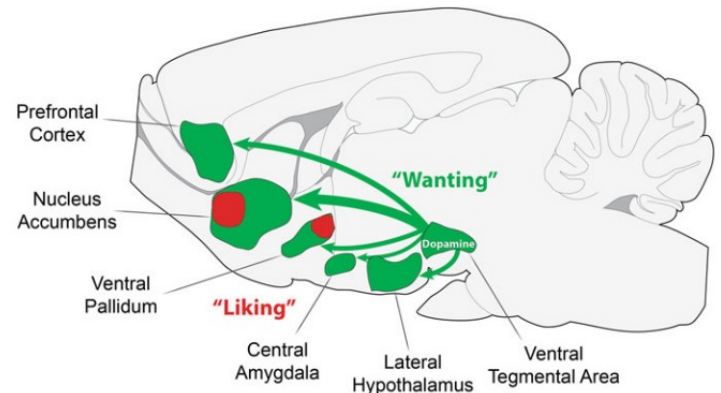


Adipose tissue

- Weight cycling은 Fat mass를 실제로 증가시키나?
- Well designed study의 부재
- 국내 국건영 연구는 큰 차이 없는것으로 보이나
- weight cycling의 정의 자체가 다양하여
- 정확한 분석은 어려움

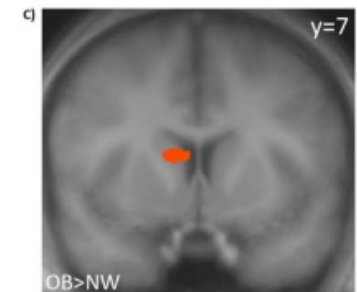
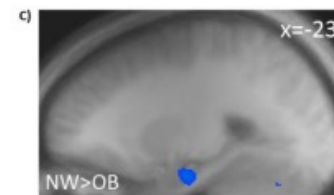
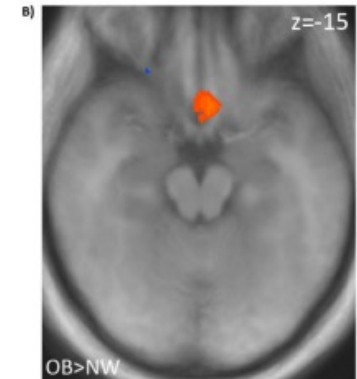
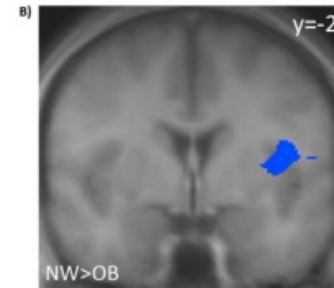
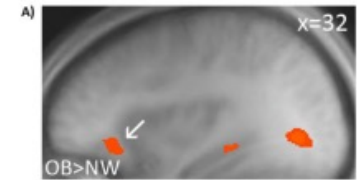
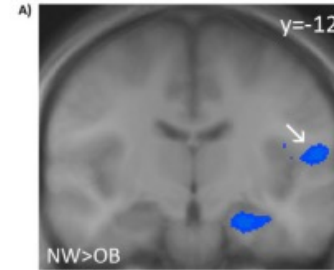
Reward

- Wanting
 - 보상을 예측할수 있는 신호에 따라 발생하는 감정
 - increased incentive salience of food
 - 음식에 대한 갈망, 초조함을 생성
 - mesocorticolimbic reward
 - dopamine, glutamate, opioid and endocannabinoid neurotransmission
- Liking (pleasure)
 - 도파민과 관련없이
 - nucleus accumbens pathway를 거침
 - opioid and endocannabinoid activity



Reward

- 음식에 대한 갈망의 증가는
 - BMI 증가할수록
 - 에너지 제한 diet
 - 비만인 경우
- fMRI로 관찰
- 비만/정상체중군의 음식자극에 대한 활성위치와 강도가 다름
- 식사전후에도 다른 모습을 보임



Hypothalamic-pituitary-thyroid axis

- 식이 칼로리 제한시
- Hypothalamic-pituitary-thyroid axis의 활성 감소
- impaired secretion of TSH
- TSH, T3감소

자율신경계

- Obesity-related increases in sympathetic nerve activity
- Chronic SNS overactivity
 - adrenoceptor sensitivity ↓
 - impaired energy expenditure
- 비만환자에서 체중감량시
 - sympathetic activity 의 감소
 - cardiac parasympathetic function ↑

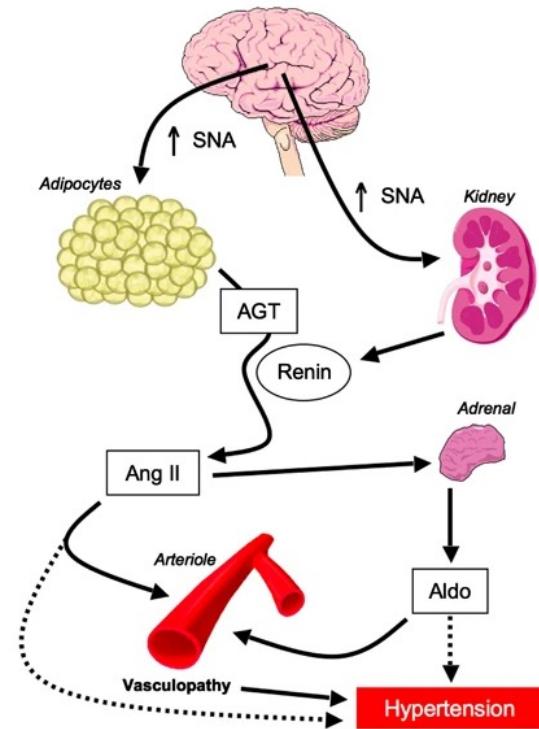
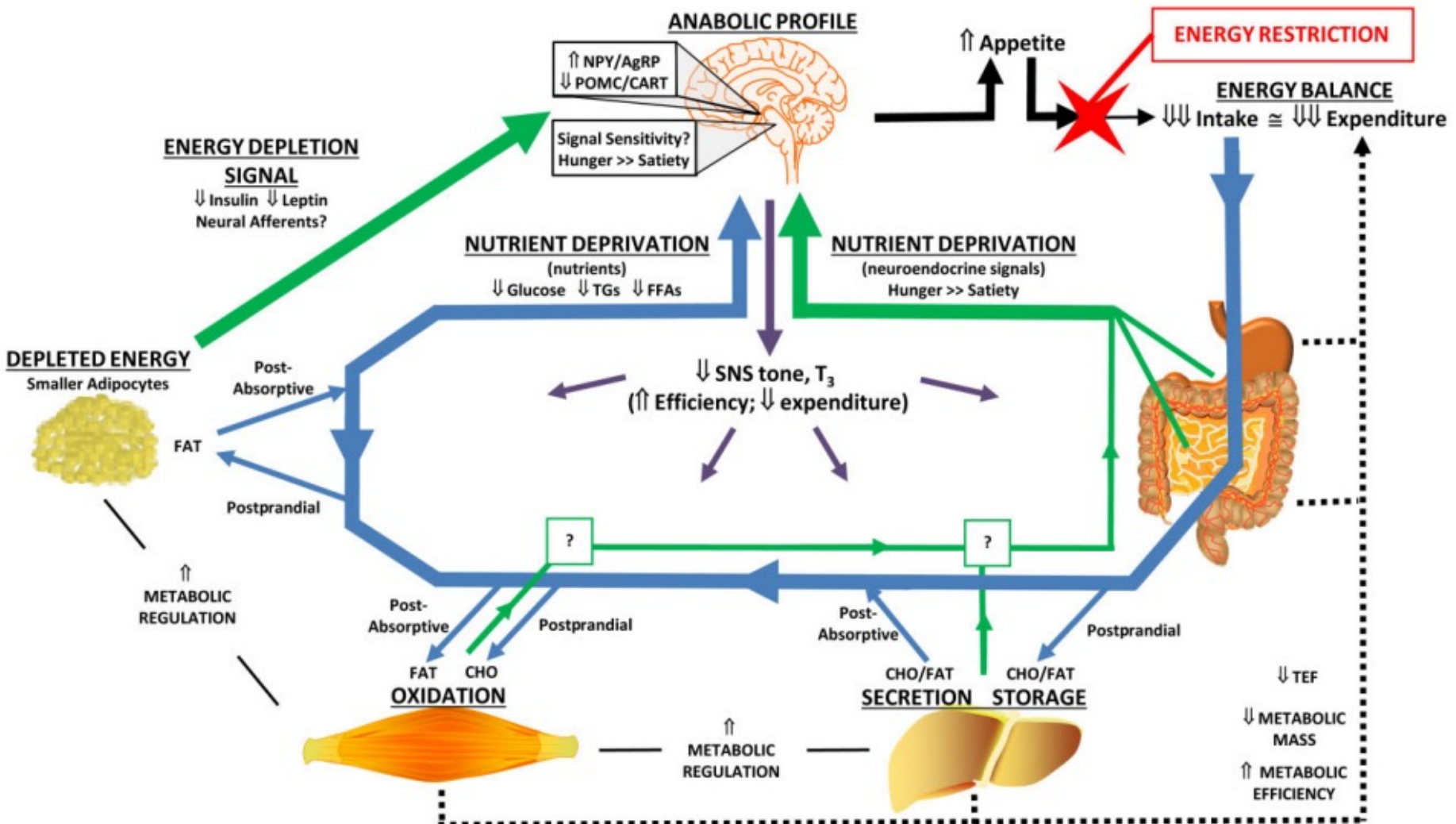


Table 1 | Predictors of weight regain after weight loss in adults with obesity

Factor	Associations	Refs
Glucose homeostasis variables at baseline or changes during diet	<ul style="list-style-type: none"> • Baseline fasting insulin associated with weight regain • Baseline insulin sensitivity (M value) inversely associated with weight regain • Change in fasting insulin and insulin resistance as defined by HOMA during weight loss inversely associated with weight regain 	<ul style="list-style-type: none"> • Kong et al. (2014)¹³⁴ • Ryan et al. (2018)¹⁷⁵ • Wong et al. (2012)¹⁷⁶ (DiOGenes study)
Total plasma cysteine level	Total plasma cysteine level 2 years after RYGB associated with weight regain between 2 and 4 years after surgery	Hanvold et al. (2017) ¹⁷⁷
Initial weight loss	<ul style="list-style-type: none"> • Increased weight loss associated with successful weight maintenance ($\geq 10\%$ weight loss maintained) • Increased weight loss associated with better weight maintenance • Increased weight loss achieved at 6 months associated with more successful 2-year weight loss ($>5\%$) • Weight loss inversely correlated with weight regain • Increased weight loss at week 3 predicts success at 1 year ($\geq 5\%$ weight loss) • Reduced BMI inversely associated with weight regain 	<ul style="list-style-type: none"> • Sawamoto et al. (2017)¹⁷⁸ • Calugi et al. (2017)¹⁷⁹ • Greenberg et al. (2009)¹⁸⁰ (DIRECT trial) • Vogels et al. (2005)¹⁸¹ • Fabricatore et al. (2009)¹⁸² • Wong et al. (2012)¹⁷⁶ (DiOGenes study)
Eating behaviour variables	<ul style="list-style-type: none"> • Reduced disinhibition and reduced food addiction at end of weight loss associated with successful weight maintenance ($\geq 10\%$ weight loss maintained) • Internal disinhibition associated with weight regain • Reduction in disinhibition during weight loss associated with less weight regain 	<ul style="list-style-type: none"> • Sawamoto et al. (2017)¹⁷⁸ • Lillis et al. (2015)¹⁸³ • Butryn et al. (2009)¹⁸⁴
Bariatric surgery aspects	A dilated gastrojejunal stoma diameter is a risk factor for weight regain	Abu Dayyeh et al. (2017) ¹⁸⁵
Exercise perception	Perceived exertion during submaximal exercise associated with weight regain	Brock et al. (2010) ¹⁸⁶
Depressive symptoms	<ul style="list-style-type: none"> • Antidepressant use associated with return to baseline weight • Reduced baseline depressive symptoms predict weight loss success at 1 year ($\geq 5\%$ weight loss) 	<ul style="list-style-type: none"> • Price et al. (2013)¹⁸⁷ (DPP study) • Fabricatore et al. (2009)¹⁸²
Satisfaction with weight loss	Increased satisfaction with weight loss associated with better weight maintenance	Calugi et al. (2017) ¹⁷⁹
Genetics	<ul style="list-style-type: none"> • SNPs in multiple genes associated with waist circumference regain • <i>PPARG2</i> genotype predicts weight regain • <i>FTO</i> genotype predicts weight regain • SNPs in multiple genes predict weight regain • SNP in the <i>ADRB2</i> gene predicts rebound weight 	<ul style="list-style-type: none"> • Larsen et al. (2012)¹⁸⁸ (DiOGenes study) • Nicklas et al. (2001)¹⁸⁹ • McCaffery et al. (2013)¹⁹⁰ (Look Ahead study) • Delahanty et al. (2013)¹⁹¹ (DPP study) • Masuo et al. (2005)¹⁹²
Epigenetics	Levels of methylation in <i>NPY</i> and <i>POMC</i> promoters associated with success of weight maintenance ($\geq 10\%$ or $<10\%$ weight regain)	Crujeiras et al. (2013) ¹⁹³

Summary



Summary

- Weight cycling은 신체내 보상작용을 포함한 다양한 과정이 복합적으로 발생하는 상태
- Gut hormone+metabolic adaptation+adipocyte+reward+++
- 이를 이해하기 위해 비만기전에 대한 이해
- Obesity stigma는 없어야 하며
- 환자의 motivation을 유지시키는 상담이 유효