OBESITA' .....

DI GENERE

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Clinica Pediatrica

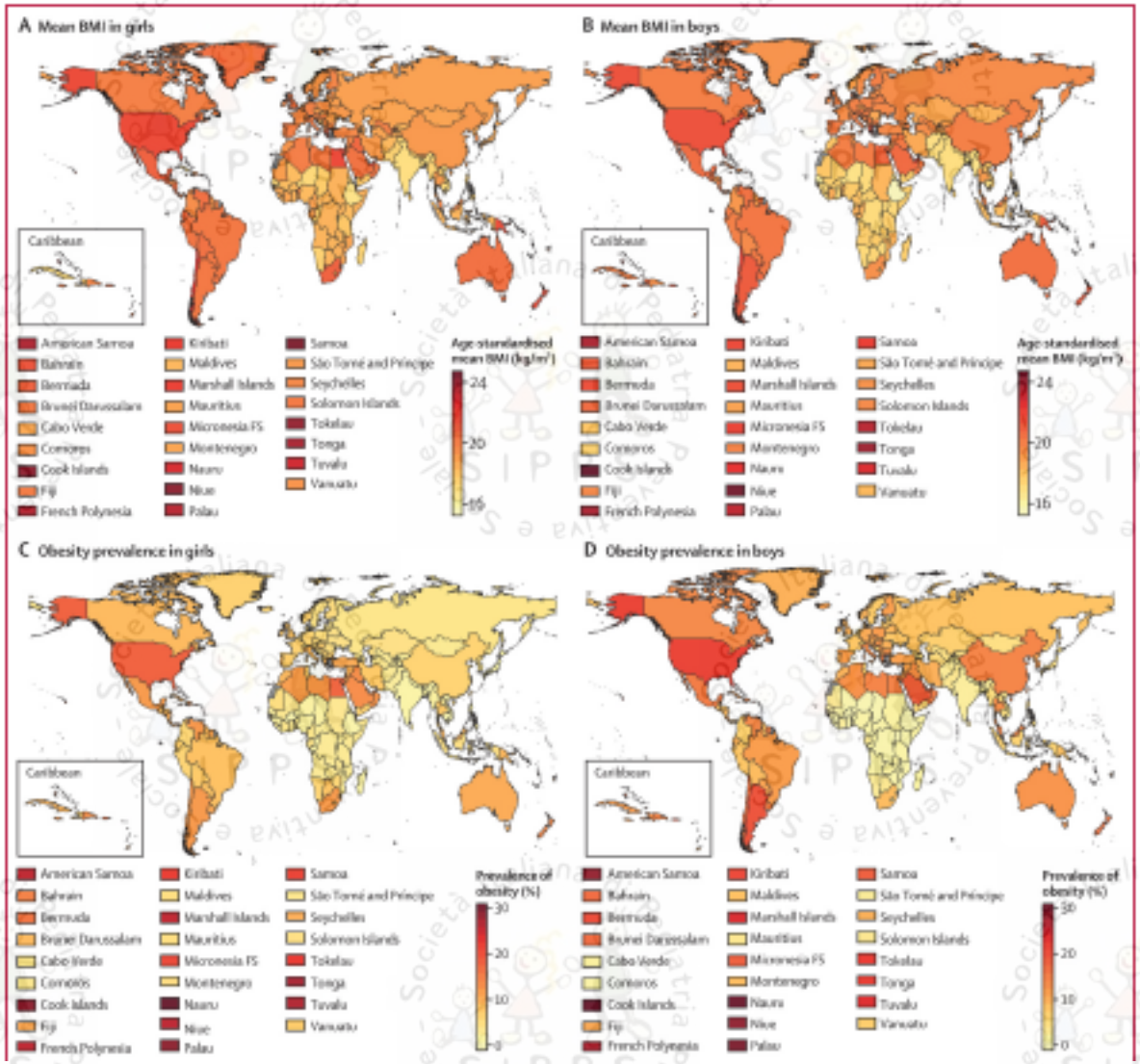
Endocrinologia Pediatrica e CRR di Diabetologia Pediatrica

Dipartimento di Medicina Clinica e Sperimentale

AOU Policlinico-Vittorio Emanuele Catania

Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults

NCD Risk Factor Collaboration (NCD-RisC)*



Lancet 2017; 390: 2627–42

Trends in Obesity Prevalence Among Children and Adolescents in the United States, 1988-1994 Through 2013-2014

Weighted Prevalence of Obesity and Extreme Obesity in US Children and Adolescents Aged 2 to 19 Years by Sex, Age NHANES 2011–2014

	Weighted Prevalence by Age Group, % (95% CI)			
	2–19 y	2–5 y	6–11 y	12–19y
Obesity (BMI at or above the sex-specific 95th percentile on the CDC BMI-for-age growth charts)				
All race/Hispanic origin groups[a]				
Both sexes	17.0 (15.5–18.6)	8.9 (7.1–11.0)	17.5 (15.2–20.1)	20.5 (17.8–23.5)
Males	16.9 (15.1–19.0)	9.2 (6.5–12.4)	17.6 (14.6–20.9)	20.1 (16.8–23.6)
Females	17.1 (15.1–19.3)	8.6 (6.2–11.6)	17.5 (14.9–20.3)	21.0 (17.3–25.2)

JAMA. 2016 June 07; 315(21)

Sex differences in obesity incidence: 20-year prospective cohort in South Africa

	1–2 years†††	4–8 years	11–12 years	13–15 years	16–18 years
BMI†§					
Boys	16.9 (16.7, 17.0)	15.8 (15.6, 15.9)	17.8 (17.5, 18.0)	19.2 (18.9, 19.5)	20.3 (20.0, 20.6)
Girls	16.7 (16.5, 16.8)	15.7 (15.6, 15.8)	18.8 (18.5, 19.2)	21.3 (21.0, 21.7)	22.8 (22.5, 23.2)
BMIZ†§					
Boys	0.3 (0.2, 0.4)	0.2 (0.1, 0.2)	–0.2 (–0.3, –0.1)	–0.4 (–0.5, –0.3)	–0.6 (–0.7, –0.5)
Girls	0.4 (0.3, 0.5)	0.1 (0.0, 0.2)	–0.03 (–0.1, 0.1)	0.2 (0.1, 0.3)	0.3 (0.2, 0.4)
Obesity¶					
WHO definition**					
Boys	8.8 (6.5, 11.2)	3.0 (1.6, 4.4)	6.0 (4.0, 8.0)	4.4 (2.7, 6.1)	2.5 (1.2, 3.8)
Girls	8.1 (5.9, 10.3)	3.1 (1.7, 4.5)	6.4 (4.5, 8.4)	7.3 (5.2, 9.3)	7.9 (5.8, 10.1)

Pediatric Obesity published by John Wiley & Sons Ltd on behalf of World Obesity. **Pediatric** Obesity **11**, 75–80

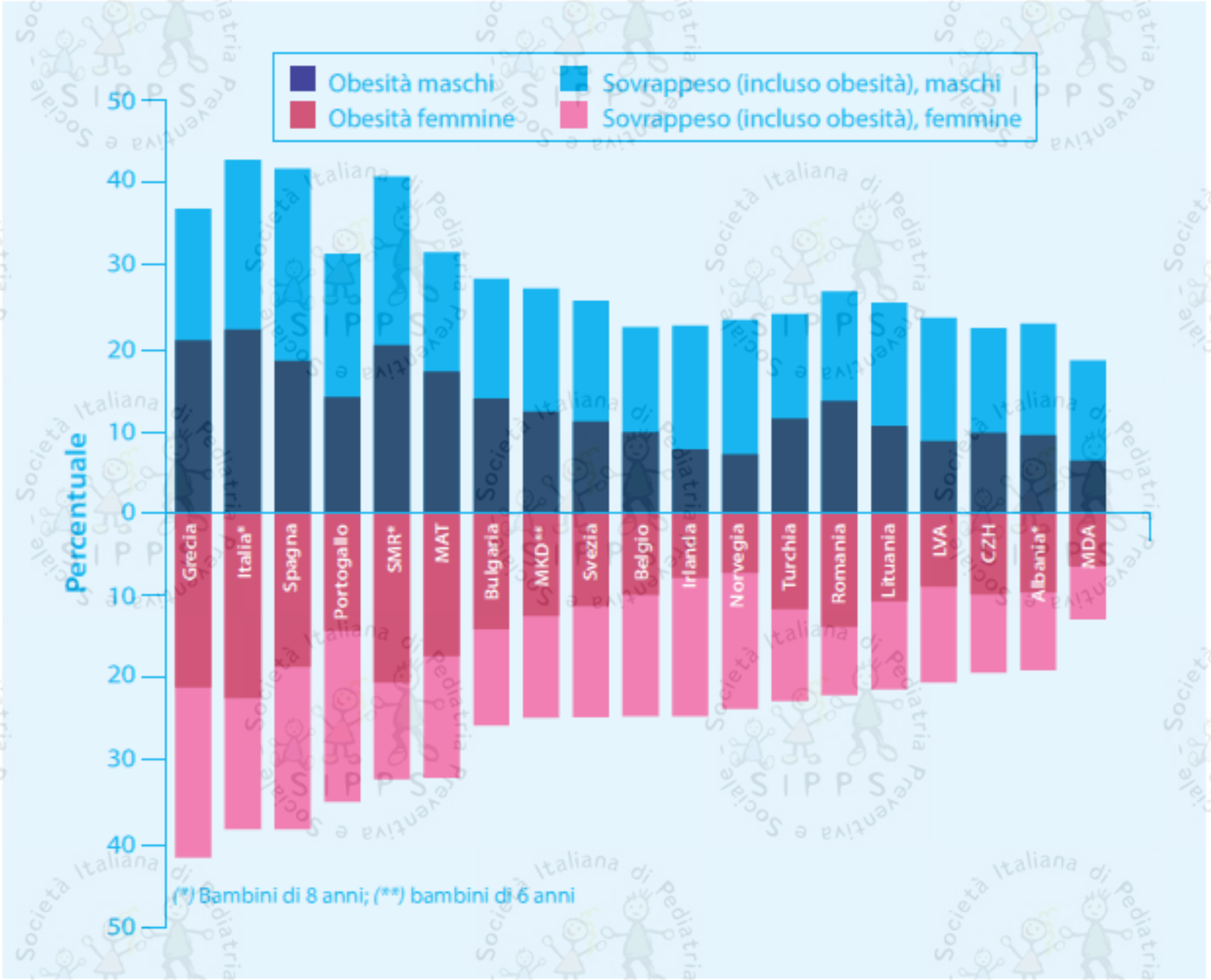
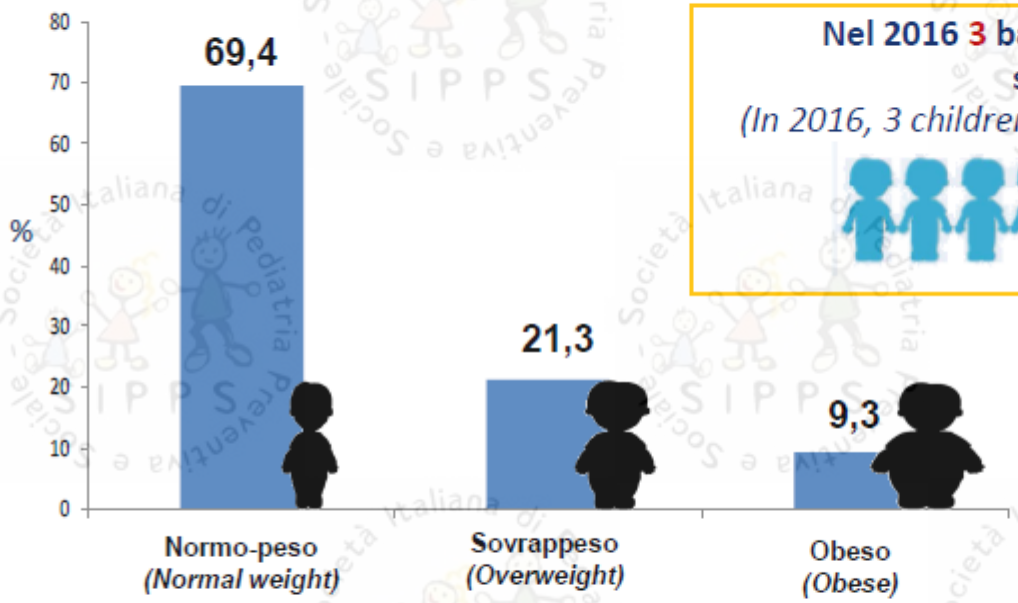


Figura 1 - Prevalenze di sovrappeso e obesità in bambini di 7 anni (utilizzando valori soglia dell'OMS) in alcuni Paesi europei. Fonte: OMS/Regione Europea - Childhood Obesity Surveillance Initiative (COSI), 2012-13

Prevalenze di sovrappeso e obesità tra i bambini di 8-9 anni*

(Overweight and obesity prevalence values among children aged 8-9 years)

OKkio alla SALUTE 2016



Nel 2016 3 bambini su 10 hanno problemi di sovrappeso/obesità

(In 2016, 3 children out of 10 were overweight or obese)

Le femmine sono meno obese dei maschi

(Girls are less obese than boys)

8,8%

9,7%

Prevalenze calcolate utilizzando i cut-off IOTF - Prevalence values based on IOTF cut-offs

Factors associated with abdominal obesity in children

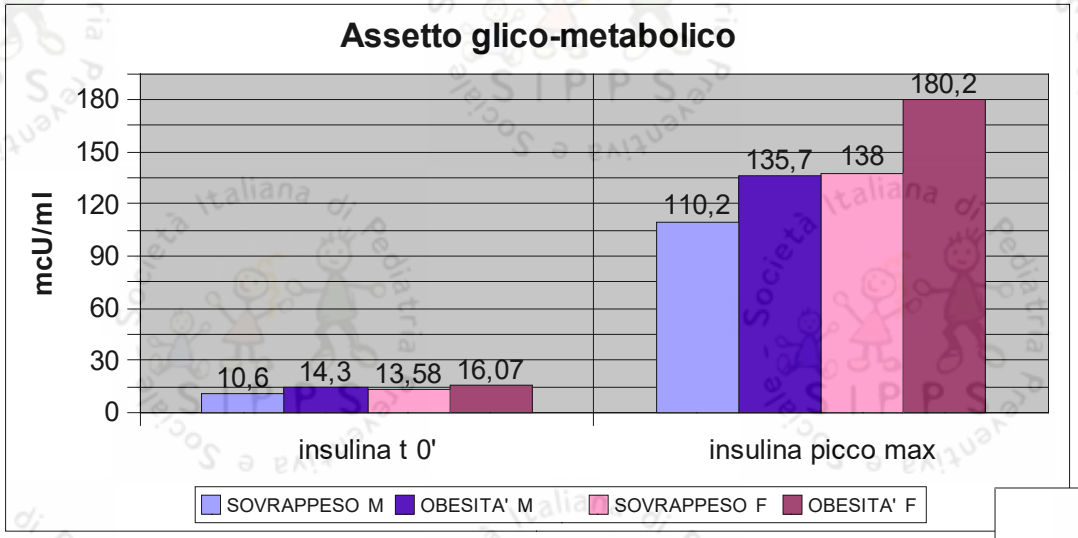
Rev Paul Pediatr. 2015;33(4):437–444

	$_{\text{Adjusted}}$OR	95%CI	*p*-value
Excess weight according to the child's BMI/age			
Yes	93.7	39.3–223.3	<0.001
No	1.0	–	
Child's gender			
Male	1.0	–	0.012
Female	4.1	1.8–9.3	
Maternal abdominal obesity			
Yes	2.7	1.2–6.0	0.01
No	1.0	–	
Socioeconomic level according to ABEP			
High	1.0	–	0.08
Low	0.5	0.2–1.0	

Table 4 Multiple logistic regression model with the children's abdominal obesity as the dependent variable. Santos, 2012 (n=356).

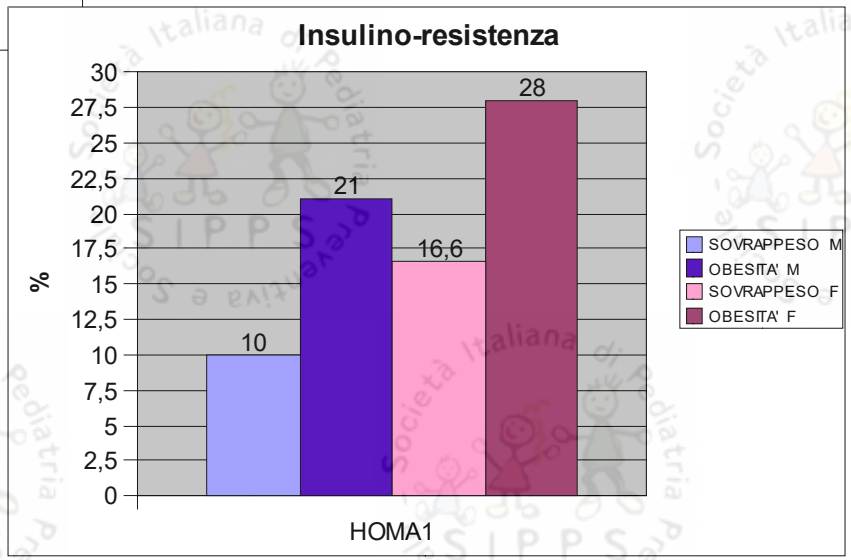
Profilo metabolico in un campione di 181 soggetti sovrappeso/obesi di età media 10,5 anni

ASSETTO GLICO-METABOLICO

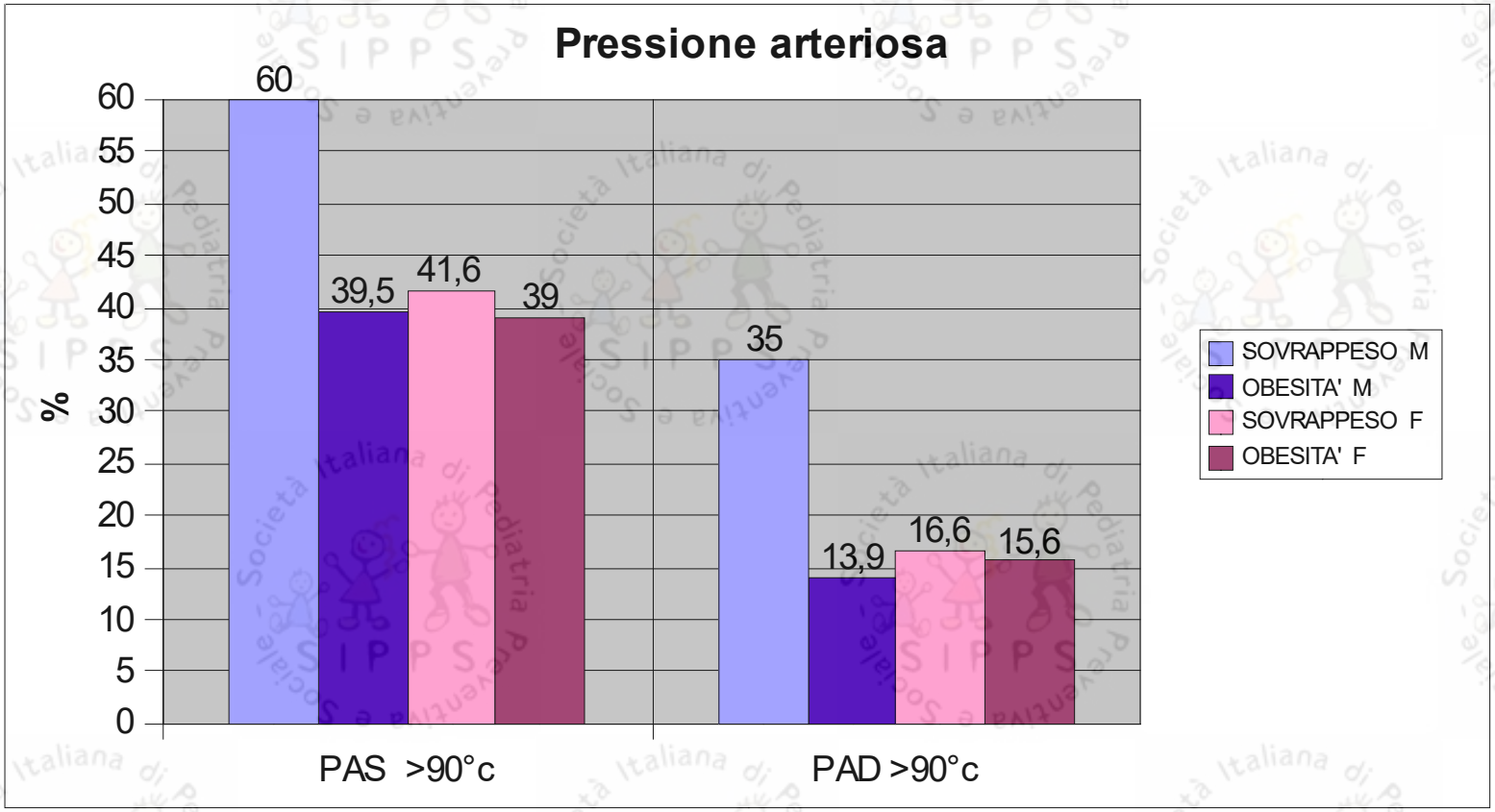


IPERINSULINEMIA

INSULINO-RESISTENZA



Profilo metabolico in un campione di 181 soggetti sovrappeso/obesi di età media 10,5 anni



Gender-related differences in cardiometabolic risk factors and lifestyle behaviors in treatment-seeking adolescents with severe obesity

Barstad *et al. BMC Pediatrics* (2018) 18:61

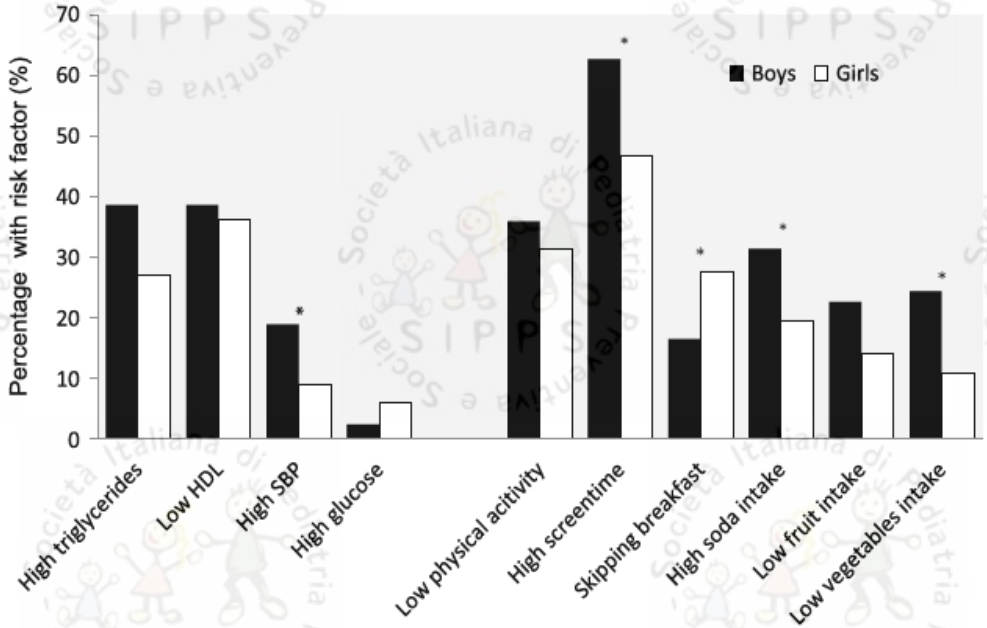


Fig. 1 Prevalence of CVD risk factors (cardiometabolic and behavioral) according to gender. *$P < 0.05$

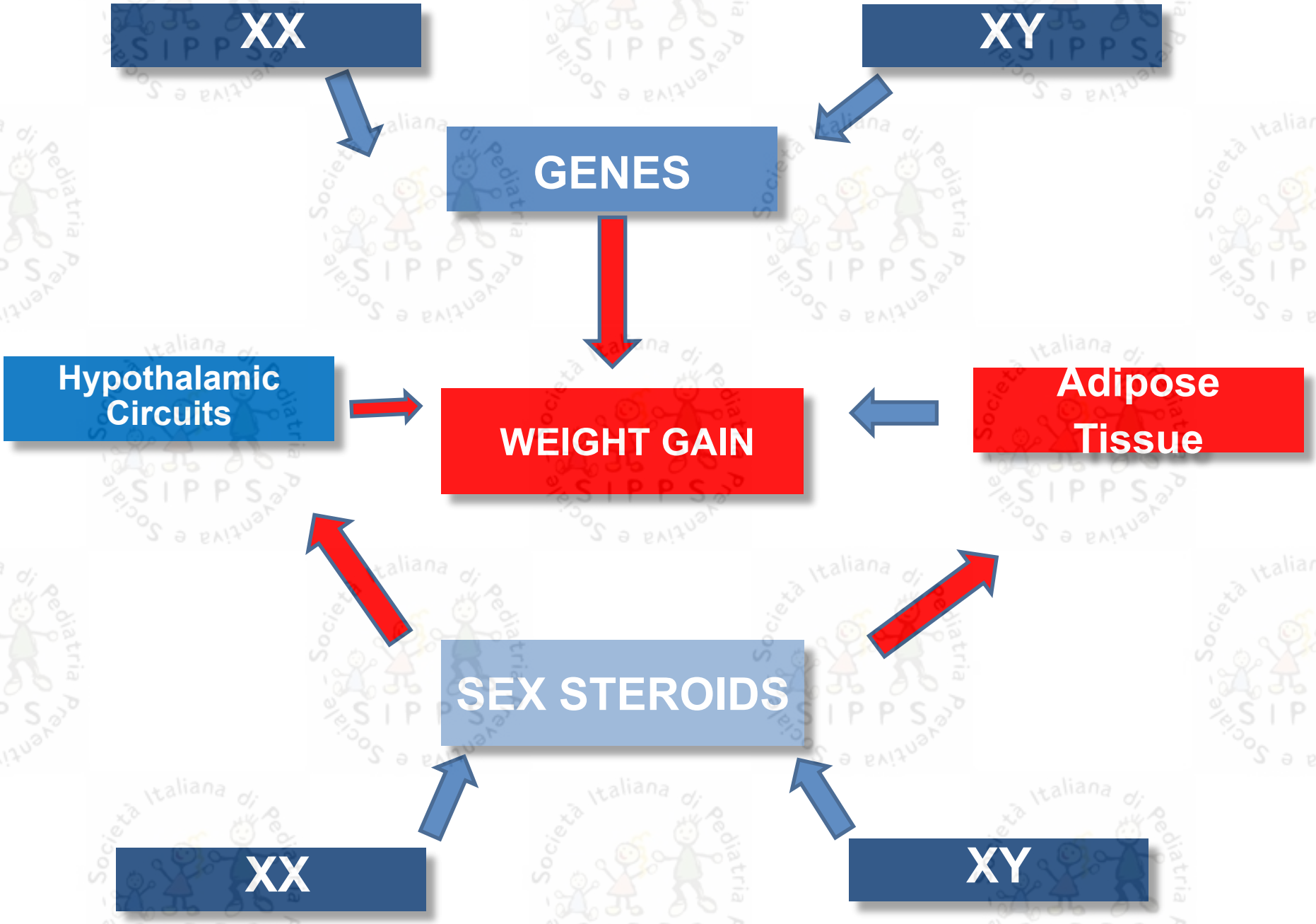
Conclusions: Male treatment-seeking adolescents with severe obesity had a more unfavorable set of metabolic and behavioral risk factors for cardiovascular disease than girls. Our results indicate that lifestyle behavioral markers should be thoroughly assessed in both genders, and possible gender-related differences in risk profile should be taken into account in future treatment programs.

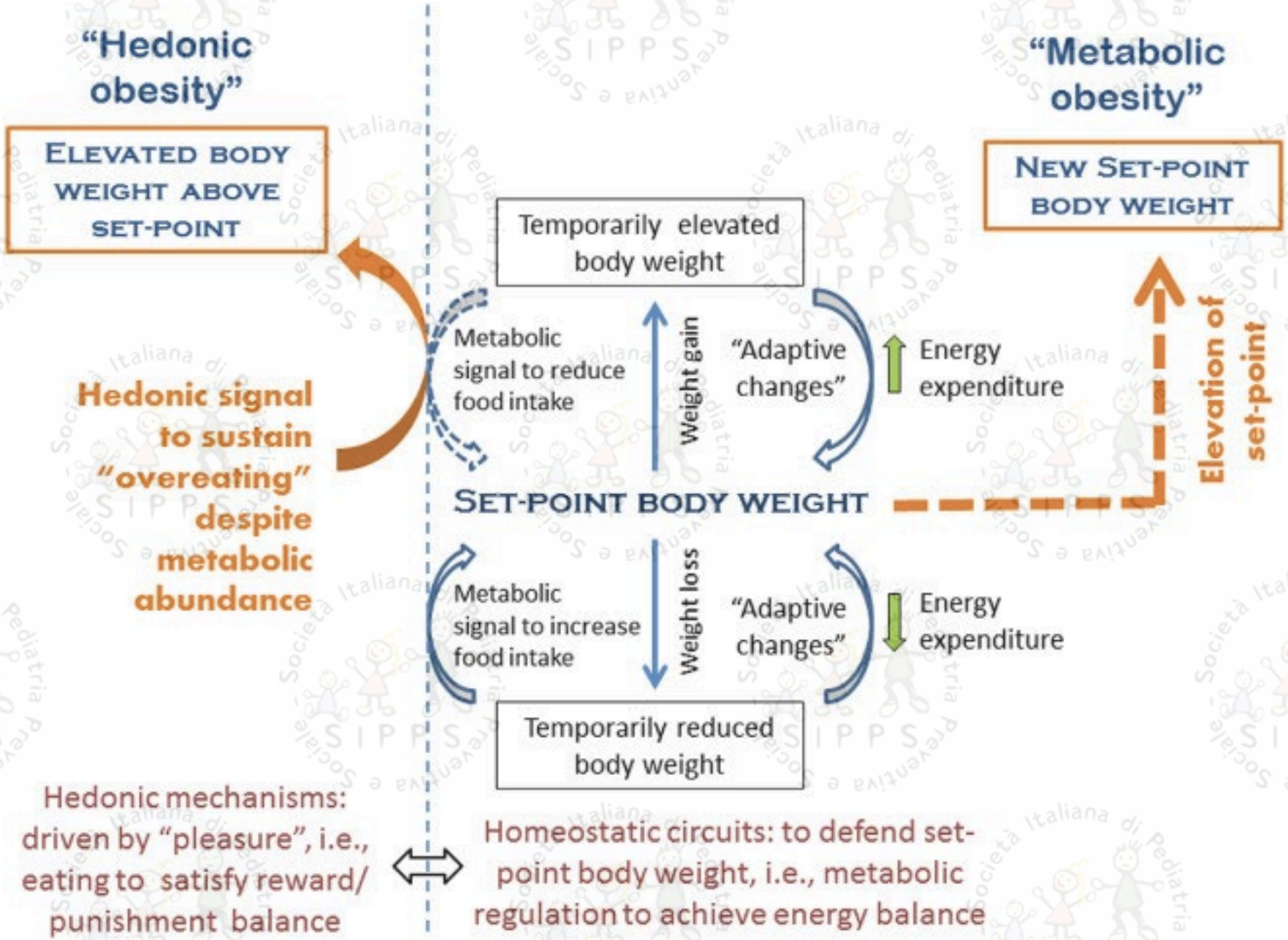
Obesità

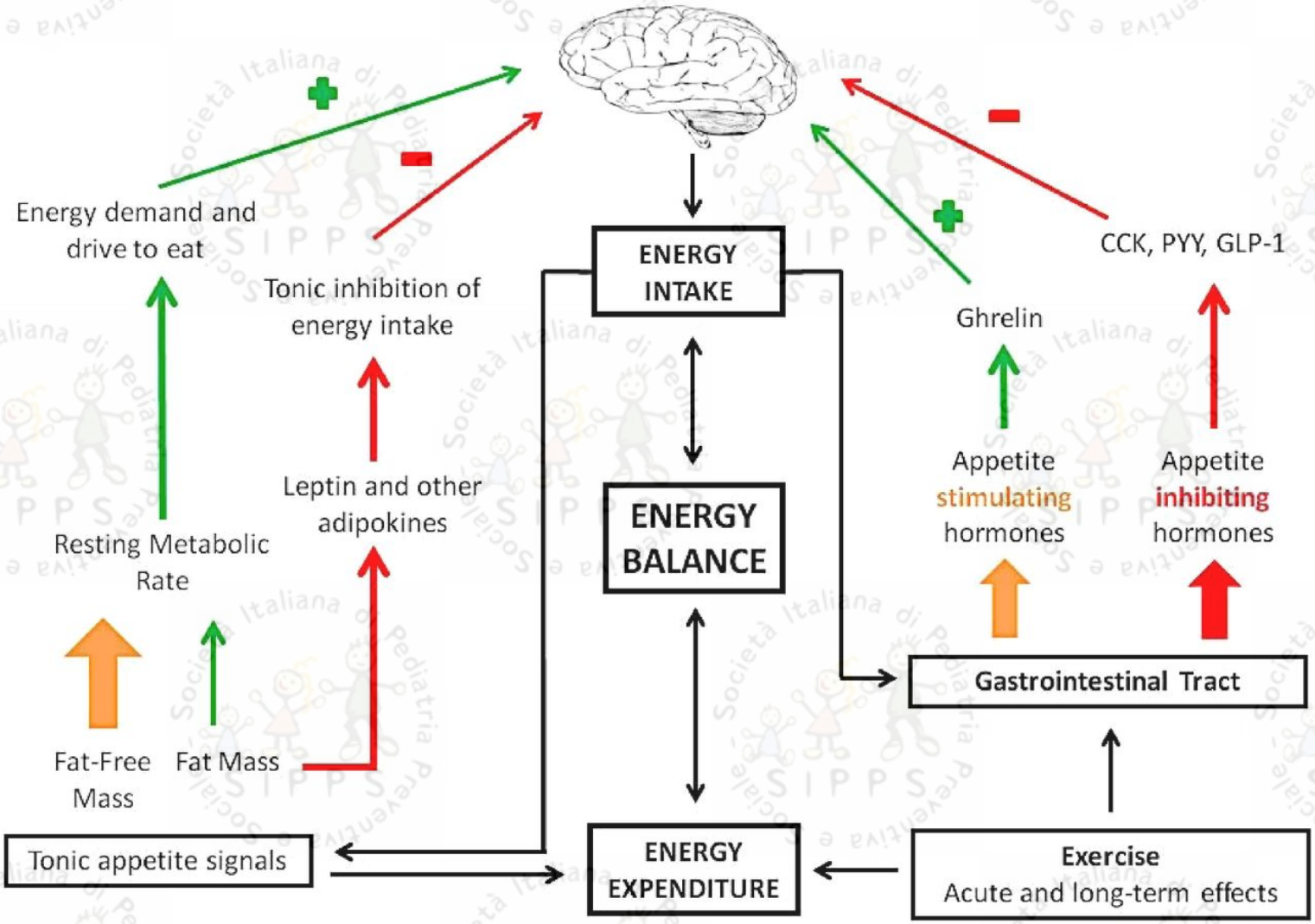
thrifty genotype

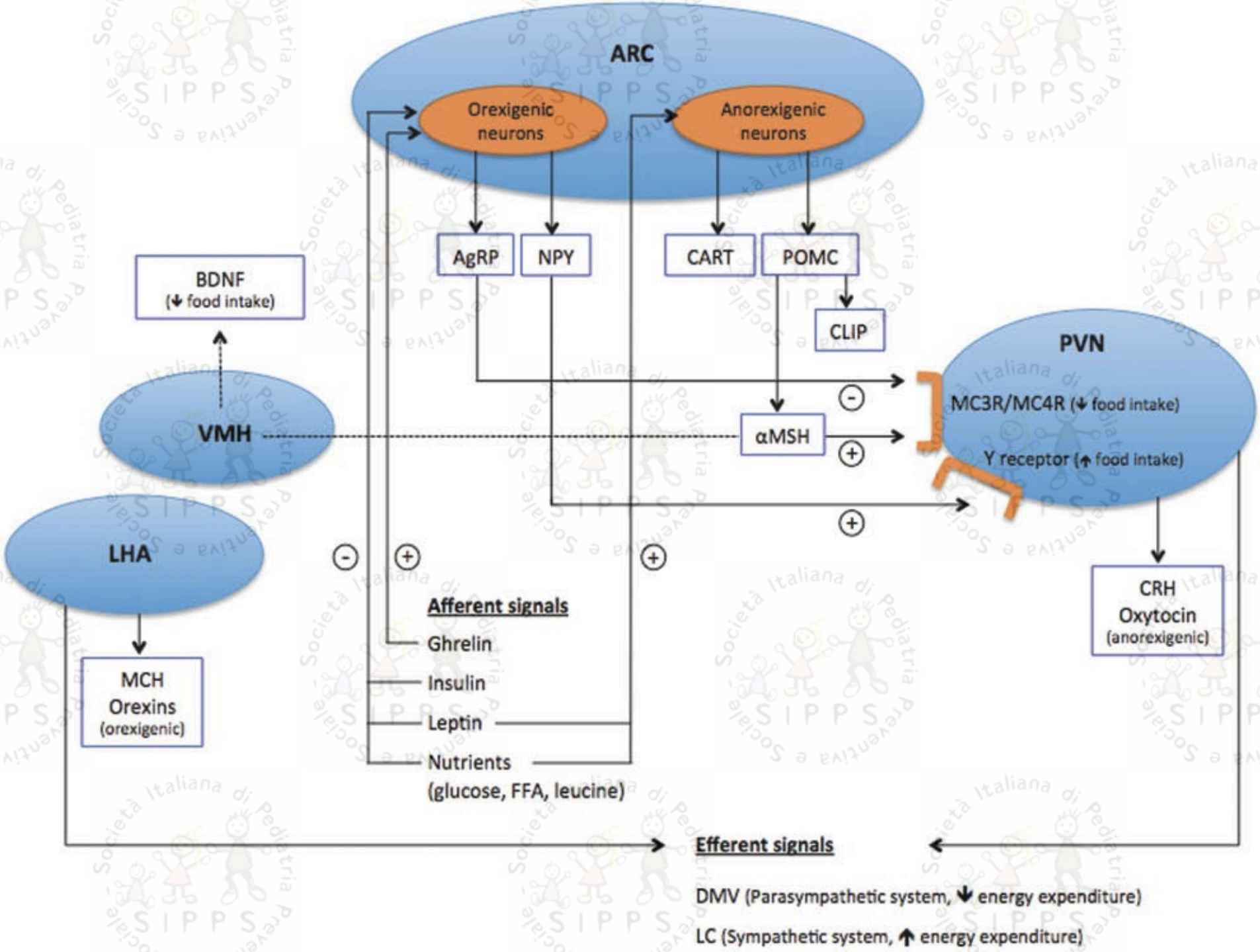
Obsogenic enviroment

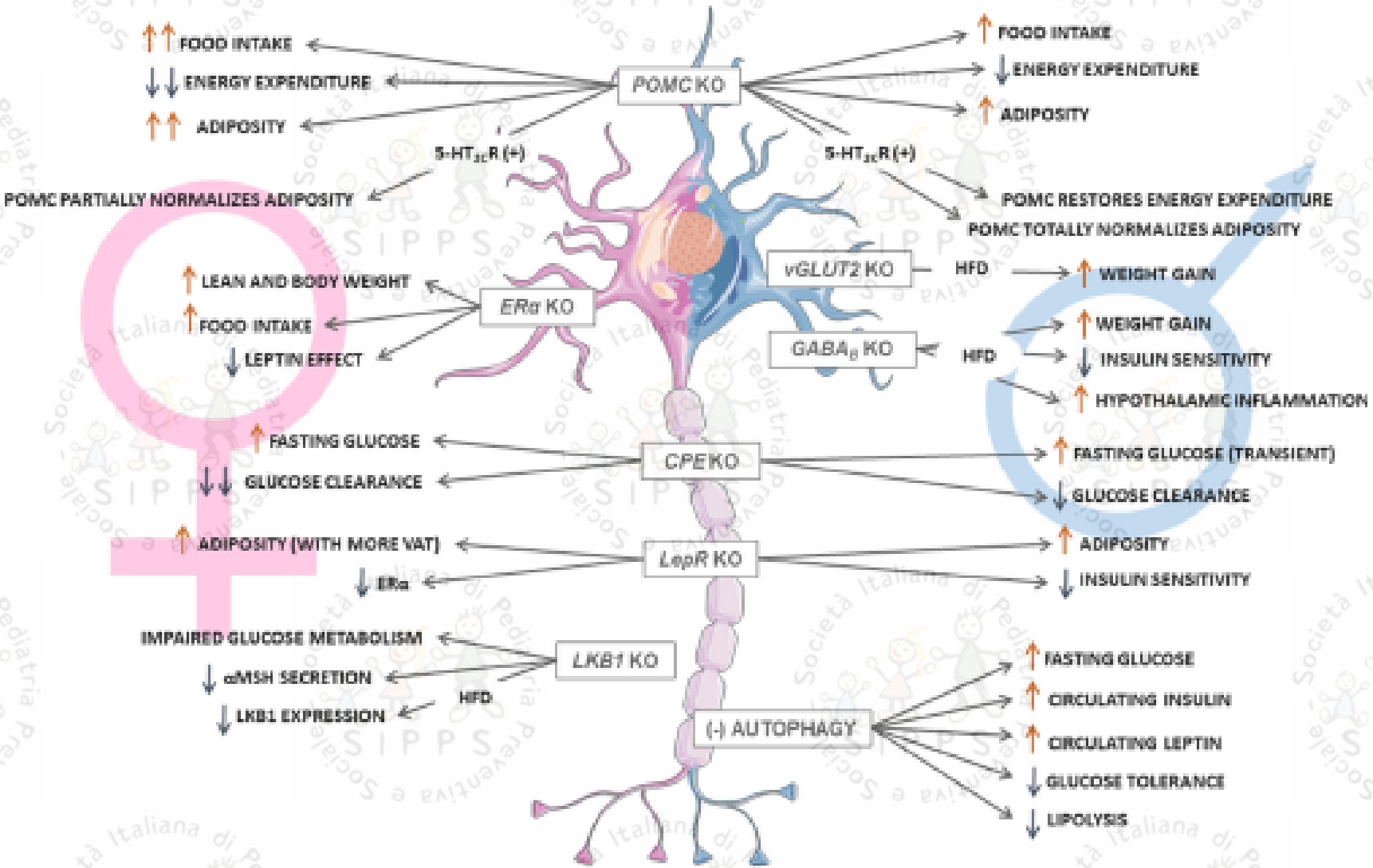
Sistema di regolazione del bilancio energetico e dell'appetito


XX
XY
GENES
Hypothalamic Circuits
WEIGHT GAIN
Adipose Tissue
SEX STEROIDS
XX
XY

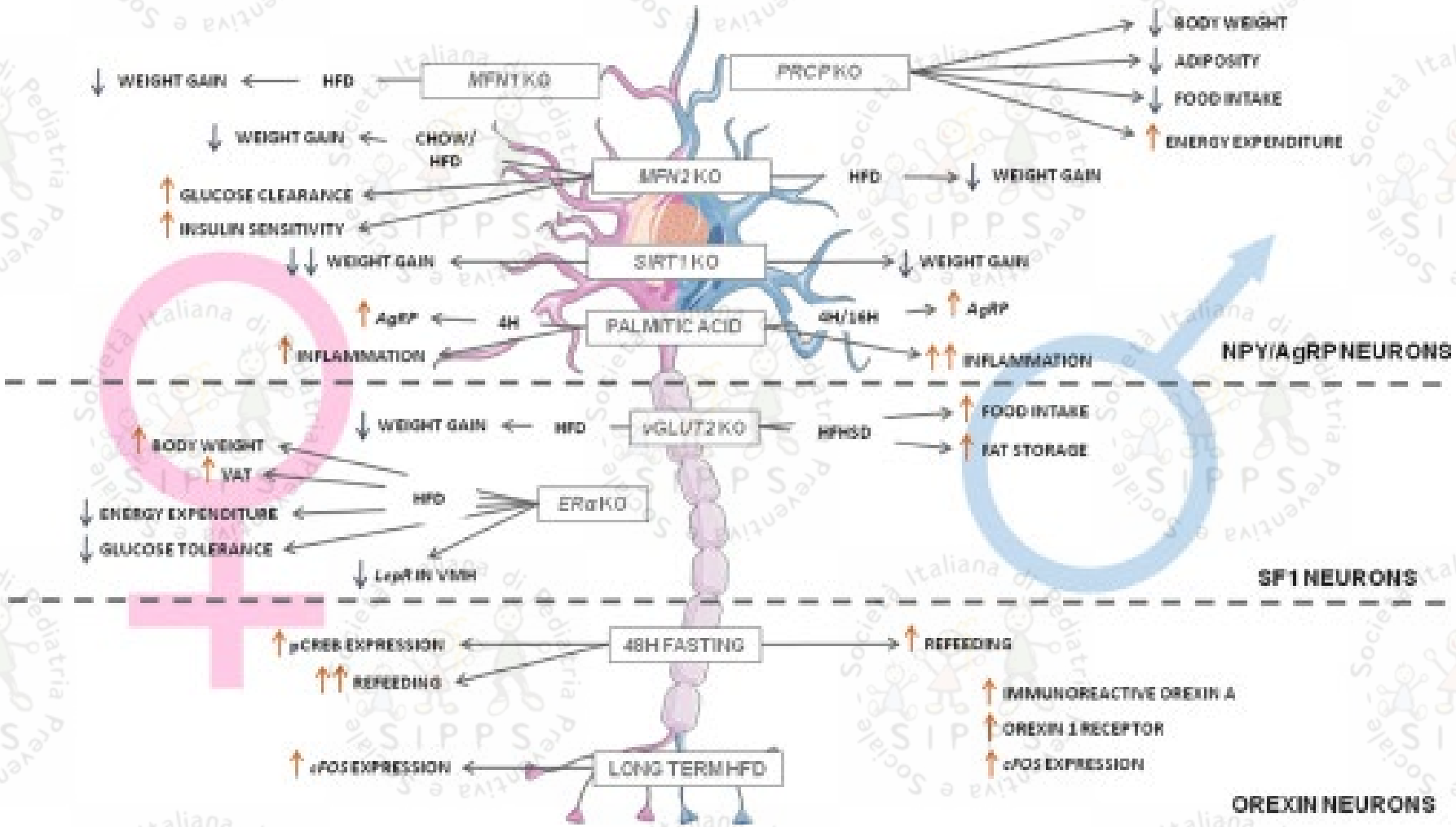

"Hedonic obesity"
ELEVATED BODY WEIGHT ABOVE SET-POINT
Hedonic signal to sustain "overeating" despite metabolic abundance
"Metabolic obesity"
NEW SET-POINT BODY WEIGHT
Temporarily elevated body weight
Metabolic signal to reduce food intake
Weight gain
"Adaptive changes"
Energy expenditure
Elevation of set-point
SET-POINT BODY WEIGHT
Metabolic signal to increase food intake
Weight loss
"Adaptive changes"
Energy expenditure
Temporarily reduced body weight
Hedonic mechanisms: driven by "pleasure", i.e., eating to satisfy reward/ punishment balance
Homeostatic circuits: to defend set-point body weight, i.e., metabolic regulation to achieve energy balance


Energy demand and drive to eat
Tonic inhibition of energy intake
ENERGY INTAKE
CCK, PYY, GLP-1
Ghrelin
Resting Metabolic Rate
Leptin and other adipokines
ENERGY BALANCE
Appetite stimulating hormones
Appetite inhibiting hormones
Gastrointestinal Tract
Fat-Free Mass
Fat Mass
Tonic appetite signals
ENERGY EXPENDITURE
Exercise
Acute and long-term effects


ARC
Orexigenic neurons
Anorexigenic neurons
AgRP
NPY
CART
POMC
CLIP
BDNF
(↓ food intake)
VMH
αMSH
PVN
MC3R/MC4R (↓ food intake)
Y receptor (↑ food intake)
LHA
MCH
Orexins
(orexigenic)
CRH
Oxytocin
(anorexigenic)
Afferent signals
Ghrelin
Insulin
Leptin
Nutrients
(glucose, FFA, leucine)
Efferent signals
DMV (Parasympathetic system, ↓ energy expenditure)
LC (Sympathetic system, ↑ energy expenditure)



Chowen, J.A., Progress in Neurobiology, https://doi.org/10.1016/j.pneurobio.2018.09.001



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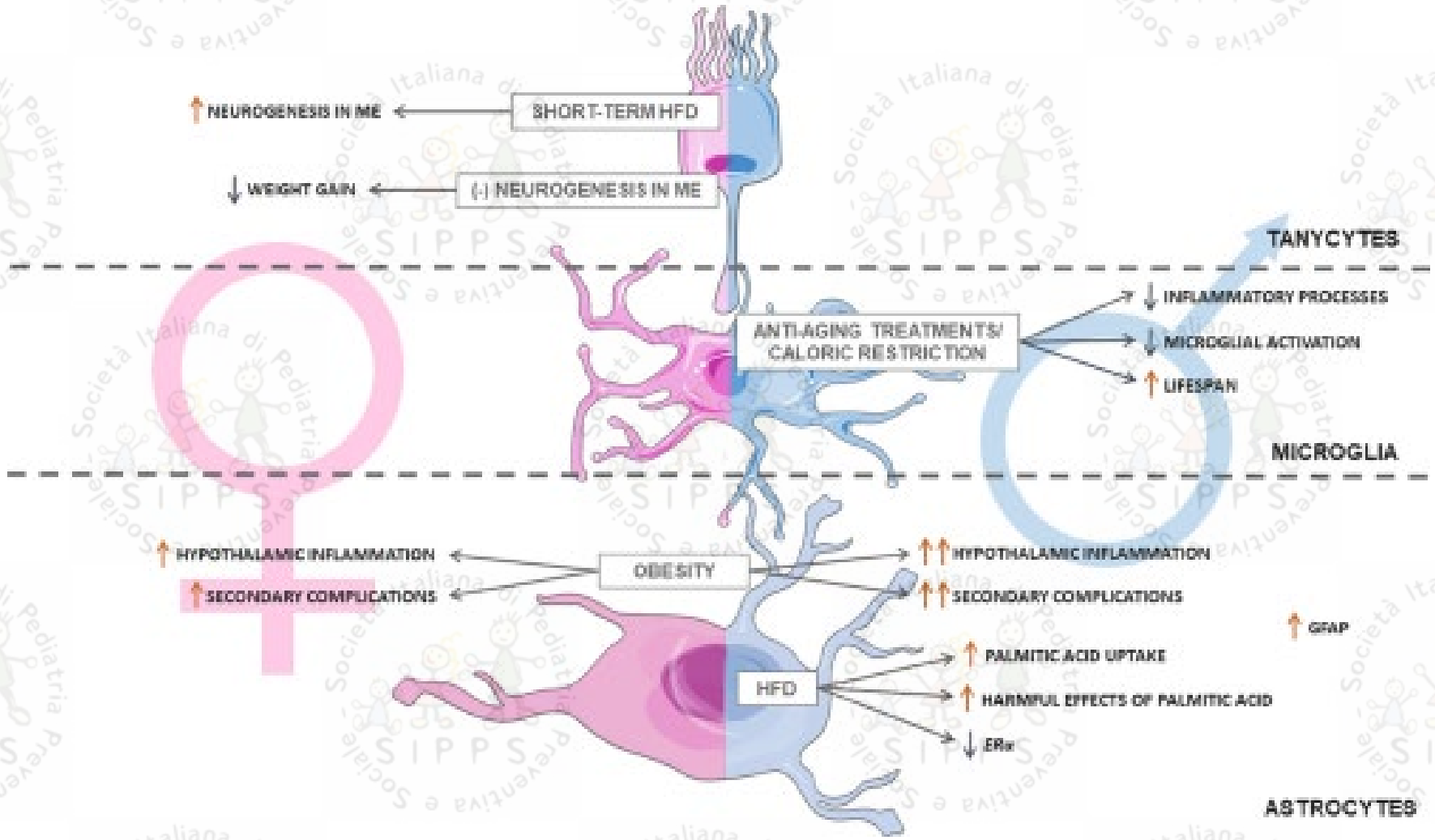


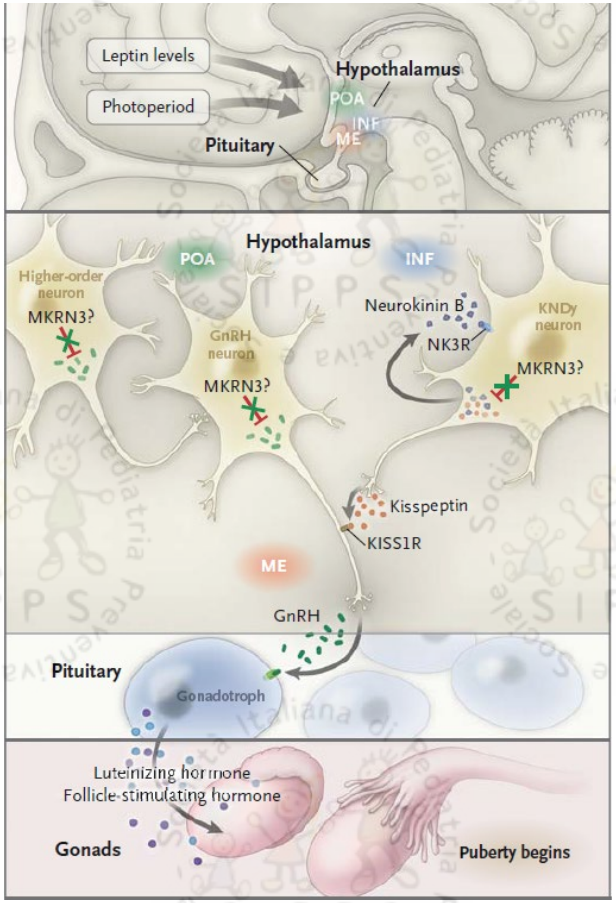
Chowen, J.A., Progress in Neurobiology, https://doi.org/10.1016/j.pneurobio.2018.09.001

OBESITA' E SVILUPPO PUBERALE

- Fattori genetici (familiari, etnici,di genere) 70-80%
- Condizioni intrauterine

- **Fattori ambientali (clima,ciclo luce/buio, fattori inquinanti)**
- **Stato Nutrizionale (peso, BMI)**

- Condizioni di salute
- Stress



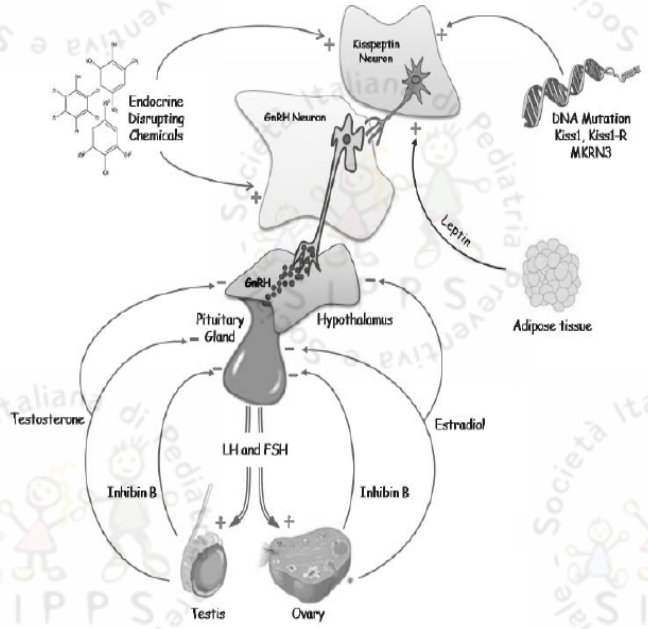
IPOTESI SUI MOTIVI DELL'ANTICIPO PUBERALE

- Aumento della prevalenza di obesità nella popolazione infantile

  Kaplowitz PB, Pediatrics 2008

  Midyett LK et al, Pediatrics 2003

  Chumlea WC et al, Pediatrics 2003



- Inquinanti ambientali → Endocrine disruptors

  Vasiliu O et al, Hum Reprod 2004

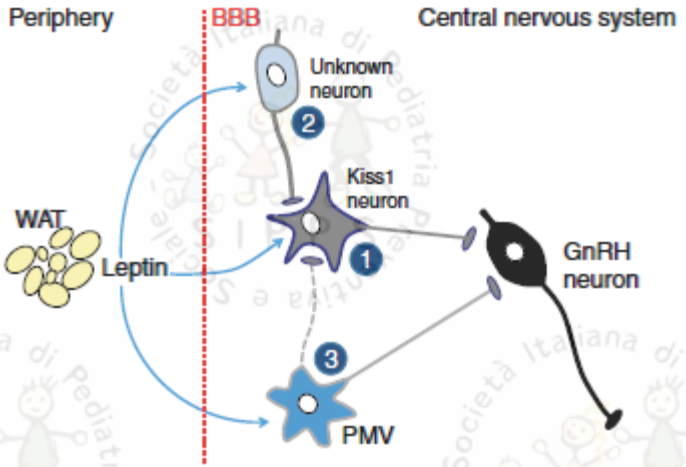
Blanck HM et al, Epidemiology 2004

Chou YY et al, J Pediatr Endocrinol Metab 2009

- Fattori psicosociali stressanti
- Inquinanti psichici : eccesso di stimoli sessuali dall'ambiente (televisione, etcc..)

TESSUTO ADIPOSO E PUBERTA' PRECOCE

- Aumentata conversione di androgeni in estrogeni
- Insulino resistenza e aumentata biodisponibilità di steroidi sessuali
- Aumentata produzione di adipokine : leptina



Dati auxologici in pazienti con sospetta pubertà precoce

GRUPPI	N°	E.C. (m±DS)	Δ E.O. (m±DS)	ALTEZZA SDS (m±DS)	BMI SDS (m±DS)	TARGET SDS(m±DS)
TPI < 2.5 aa	22	1.5 ± 1.2		0.0 ± 0.8	-0.4 ± 1	-1.1 ± 1.8
TPI	26	7.1 ± 1.2	0.6 ± 0.9	0.6 ± 1.0	0.9 ± 1.3	-0.7 ± 0.8
PPI	43	7.1 ± 0.9	0.9 ± 1	0.9 ± 1.0	2.9 ± 2.3	-0.5 ± 0.9
PA	17	8.3 ± 1.2	1.2 ± 0.8	1.2 ± 1.0	2.2 ± 2.4	-0.8 ± 0.7
PP	35	7.7 ± 0.7	2.2. ± 1	1.4 ± 1.0	2.2 ± 1.6	-0.7 ± 0.8

PAZIENTI CON COMPARSA ANTICIPATA DEI CARATTERI SESSUALI

DIAGNOSI NELLE FEMMINE

- N° 10 Pubarca prematuro isolato
- N° 15 Telarca prematuro isolato
- N° 10 Pubertà precoce gonadotropino-dipendente
  (9 idiopatiche, 1 displasia setto-ottica)

DIAGNOSI NEI MASCHI

- N° 1 Pubarca prematuro isolato
- N° 2 Pubertà anticipata
- N° 1 Pubertà precoce gonadotropino-indipendente da SAG
- N° 4 Pubertà precoce gonadotropino-dipendente
  (2 idiopatiche, 1 amartoma ipotalamico, 1 associata a S. di Williams)

ENDOCRINE DISRUPTORS E PUBERTA' PRECOCE

- ED naturali: fitoestrogeni
- ED chimici: BPBs; PCBs; DDT; DDE; PCB; Diossina; Ftalati

Possono agire: legandosi ai recettori degli ormoni, interferendo con la sintesi degli steroidi, direttamente sul SNC

Influenzano negativamente lo sviluppo e/o il funzionamento del sistema endocrino

- ✓ Azione **estrogenica** o antiestrogenica
- ✓ Azione androgenica o **antiandrogenica**
- ✓ Interferenza con il GnRH

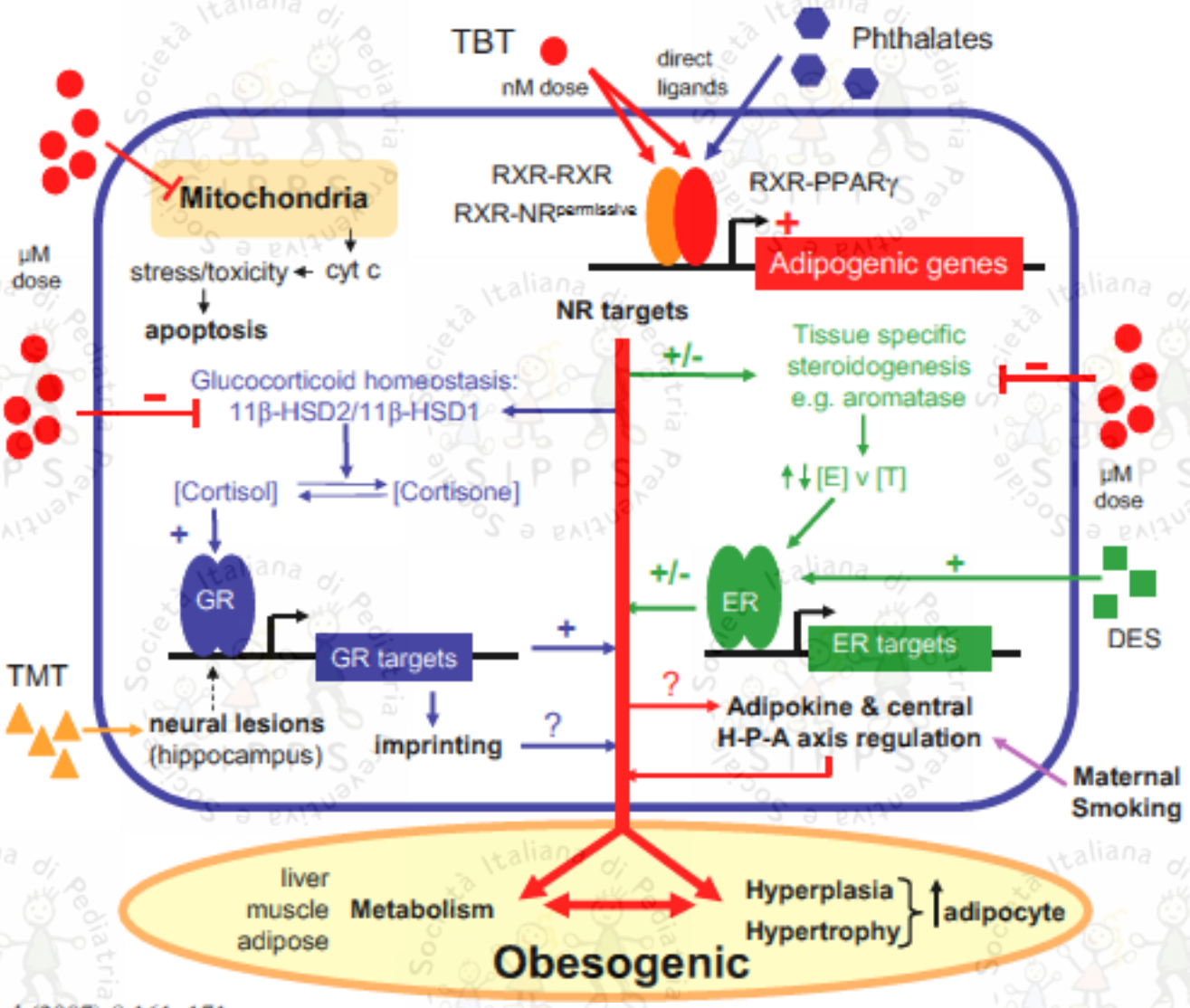
ENDOCRINE DISRUPTORS E OBESITA'

- ED naturali: fitoestrogeni
- ED chimici: BPBs; PCBs; DDT; DDE; PCB; Diossina; Ftalati

Possono agire: legandosi ai recettori degli ormoni, interferendo con la sintesi degli steroidi, direttamente sul SNC

- ✓ Reclutamento e differenziazione degli adipociti
- ✓ Accumulo di trigliceridi negli adipociti /dimensione degli adipociti
- ✓ Alterazione rapporto prolif./distruzione adipociti
- ✓ Influenzano MR ed equilibrio energetico

Perturbed nuclear receptor signaling by environmental obesogens as emerging factors in the obesity crisis



Rev Endocr Metab Disord (2007) 8:161–171
DOI 10.1007/s11154-007-9049-x

Journal of Epidemiology 27 (2017) 228–234

Contents lists available at ScienceDirect

Journal of Epidemiology

journal homepage: http://www.journals.elsevier.com/journal-of-epidemiology/

Original Article

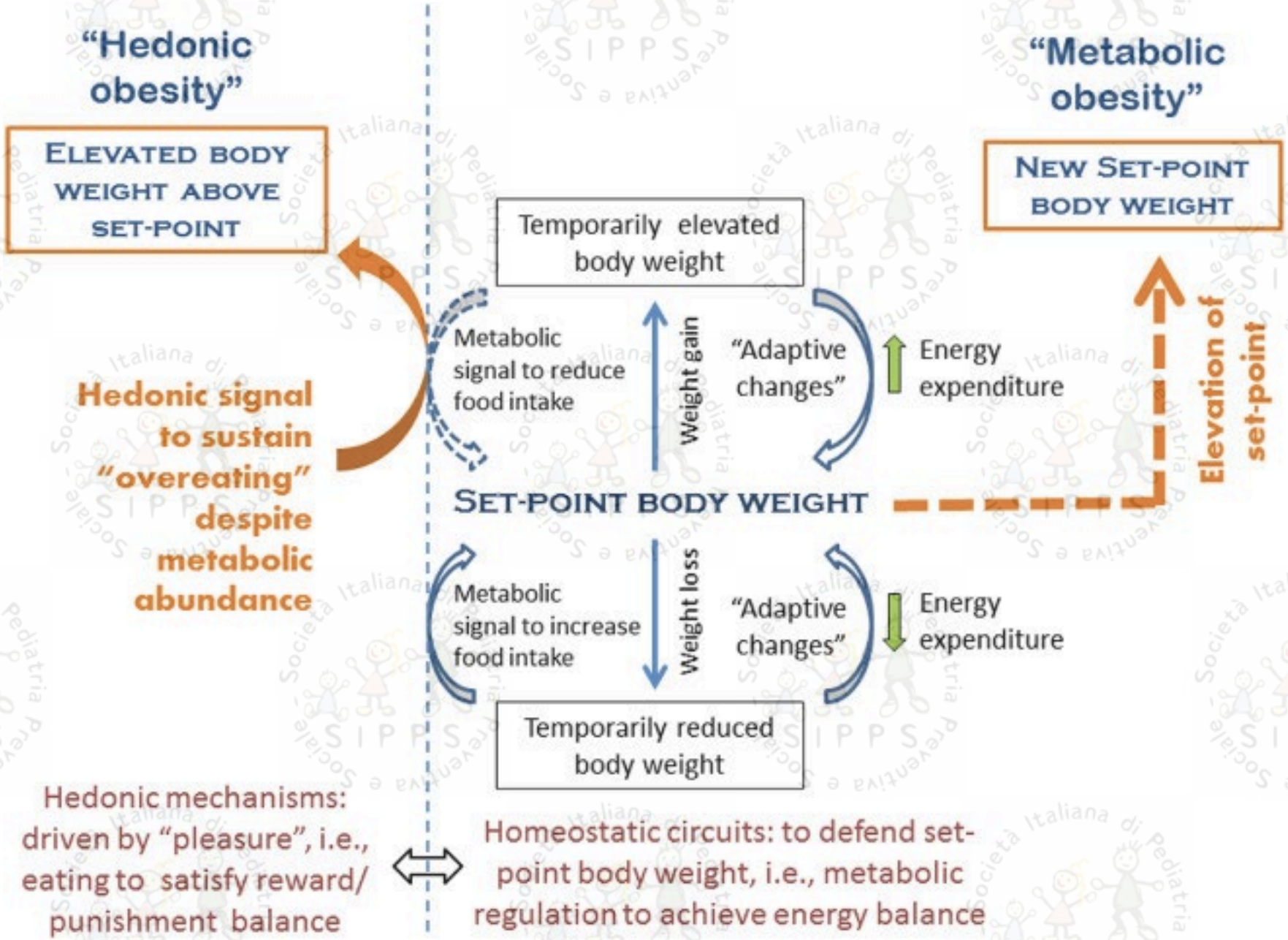
Gender differences in the associations between urinary bisphenol A and body composition among American children: The National Health and Nutrition Examination Survey, 2003–2006

Ji Li [a], Hong Lai [b], Shaoguang Chen [a], Hong Zhu [a, c], Shenghan Lai [a, b, d, *]

Background: As an endocrine disruptor, bisphenol A (BPA) exposure has been implicated as a potential risk factor in childhood obesity, which is defined using percentiles of body mass index for age. We aimed to examine the associations between BPA exposure, reflected by urinary BPA concentration, and body composition in American children.

Methods: Data of 1860 children aged 8–19 years who participated in the 2003–2006 National Health and Nutrition Examination Survey (NHANES) were analyzed in this study. Urinary BPA concentration (ng/mL) was used to indicate BPA status in the body. Body composition was measured by dual-energy X-ray absorptiometry (DXA). Multivariate linear regression models were fitted using survey procedures to investigate the associations between urinary BPA level and body composition separately for boys and girls.

Conclusions: Higher BPA levels may be associated with elevated LBM in boys, but not in girls, while higher BPA levels may be associated with elevated FM in girls, but not in boys.


"Hedonic obesity"
ELEVATED BODY WEIGHT ABOVE SET-POINT
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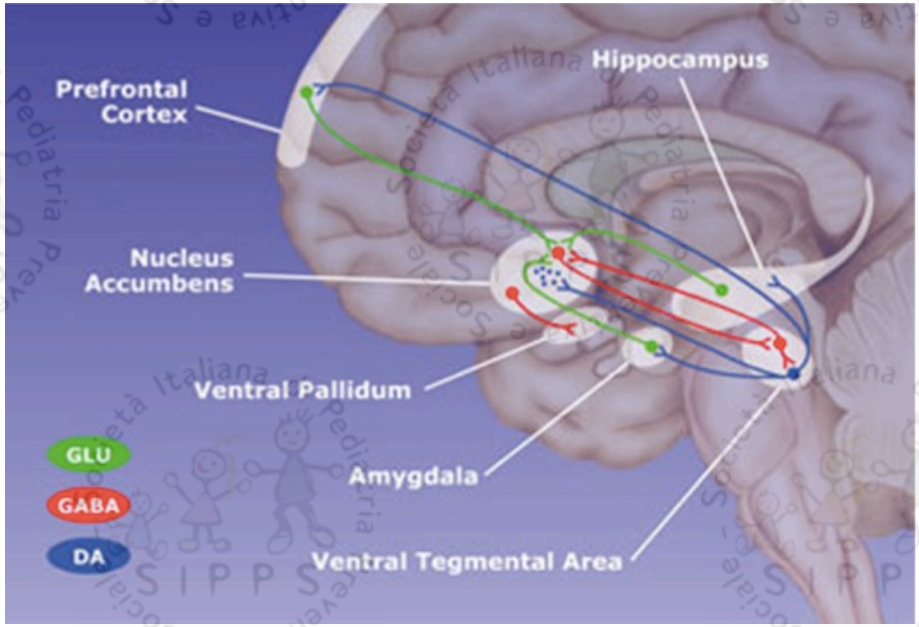
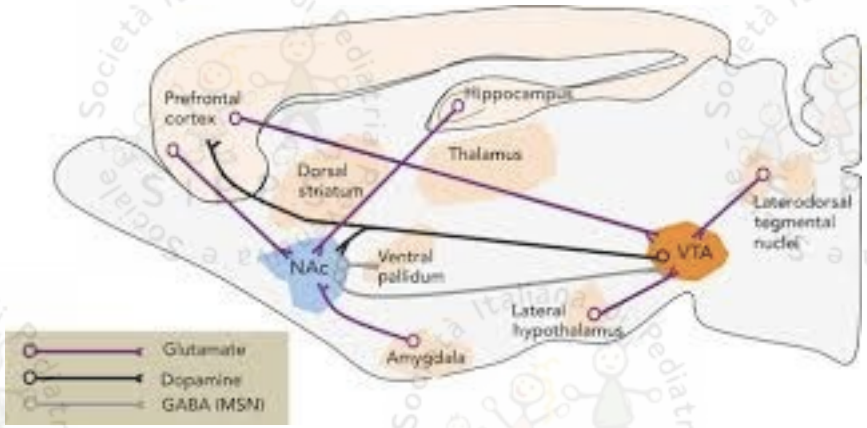
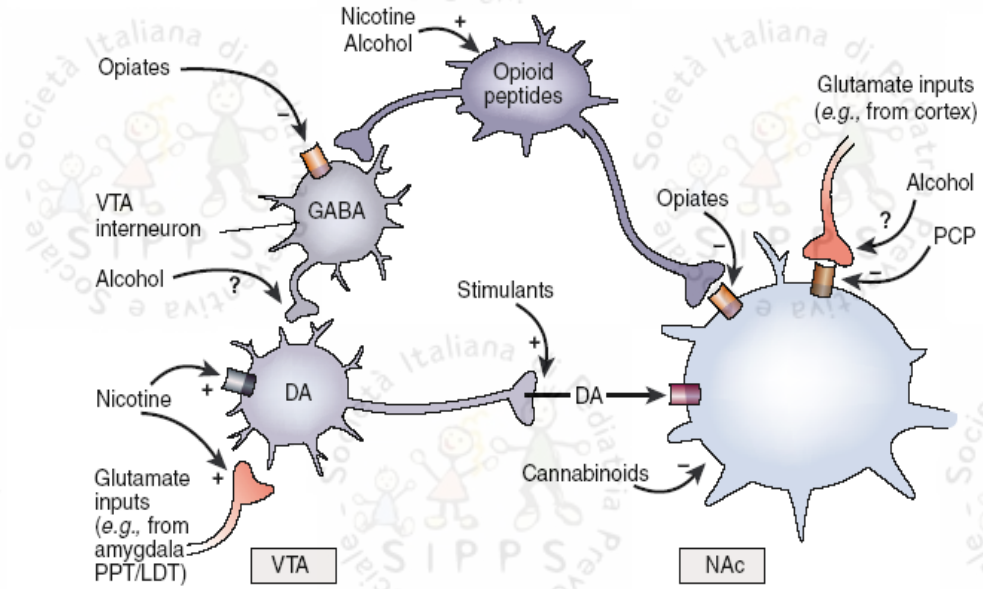
Hedonic mechanisms: driven by "pleasure", i.e., eating to satisfy reward/ punishment balance
Homeostatic circuits: to defend set-point body weight, i.e., metabolic regulation to achieve energy balance

Il "palatable food" attiva il sistema dopaminergico mesolimbico (dall'area ventrale del tegmento al nucleo accumbens)







Addiction Biology

SSA SOCIETY FOR THE STUDY OF ADDICTION

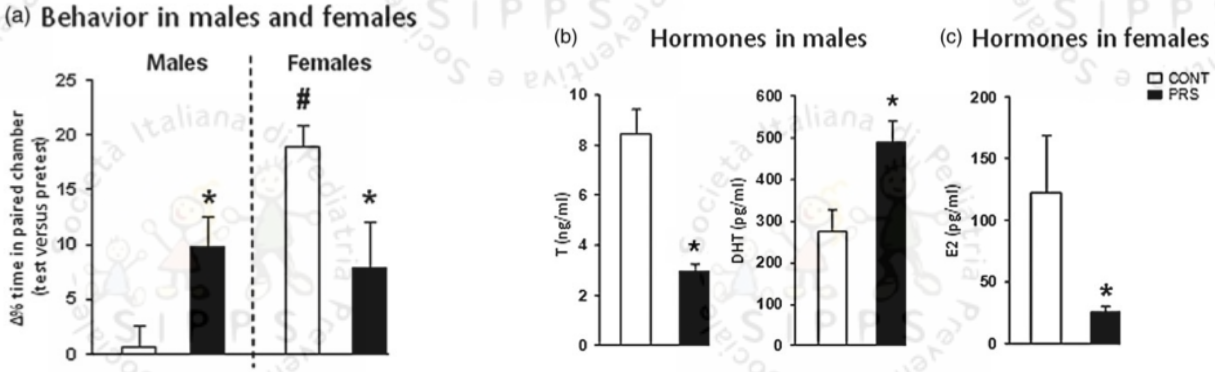
PRECLINICAL STUDY

doi:10.1111/adb.12270

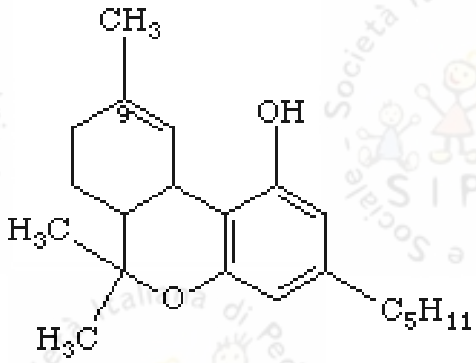
Hedonic sensitivity to natural rewards is affected by prenatal stress in a sex-dependent manner

Marie-Line Reynaert[1,2], Jordan Marrocco[3], Jérôme Mairesse[1,2], Luana Lionetto[4], Maurizio Simmaco[4], Lucie Deruyter[1,2], Delphine Allorge[5], Anna Moles[6,7], Anna Pittaluga[8], Stefania Maccari[1,2], Sara Morley-Fletcher[1,2], Gilles Van Camp[1,2]* & Ferdinando Nicoletti[1,2]*

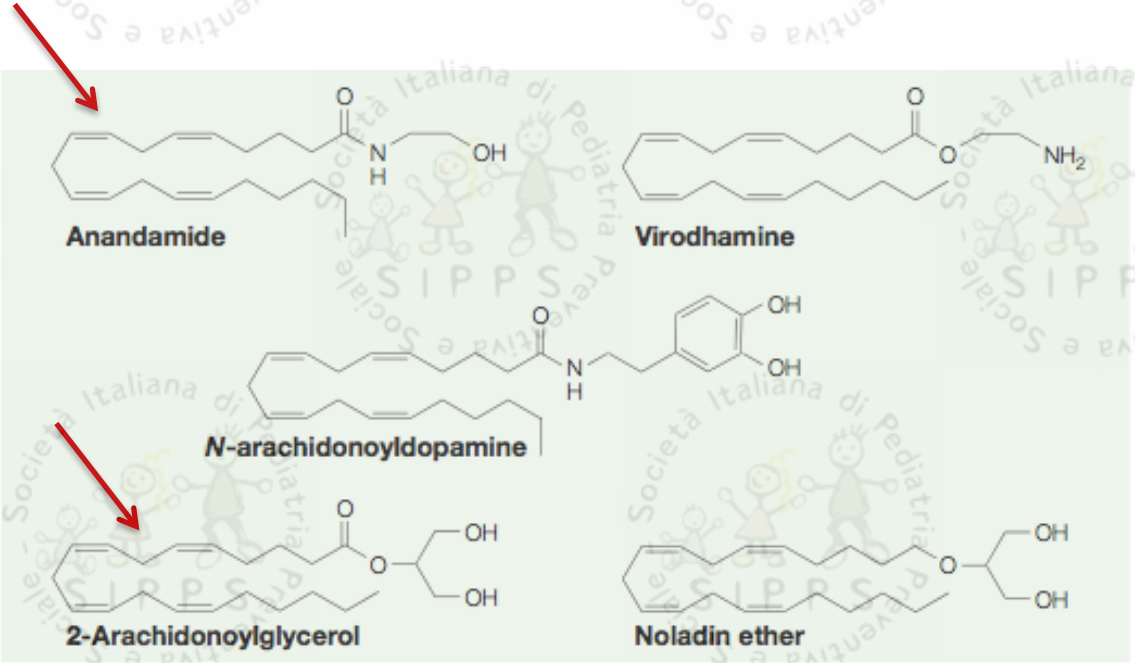
Le femmine hanno una maggiore sensibilità edonica nei confronti del « palatable food » rispetto ai maschi. Le differenze sono annullate dallo stress perinatale che aumenta il DHT nei maschi e riduce l'E2 nelle femmine

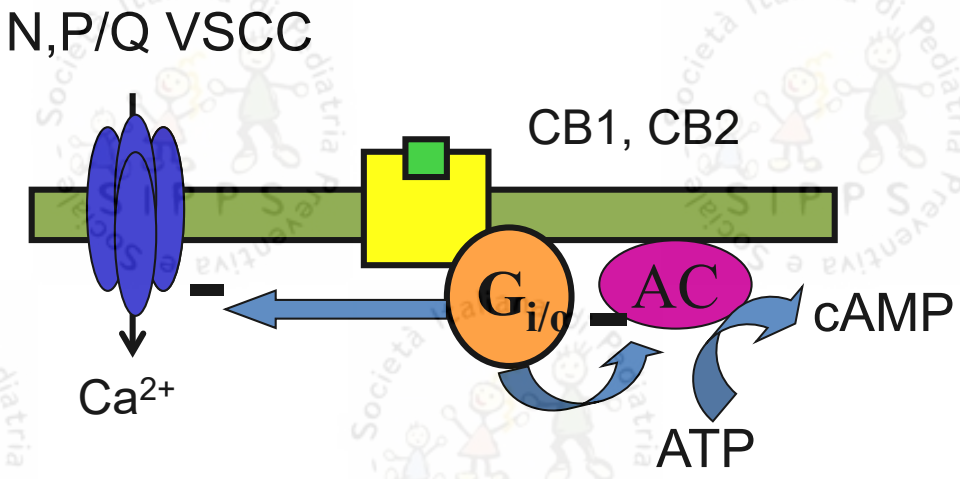


I recettori CB1 sono attivati dagli endocannabinoidi



Δ^9-tetraidrocannabinolo (THC)





The CB1 receptor as the cornerstone of exostasis

(Piazza, Cota, and Marsicano, Neuron, 2017)

NeuroImage 184 (2019) 834–842

Contents lists available at ScienceDirect

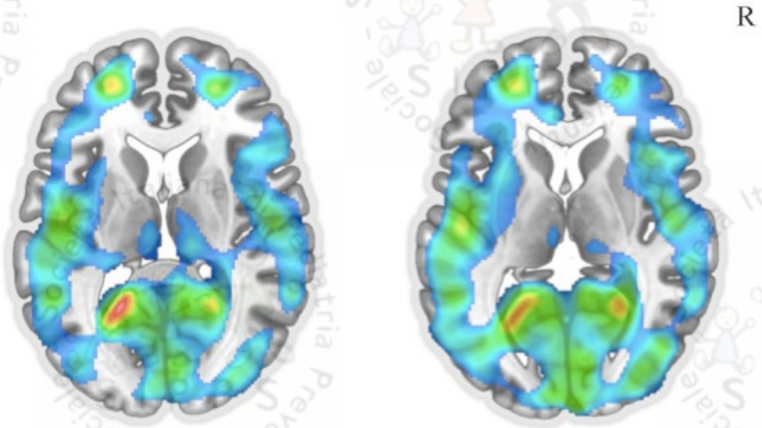
NeuroImage

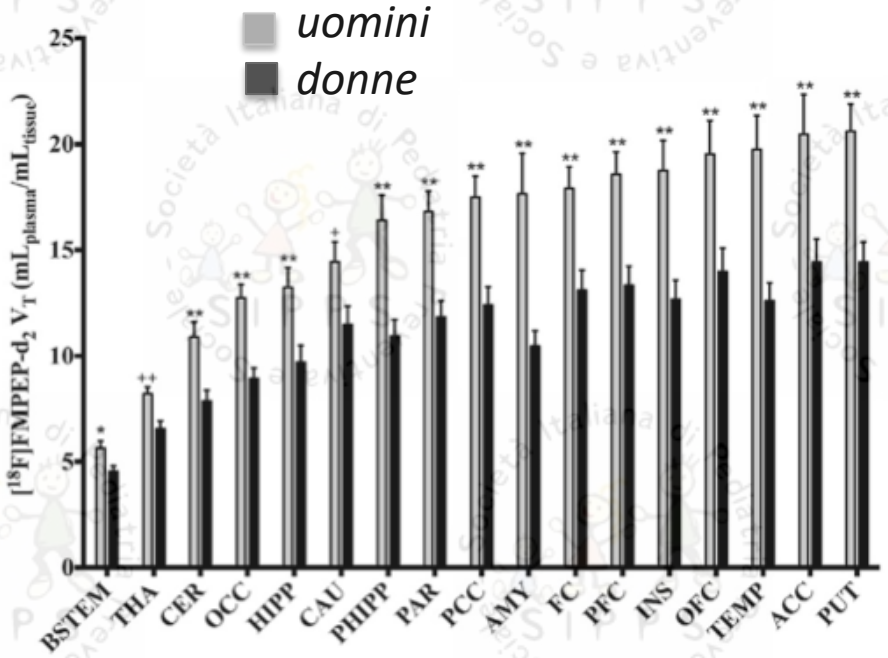
journal homepage: www.elsevier.com/locate/neuroimage

Sex difference in brain CB1 receptor availability in man

Heikki Laurikainen [a,b], Lauri Tuominen [a,b,e], Maria Tikka [b], Harri Merisaari [a], Reetta-Liina Armio [a,b], Elina Sormunen [a,b], Faith Borgan [c], Mattia Veronese [d], Oliver Howes [c], Merja Haaparanta-Solin [a], Olof Solin [a], Jarmo Hietala [a,b,*], METSY group

Maggiore densità dei recettori CB1 nel SNC dell'uomo rispetto alla donna





Hormonal Milieu/ Nutrition / Enviroment (EDC obesogeni)

Developmental Critical Periods

(Gestation, Neonatal, etc….)

Hypothalamic Circuits

Homeostatic Control of Metabolism

Obesity