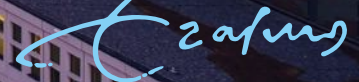


Drug induced obesity

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Erasmus MC
Universitair Medisch Centrum Rotterdam



DISCLOSURES	Name all entities with whom you have this relationship	Specifications/Comments (e.g., if payments were made to you or to your institution)
Grants or contracts from any entity	Nederlandse Hartstichting/ ZonMW	All payments to institution: Erasmus MC. Research project on Obesity
	ESPE (European Society for Paediatric Endocrinology) research unit	All payments to institution: Erasmus MC. Research project on CAH
	Stichting Erasmus Trustfonds	All payments to institution: Erasmus MC. Research project on Obesity
	NVK SKMS	All payments to institution: Erasmus MC. Guideline chair “treatment of children with obesity”
	Rhythm Pharmaceuticals Inc	All Payments to institution: Erasmus MC. Funding clinical trials: research personnel, research visits, diagnostics, treatment, provision of study materials, medical writing, article processing charges.
Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	European Society Pediatric Endocrinology Clinical practice Committee	unpaid
	European Reference Network RareEndoERN member main thematic group growth&obesity	unpaid
	Partnership Obesity Netherlands (PON) – NVK representative	unpaid
	Rare EndoERN guideline pubertal induction and HRT	unpaid
	Rare EndoERN guideline Bardet Biedl syndrome	unpaid

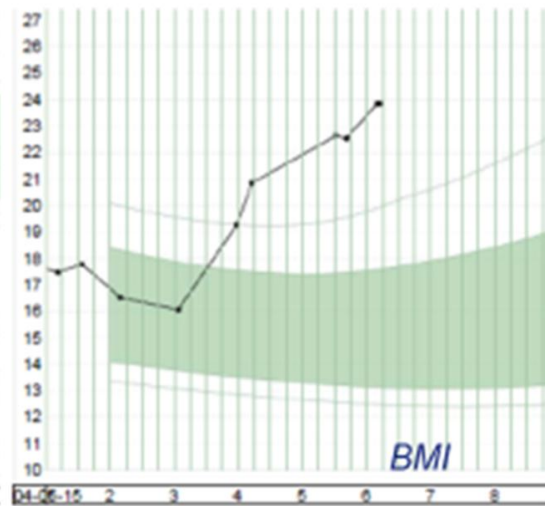
DRUG INDUCED OBESITY

- ☐ Definition
- ☐ Diagnoses
- ☐ Etiology
- ☐ Treatment
- ☐ Summary

DEFINITION DRUG INDUCED OBESITY

- No definition medical literature or www
- Pubmed: main literature on drug induced weight gain caused by side-effects of antipsychotics, antidepressive drugs

DEFINITION DRUG INDUCED OBESITY



The start or intensification of known weight-inducing medication coinciding with a sudden progression of obesity (seen as a clear visual slope discontinuity in the growth curve) and the absence of other plausible explanations for the sudden weight gain.

WEIGHT INDUCING MEDICATION

Corticosteroids

Psychiatric drugs:

- Anti-psychotics

- Anti-depressants

- Anti-anxiety

Antiepileptics

DRUG INDUCED WEIGHT GAIN

- Corticosteroids 70% of patients gain weight; in 20% +10kg in first year
- Anti-psychotics 80% of patients >+ 7% first episode; +13-18kg longterm
- Anti-anxiety on average + 5 to +16 kg
- Antiepileptics
 - Valproaat: 60% of patients; +4-7,5 kg (up to 20kg)

Verhagen et al JCI 2017.

Fitzgerald et al. Evid Based Ment Health . 2022 Feb;25(1):15-22. doi: 10.1136/ebmental-2021-300291. Epub 2021 Sep 29. Metformin in the management of antipsychotic-induced weight gain in adults with psychosis: development of the first evidence-based guideline using GRADE methodology

Breum et al. Drug-induced Obesity. Int textbook of obesity 2001

WEIGHT INDUCING MEDICATION

Corticosteroids
Anti-psychotics
Anti-depressants
Anti-anxiety
Antiepileptics

Insulin
Antimigraine
Antihistaminergic
Beta blockers
Estrogen- high dose
Omeprazole

DRUG INDUCED OBESITY

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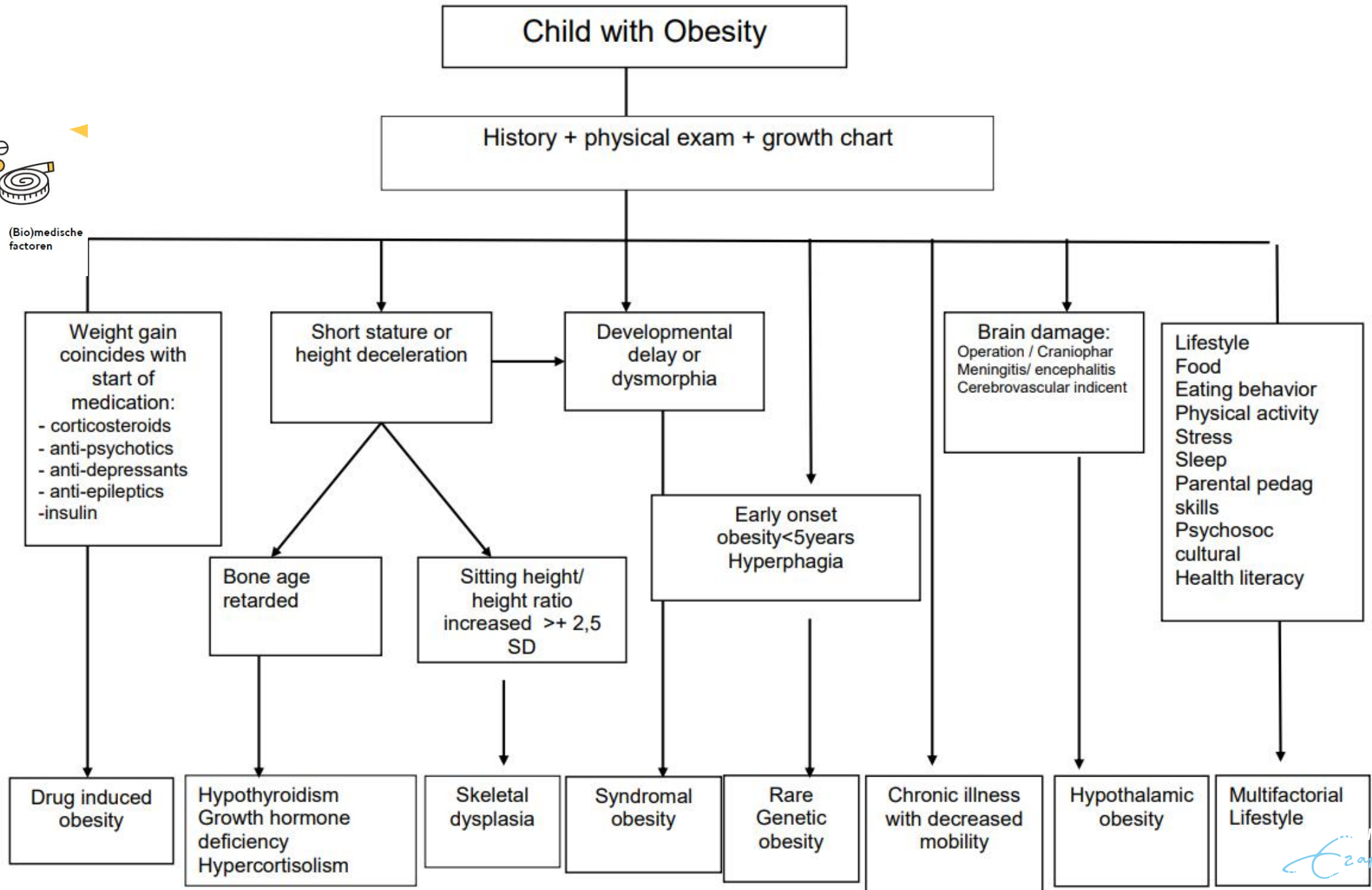
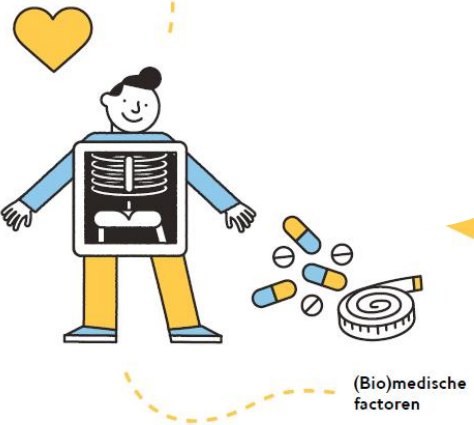
IN WHOM TO SUSPECT DRUG INDUCED OBESITY?

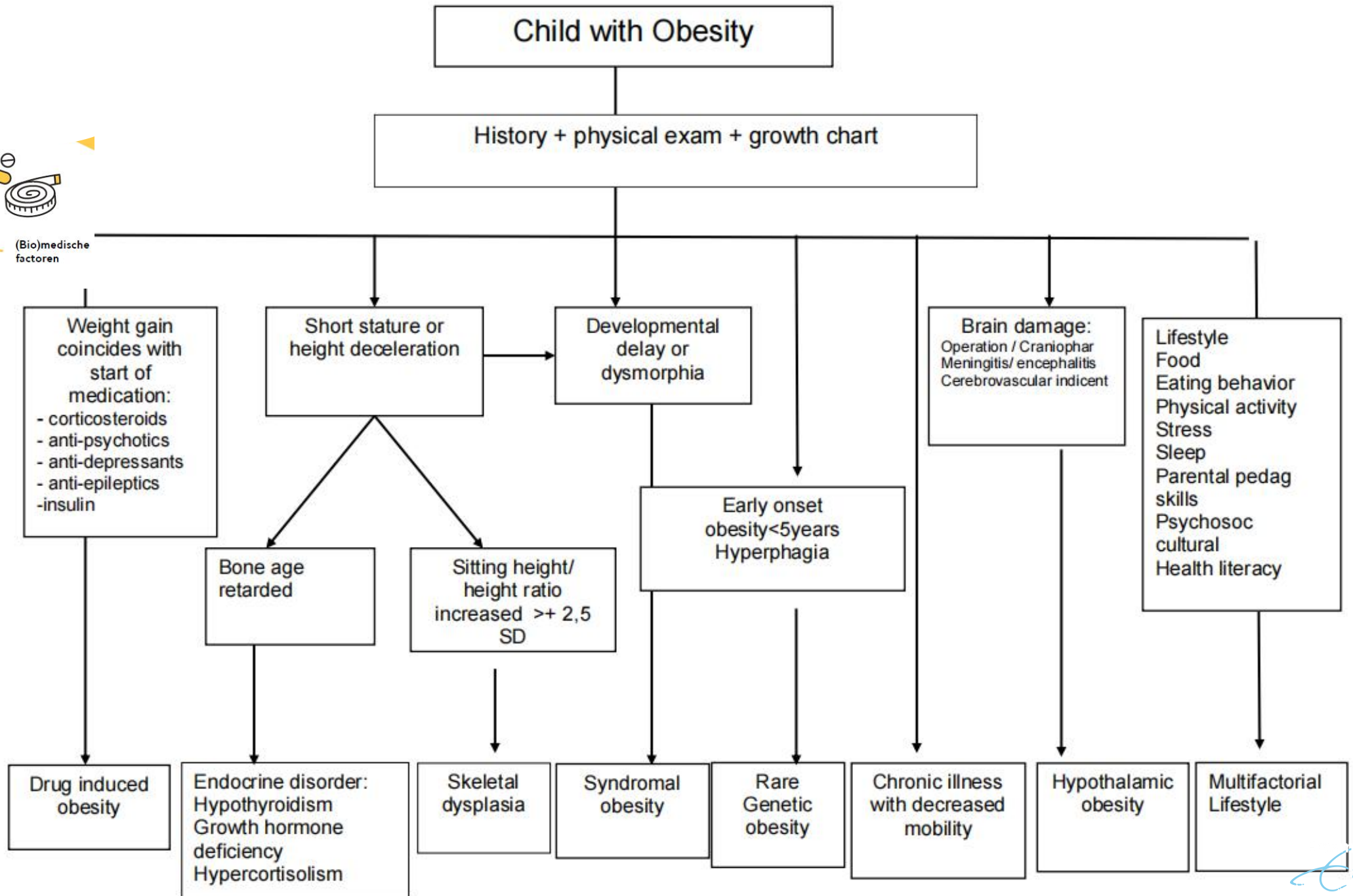
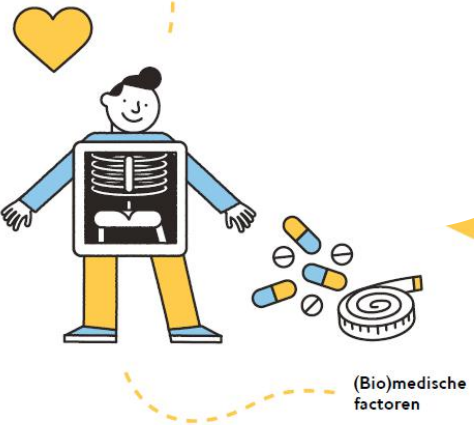
Health care professionals need a structured diagnostic approach



CAUSES OF (UN)HEALTHY LIFESTYLE AND WEIGHT GAIN









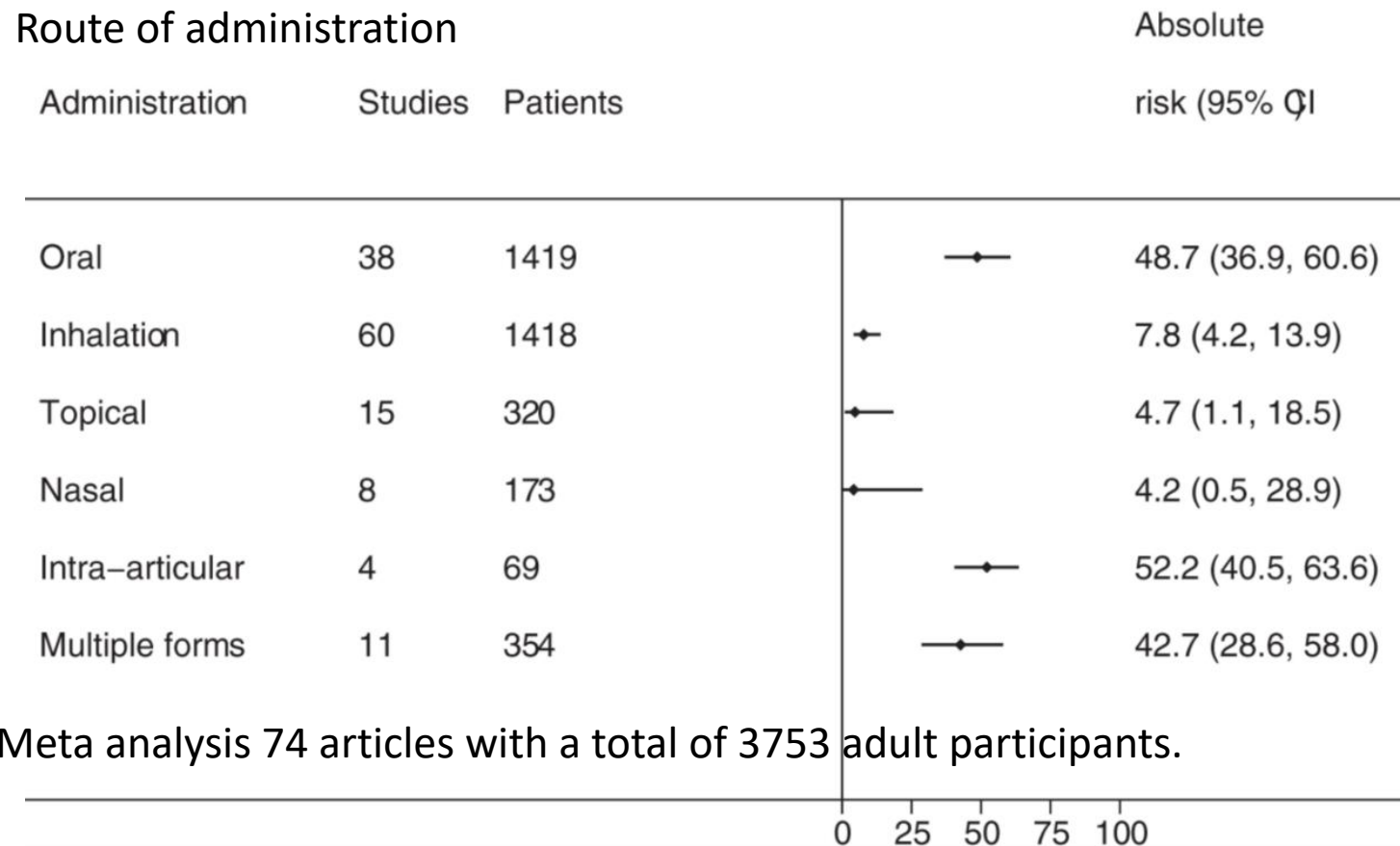
CORTICOSTEROID USE is not rare

Type	Most used corticosteroids NL	Users (2015)
Inhaled	Fluticason (Seretide®), Fluticason (Flixotide®) Symbicort®, Foster®, Qvar®, Pulmicort®, Alvesco®	1.032,020
Nasal	Fluticason (Flixonase®)	427,470
Dermal	Triamcinolon, hydrocortison, betamethason etc	2.352,980
Tablet	Prednisolon, dexamethason, Prednison	623,656
Local injection	Triamcinolon (Kenacort-a ®)	198,230



Adrenal Insufficiency in Corticosteroids Use: Systematic Review and Meta-Analysis.

Systemic effect can also be present in nasal or inhaled or topical corticosteroids.



From: Adrenal Insufficiency in Corticosteroids Use: Systematic Review and Meta-Analysis
J Clin Endocrinol Metab. 2015;100(6):2171-2180. doi:10.1210/jc.2015-1218
J Clin Endocrinol Metab | Copyright © 2015 by the Endocrine Society



'local' CORTICOSTEROID use and metabolic syndrome (N=140,879)



BMI: +0.25 kg/m²

waist : +1.44 cm



BMI: +0.86 kg/m²

wais : +2.43 cm



Higher blood pressure and glucose
Lipid profile

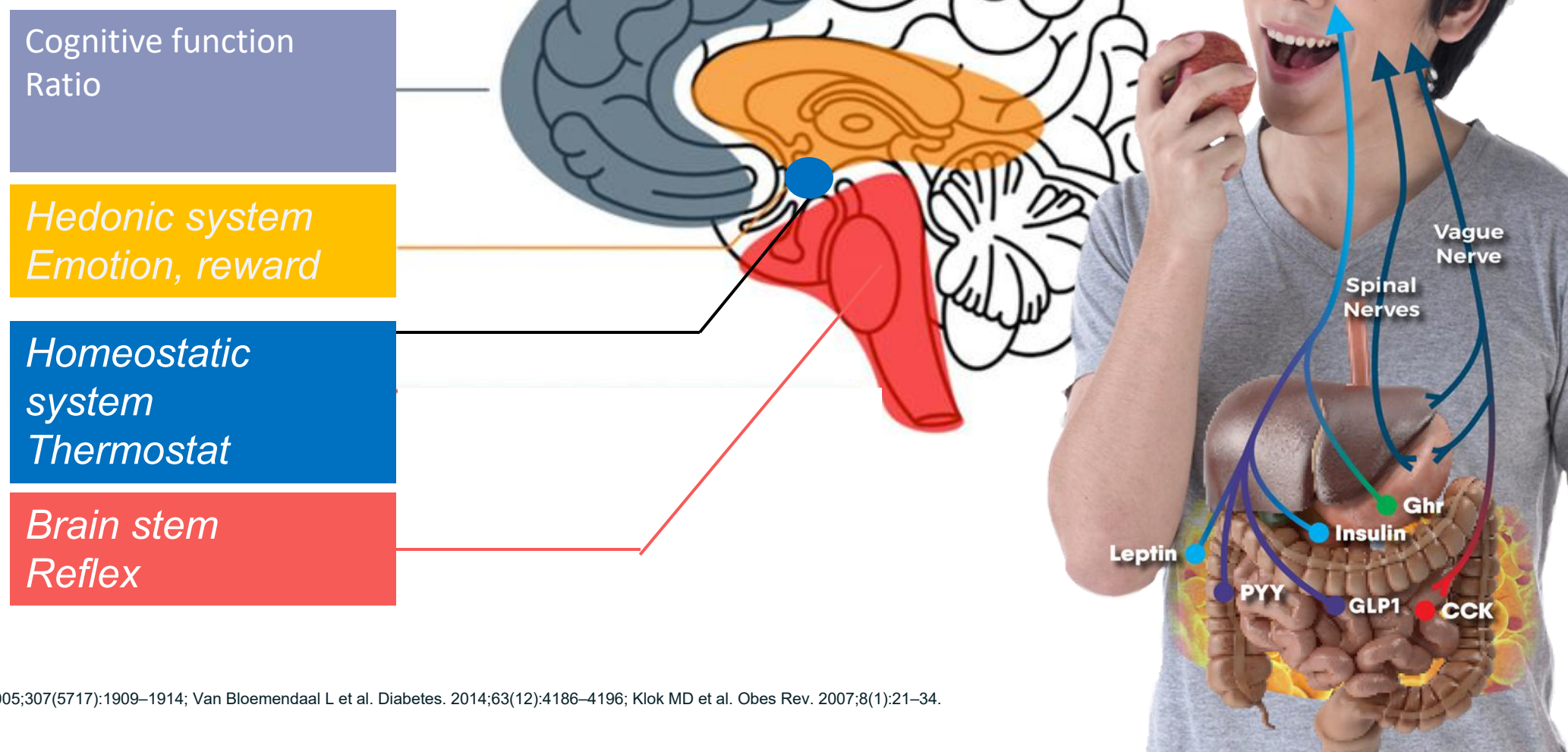
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POSSIBLE MECHANISMS

- Decreased serotonergic and dopaminergic activity
- Impaired mitochondrial beta-oxidation of fatty acids and
- other changes in substrate oxidation
- Reduced sympathetic nervous system activity
- Decreased energy expenditure
- Anticholinergic side effects causing dry mouth and
- increased intake of caloric beverages
- Altered activity of hypothalamic leptin and neuropeptide Y

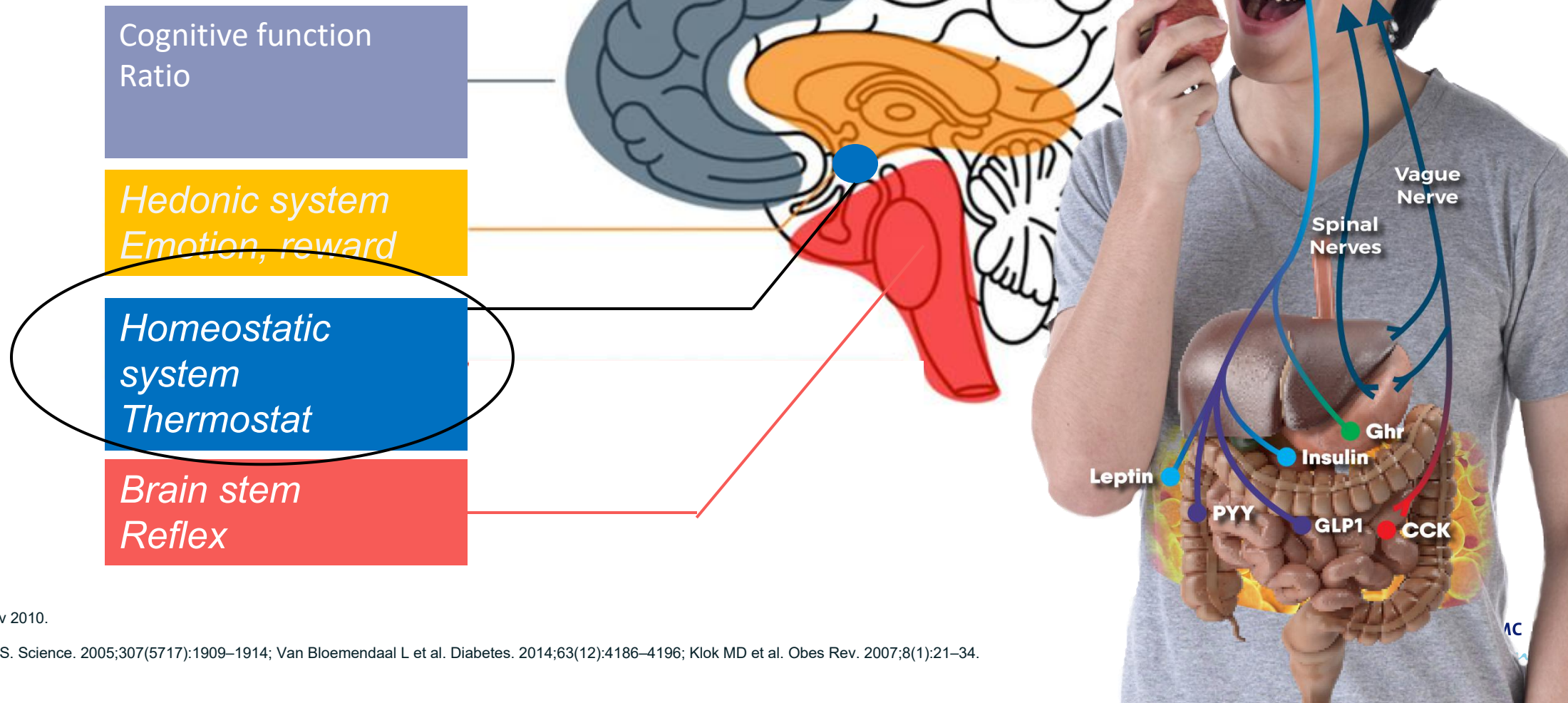
Weight regulation in the brain



Hochberg et al Ob Rev 2010.

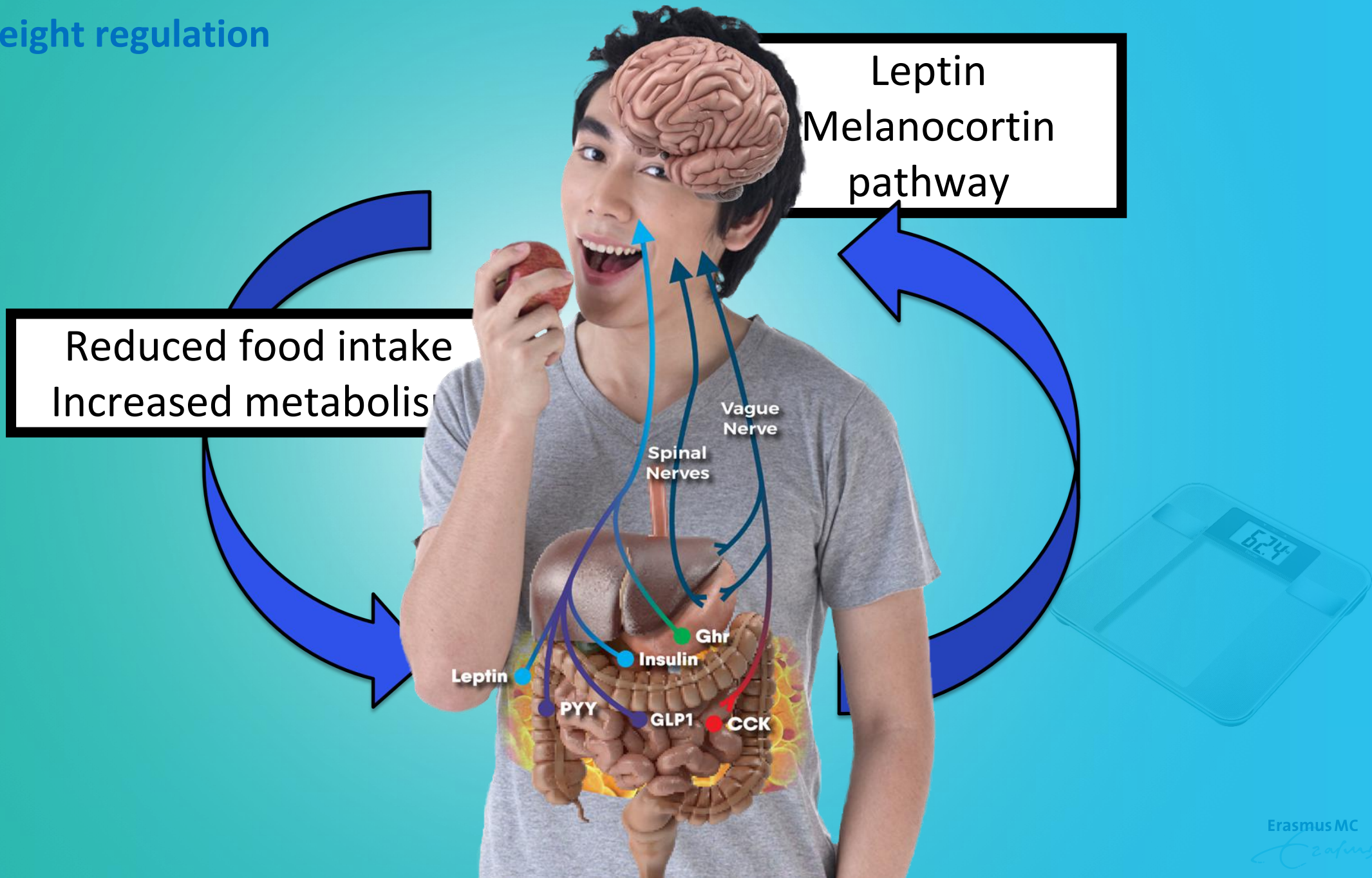
Badman MK & Flier JS. Science. 2005;307(5717):1909–1914; Van Bloemendaal L et al. Diabetes. 2014;63(12):4186–4196; Klok MD et al. Obes Rev. 2007;8(1):21–34.

Weight regulation in the brain

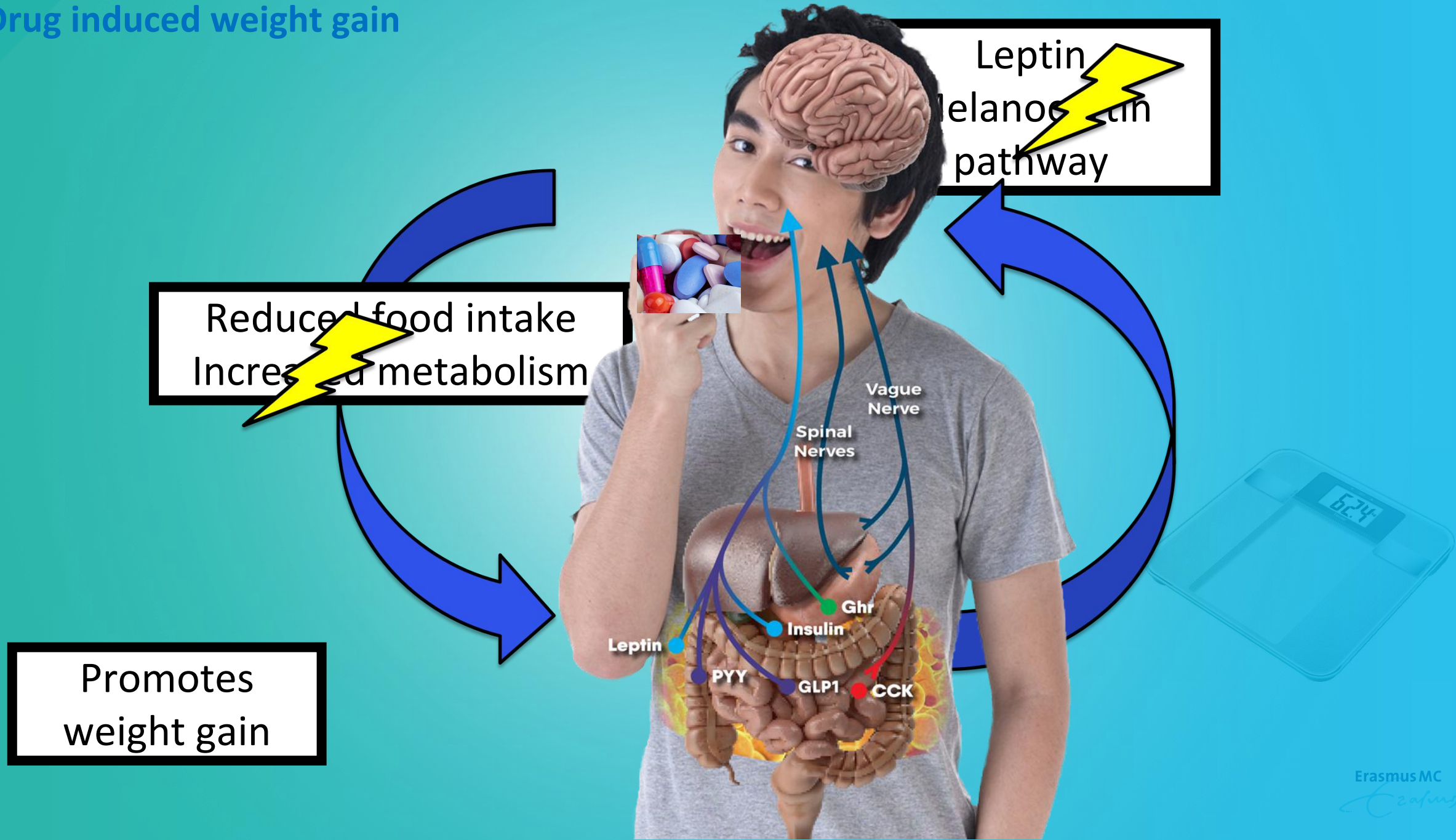


Hochberg et al Ob Rev 2010.

Normal weight regulation

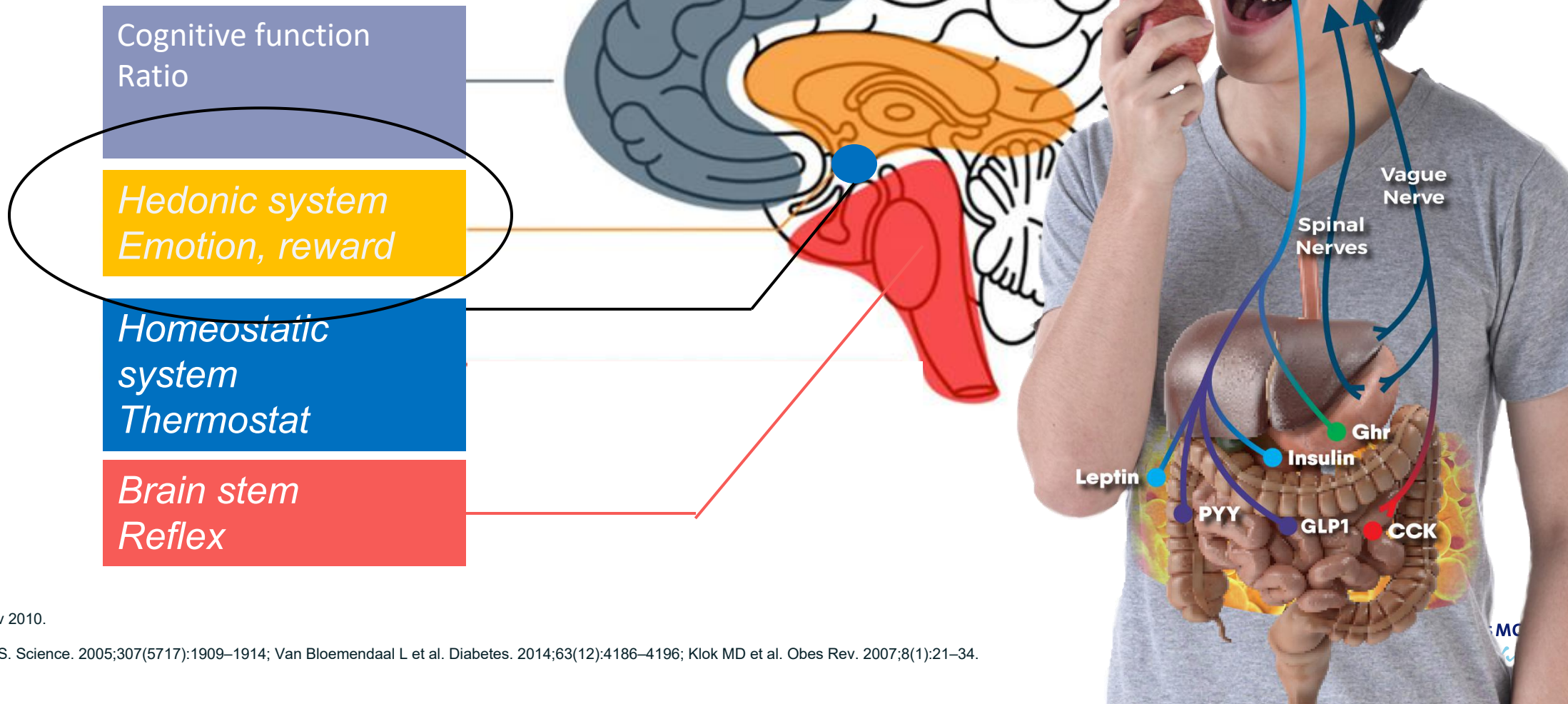


Drug induced weight gain



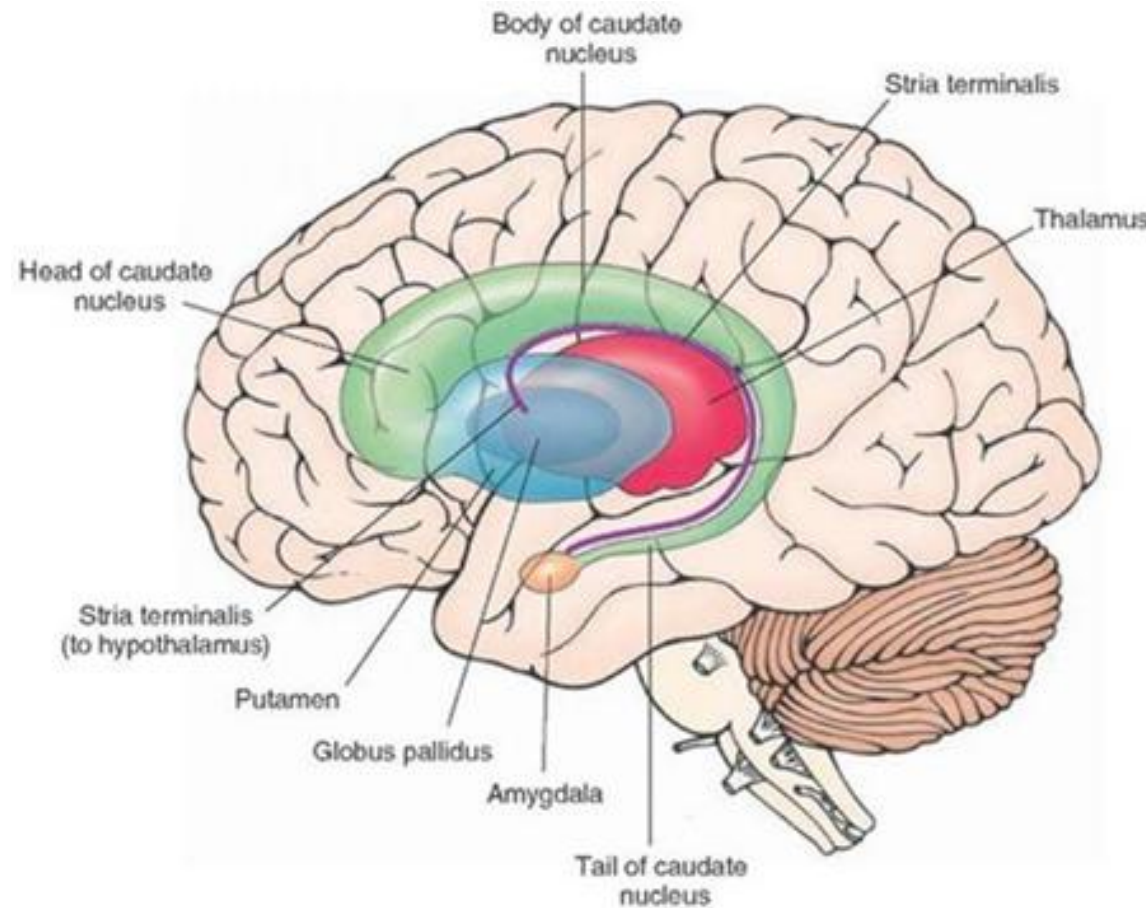
Definition Hypothalamic Obesity (HO)

HO is a result of impairment in hypothalamic regulatory centres of body weight and energy expenditure. Regardless of aetiology!



SATIETY AND HUNGER REGULATION

<https://youtu.be/leufqzTuu4s>



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TREATMENT

Are the benefits of the weight inducing drug still outweighing the effect?

- Make choices (ask prescribing HCP for options)
- Change formula
- Taper dose or try to stop
- Alternate day

Anti-epileptic drugs.

- Valproate weight inducing
- Carbamazepine weight inducing
- Gabapentin weight inducing
- Lamotrigine weight-neutral
- Topiramate weight loss

METFORMIN

ORIGINAL RESEARCH

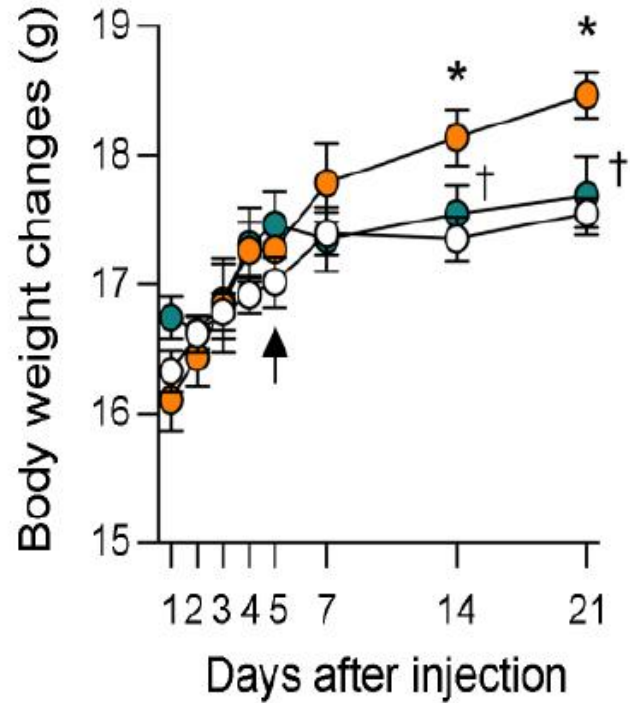
Metformin in the management of antipsychotic-induced weight gain in adults with psychosis: development of the first evidence-based guideline using GRADE methodology

Ita Fitzgerald ^{1,2} Jean O'Connell,^{3,4} Dolores Keating,⁵ Caroline Hynes,⁶ Stephen McWilliams,^{7,8} Erin K Crowley⁹

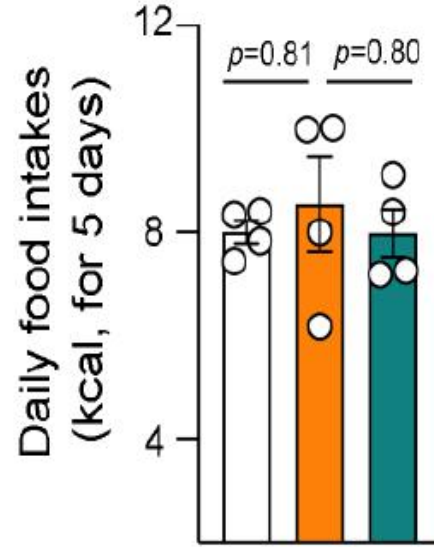
BMB; 2022

Metformin ameliorates olanzapin induced disturbance in pomc neuron number, and hypothalamic leptin resistance

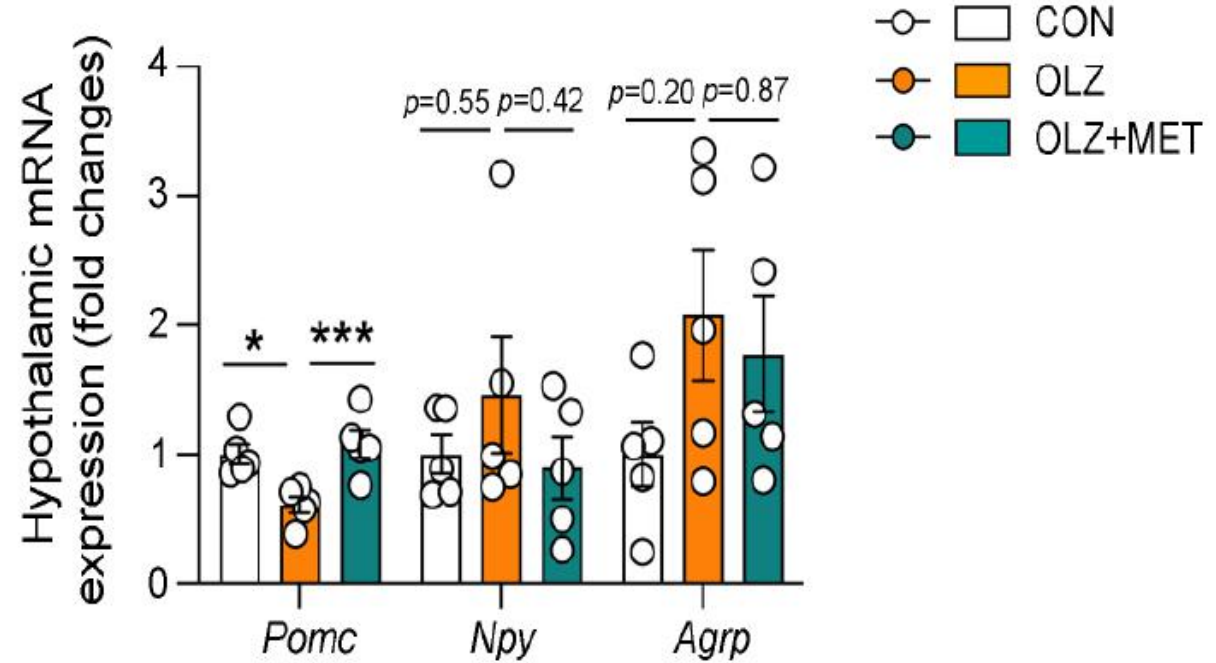
B



C



D



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SUMMARY

- Drug induced weight gain is common
- Corticosteroids, psychiatric drugs and antiepileptics
- Ask specifically for the use of drugs, many are not mentioned at first, especially inhaled, intranasal, topical or intra-articular corticosteroid
- Also drugs with small effects on weight can be worthwhile to consider.
- Weigh the benefit of drug against side-effect
- Explore the options
- Consider metformin at start of anti-psychotics.

Thank you for your attention

On behalf of Obesity Center CGG team Rotterdam



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Jenny Visser
Patrick Delhanty
Alejandra Rodriguez

Amsterdam UMC clinical genetics

Mieke van Haelst
Lotte Klemmendorp
Niels Vos

THANK YOU FOR YOUR ATTENTION



HEALTHCARE



RESEARCH



EDUCATION

Erasmus MC
University Medical Center Rotterdam

