

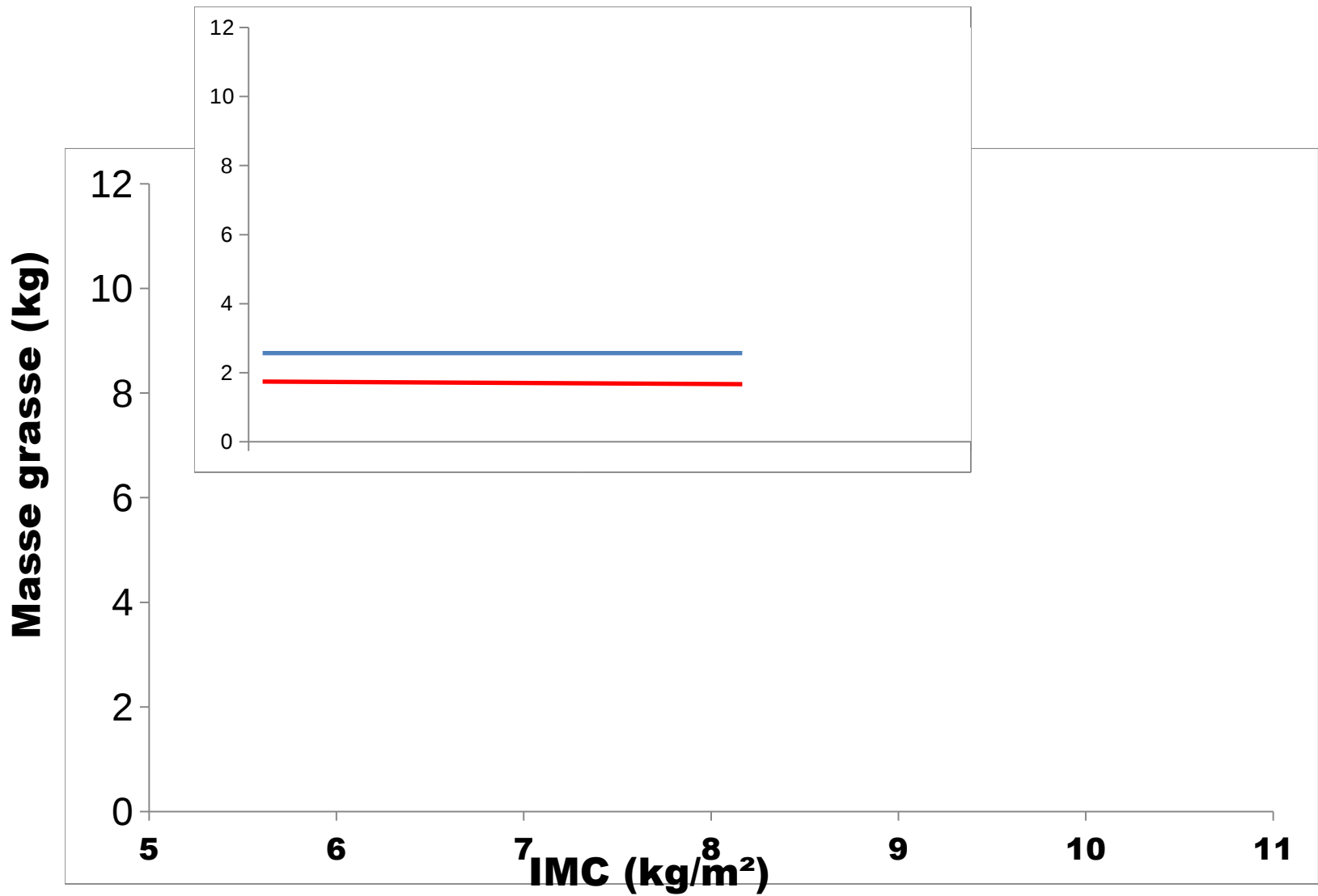


Existe t'il un seuil critique de masse grasse?

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The limit of human adaptation to starvation

STEVE COLLINS

Concern Worldwide, Camden Street, Dublin 2, Ireland and

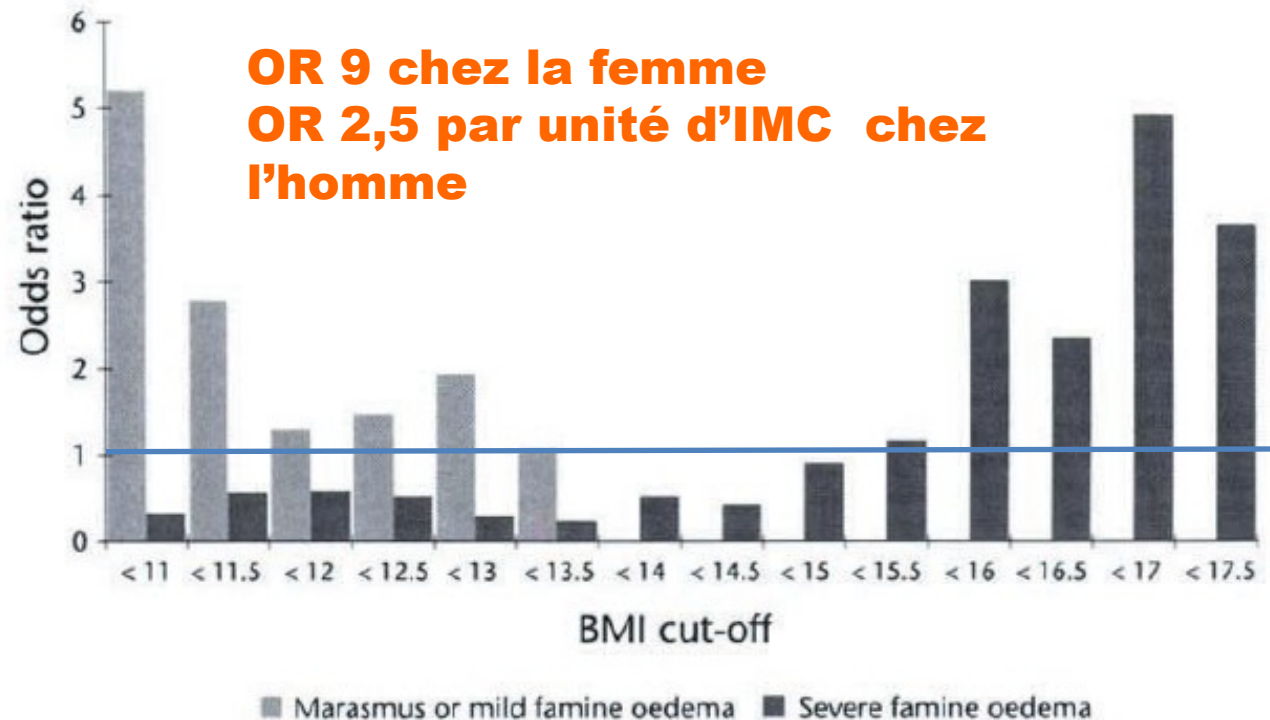


Fig. 2 The risk of mortality associated with various BMI cut-offs.

The limit of human adaptation to starvation

STEVE COLLINS

Concern Worldwide, Camden Street, Dublin 2, Ireland and

IMC les plus bas

- Observés à l'admission: **10,4** (>25 ans) **9,6** (15-24 ans)
- Compatibles avec survie: **10,1** **8,7**

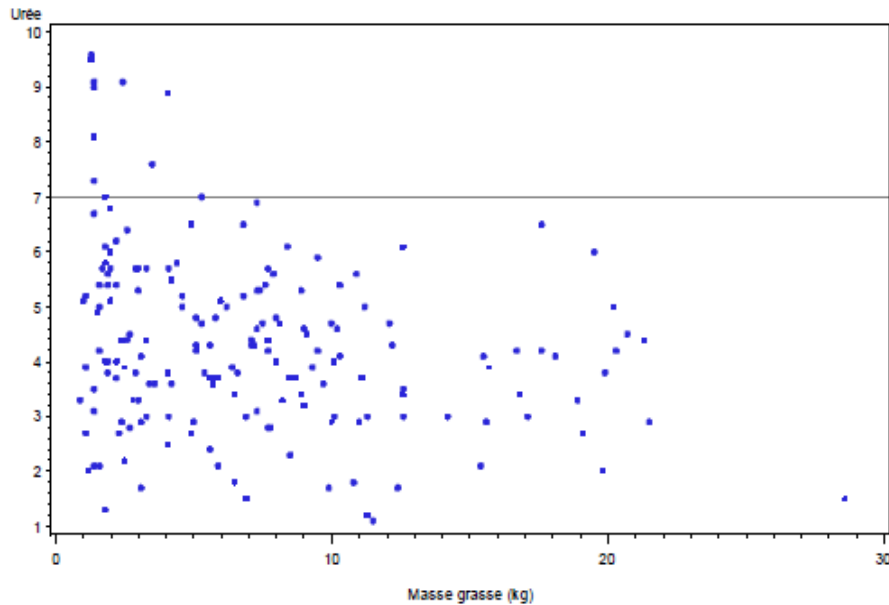
Survie si IMC <11 admission,

65%

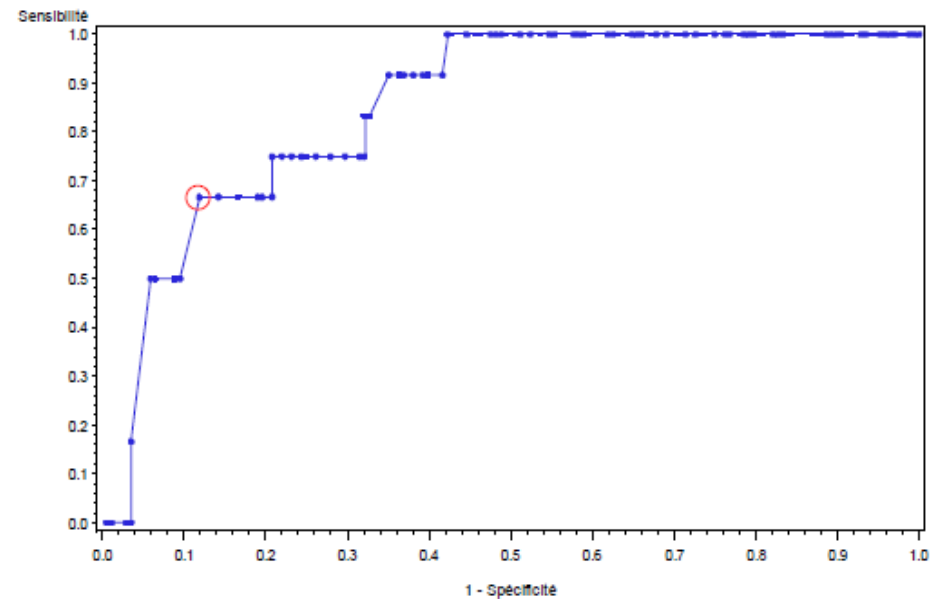
82%

Résultats: recherche de seuil de MG

Urée



ROC Curve Urée



AUC = 0.853

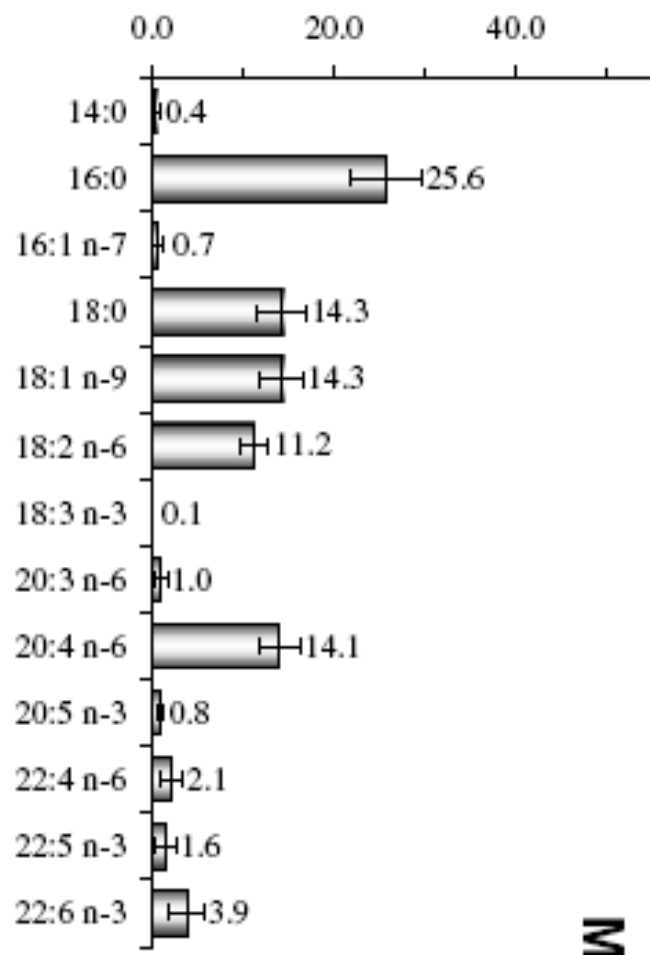
Le seuil de masse grasse ainsi calculé est de 1,8 kg. Le taux de faux positifs est de 11,9% et le taux de faux négatifs est de 33,33%

Résultats: recherche de seuil de MG

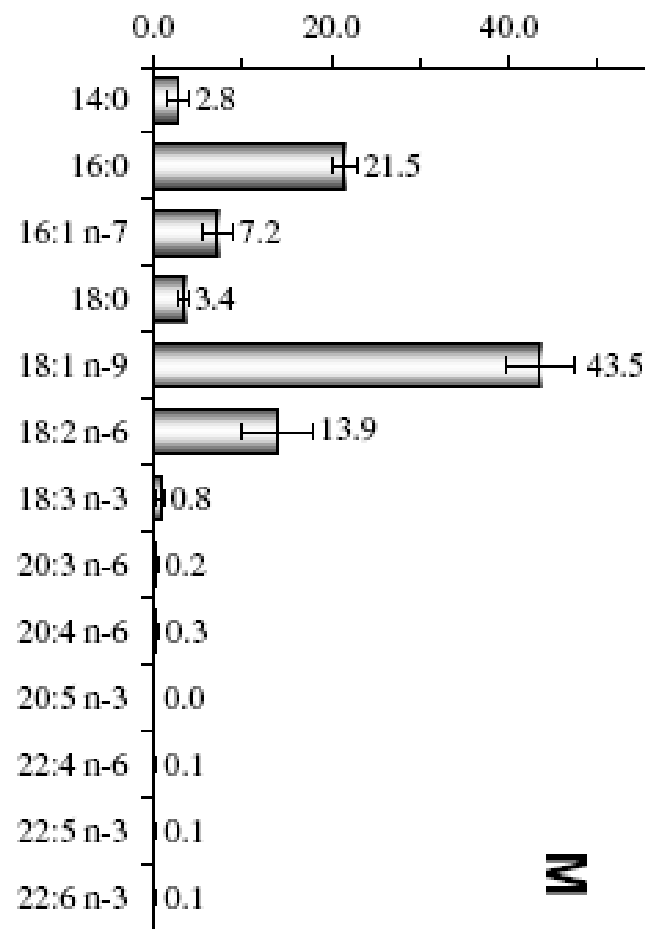
Variable	AUC	Seuil de masse grasse (kg)	Taux de vrais négatifs (%)	Taux de faux positifs (%)	Taux de vrais positifs (%)	Taux de faux négatifs (%)
Phosphore	0.790	2.5	76.00	24.00	80.00	20.00
Sodium	0.761	3.1	72.33	27.67	71.43	28.57
Calcium	0.764	2.5	77.98	22.02	75.00	25.00
Ferritine	0.752	3	72.26	27.74	70.00	30.00
Gamma GT	0.729	4.6	62.50	37.50	75.00	25.00
TGP	0.752	3	78.47	21.53	68.57	31.43
Protéines	0.732	2.5	79.14	20.86	70.59	29.41
Urée	0.853	1.8	88.10	11.90	66.67	33.33
Acide urique	0.664	3.3	73.24	26.76	63.16	36.84
Hématies	0.782	2.5	78.66	21.34	63.64	36.36
VGM	0.632	4.6	58.62	41.38	100.00	0.00
CGMHb	0.816	1.3	96.51	3.49	66.67	33.33
TGMHb	0.798	3.6	72.41	27.59	76.67	23.33
LDH	0.698	5.3	64.80	35.20	71.70	28.30

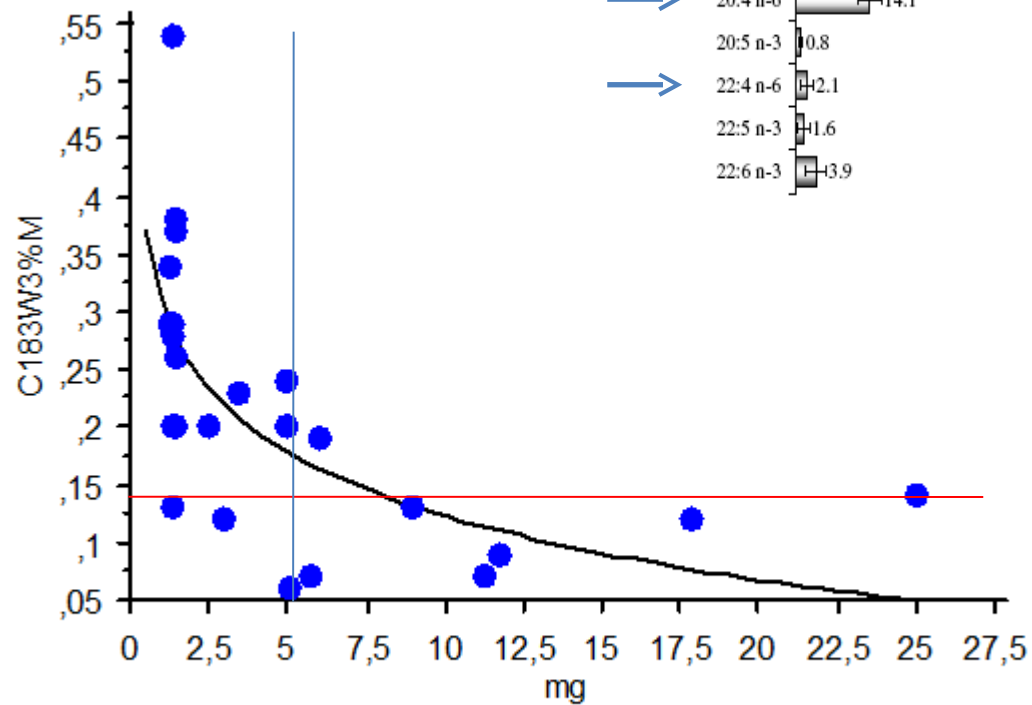
=> Seuils de MG compris entre 1,3 et 5 kg

Erythrocyte total PL (mol%)

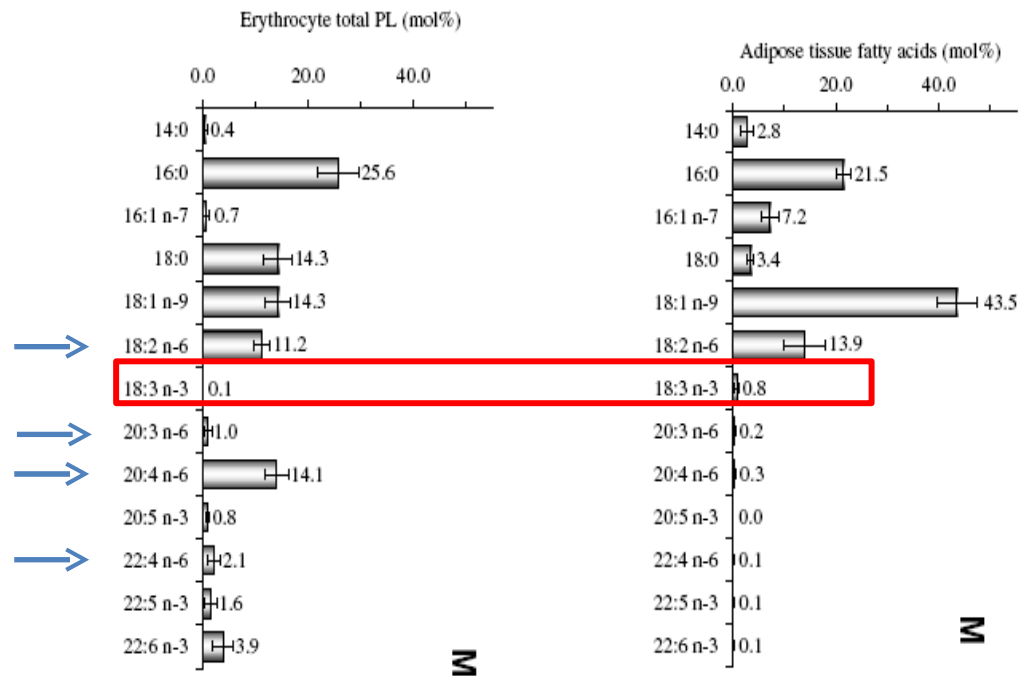


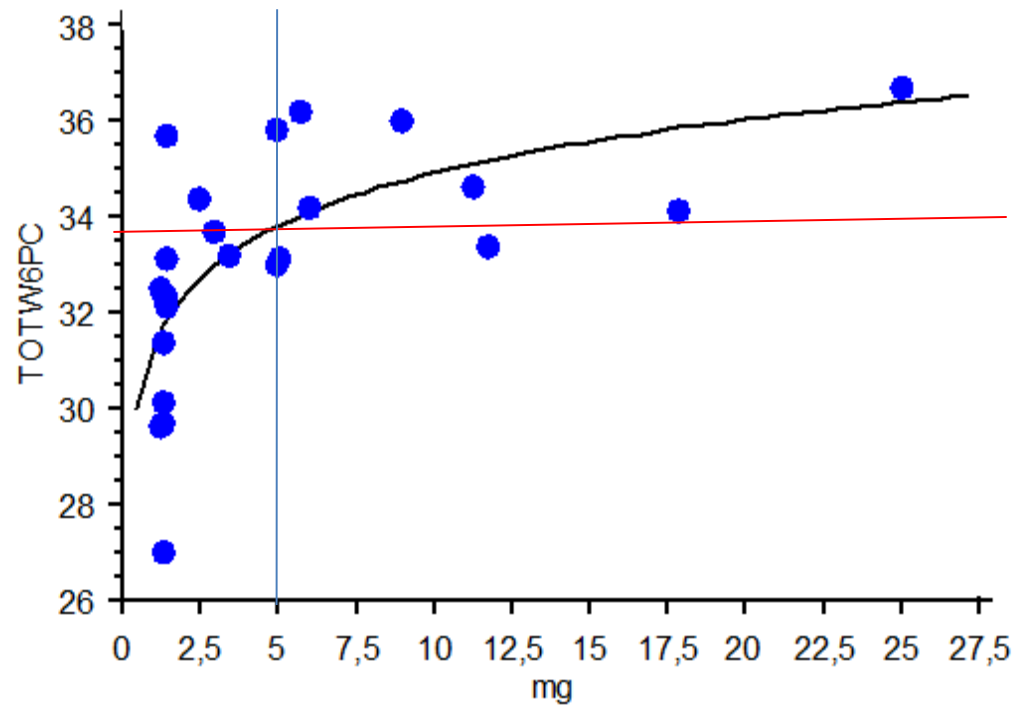
Adipose tissue fatty acids (mol%)





$$Y = ,308 - ,08 * \ln(X)$$





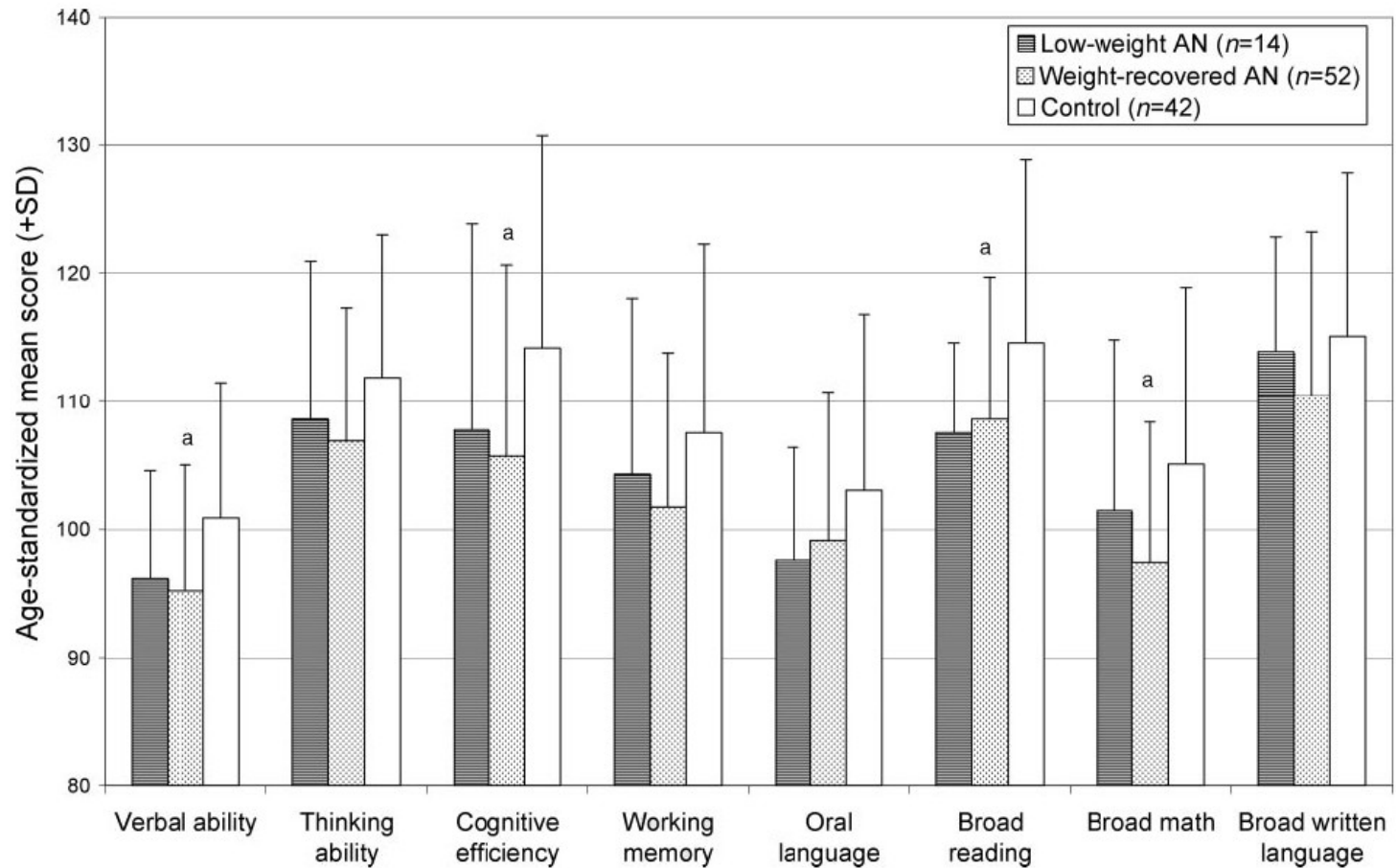
Conséquences cognitives psychologiques de l'anorexie mentale

Comparison of Regional Brain Volumes According to Weight Recovery

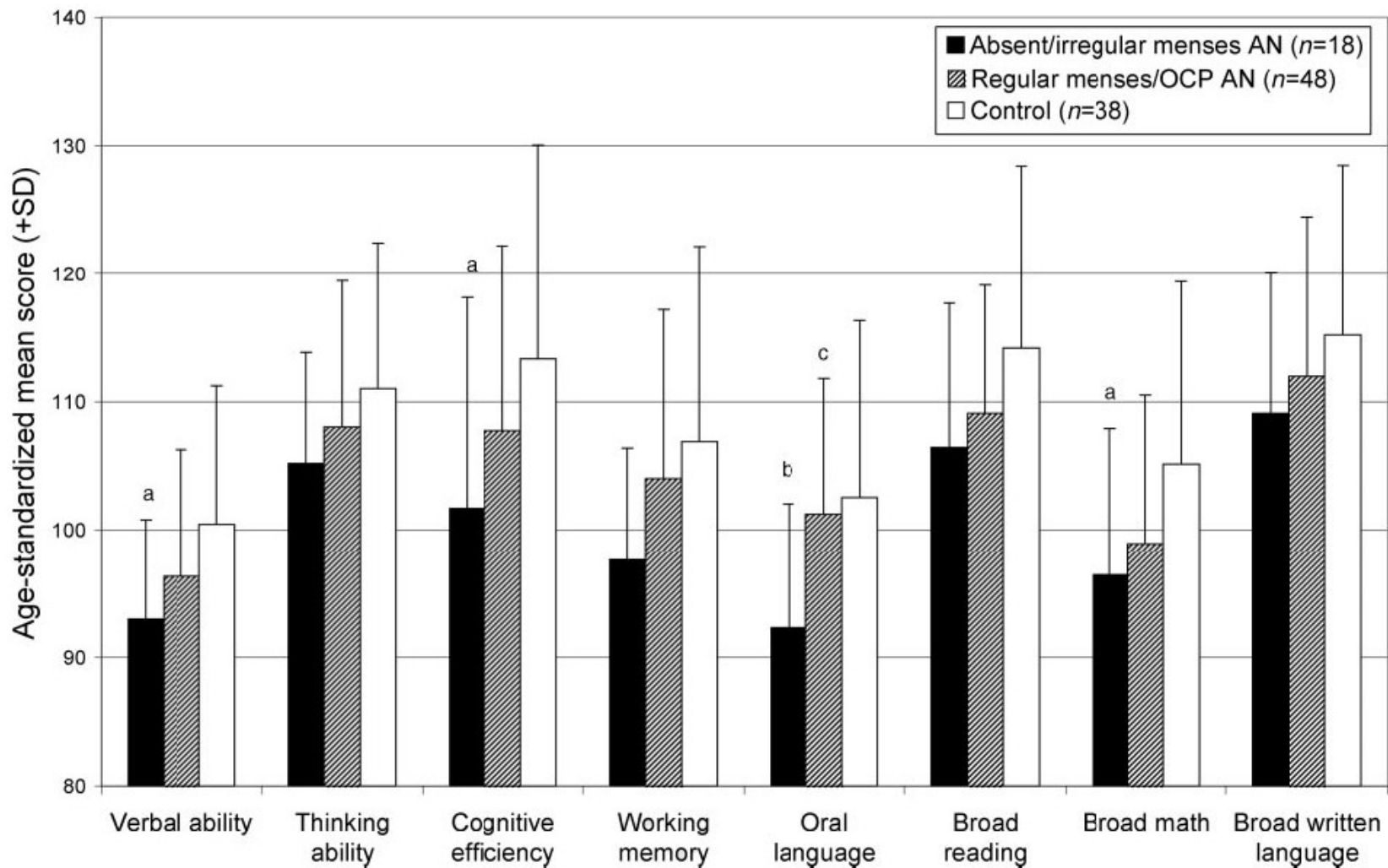
Brain Region	Mean \pm SD, Volume per mL			ANOVA, <i>P</i>
	Low-weight AN (<i>n</i> = 12)	Weight-Recovered AN (<i>n</i> = 48)	Control (<i>n</i> = 37)	
Third ventricle	2.1 \pm 0.4	2.0 \pm 0.4	1.8 \pm 0.5	.05
Lateral ventricles ^a	17.0 \pm 6.6	14.9 \pm 5.2	12.7 \pm 5.4	.04
Temporal horns ^b	3.6 \pm 1.8	3.1 \pm 0.9	2.7 \pm 0.8	.03
Hippocampi ^b	7.2 \pm 0.7	7.1 \pm 0.8	7.3 \pm 0.9	.43

Compared with control subjects, low-weight AN has greater lateral ventricle volumes (*P* = .05), and temporal horn volumes (*P* = .03)

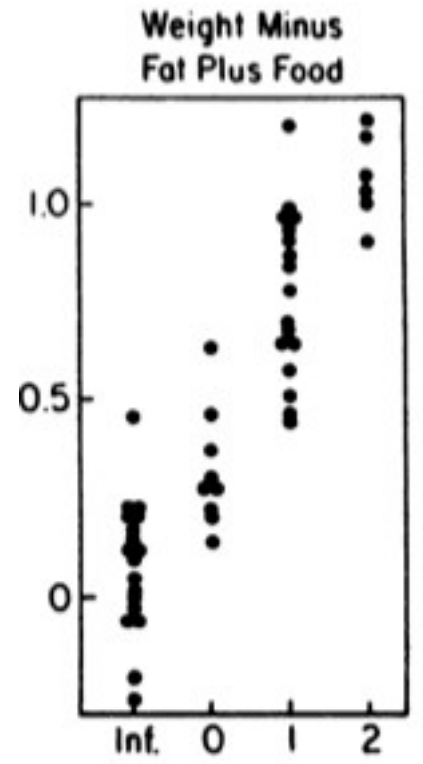
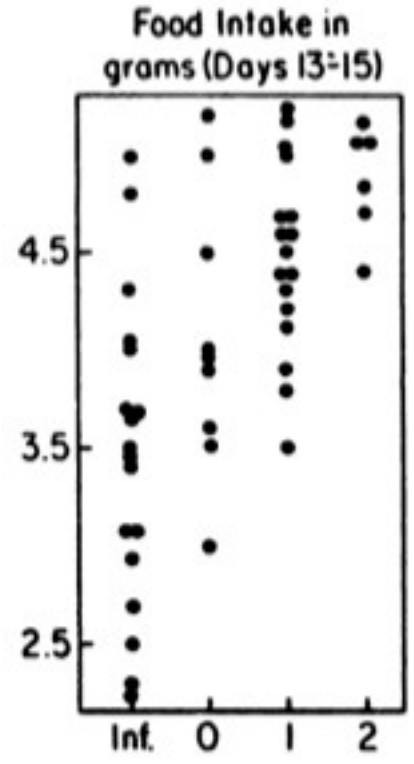
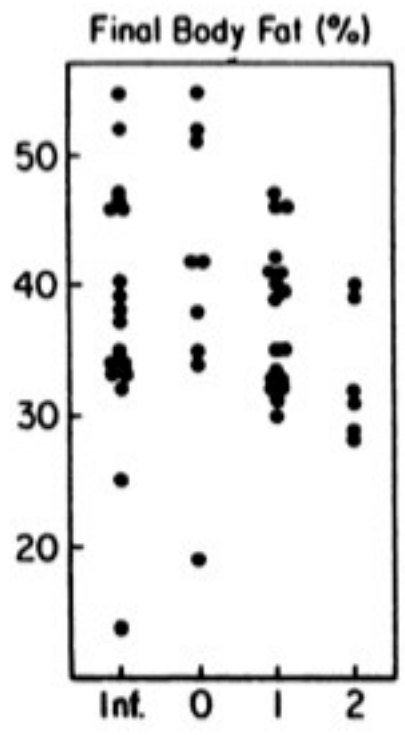
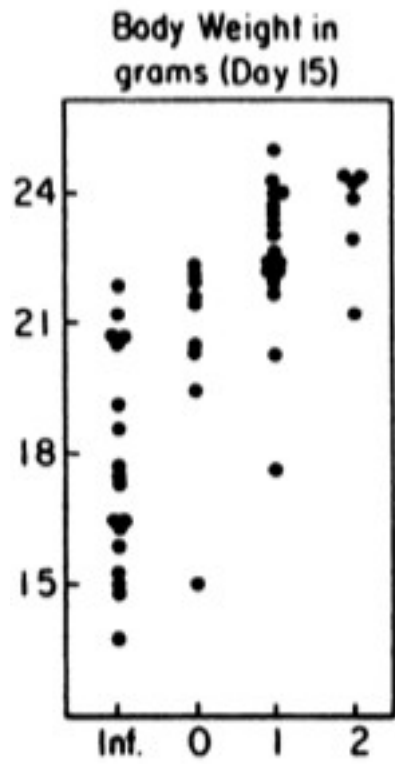
Volumes de substances blanches ou grises identiques
C ne corrèle pas avec les volumes
Plus le cortisol plasma est élevé, plus les volumes des ventricules sont augm



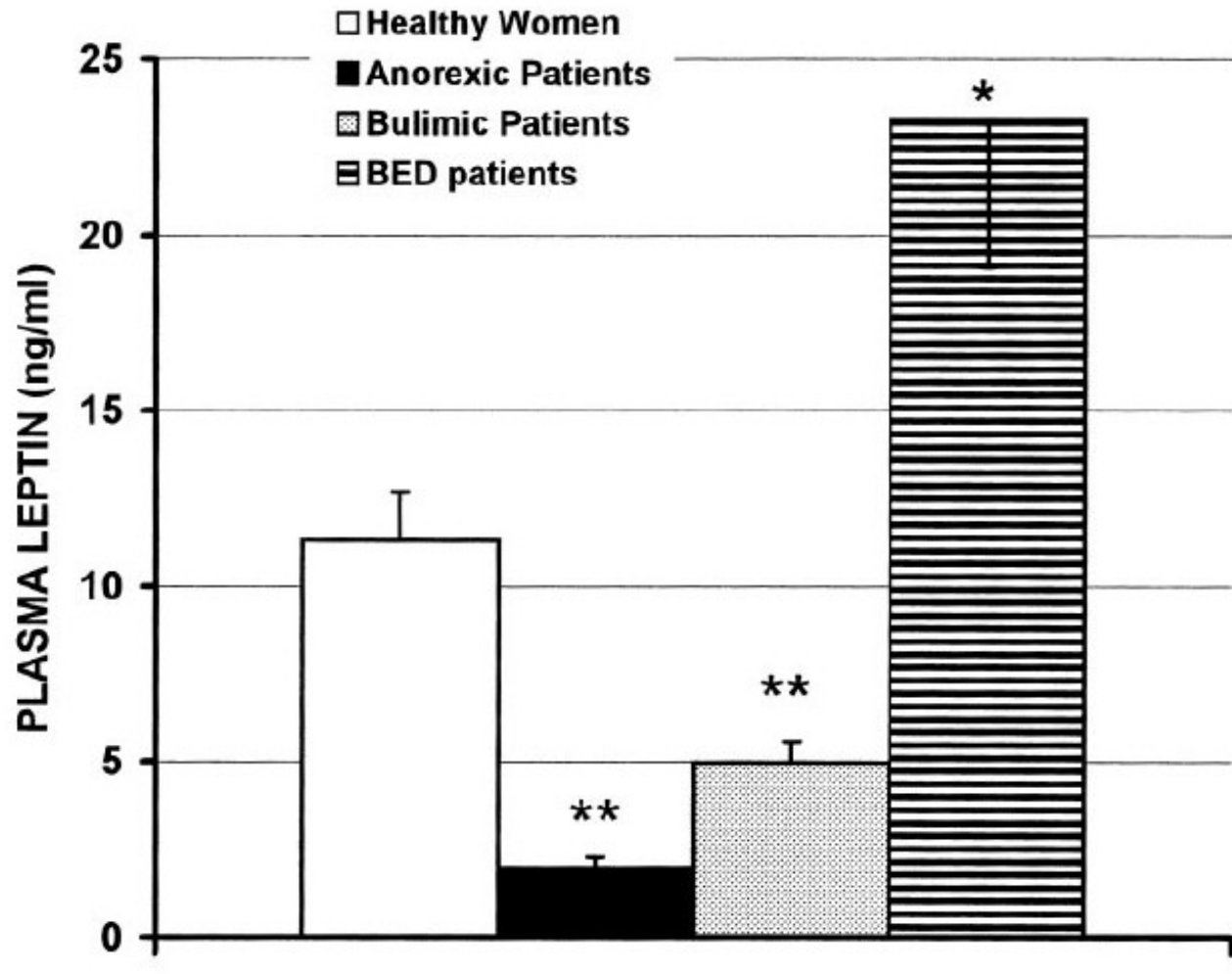
Stabilisation des facultés cognitives
Le gain de poids ne permet pas de récupérer
Les facultés cognitives sont moins bonnes chez celles qui ne sont pas réglées



**Les facultés cognitives sont moins bonnes chez celles qui ne sont pas réglées
L'œstrogène module les fonctions 5HT dépendantes**



There is no known metabolic/neuroendocrine pathway that provides a robust linkage between the magnitude of female's fat stores and the GnRH « pulse generator »



Factors promoting leptin secretion

* Excess energy stored as fat (obesity)

* Overfeeding

Glucose

Insulin

Glucocorticoids

Estrogens[†]

Inflammatory cytokines, including Tumor Necrosis Factor- α and Interleukin-6 (acute effect)

Factors inhibiting leptin secretion

* Low energy states with decreased fat stores (leanness)

* Fasting

Catecholamines and adrenergic agonists

Thyroid hormones

Androgens[†]

Peroxisome Proliferator-activated Receptor- γ (PPAR γ) agonists[†]

Inflammatory cytokines, including Tumor Necrosis Factor- α (prolonged effect)

* Denotes major factor influencing leptin levels.

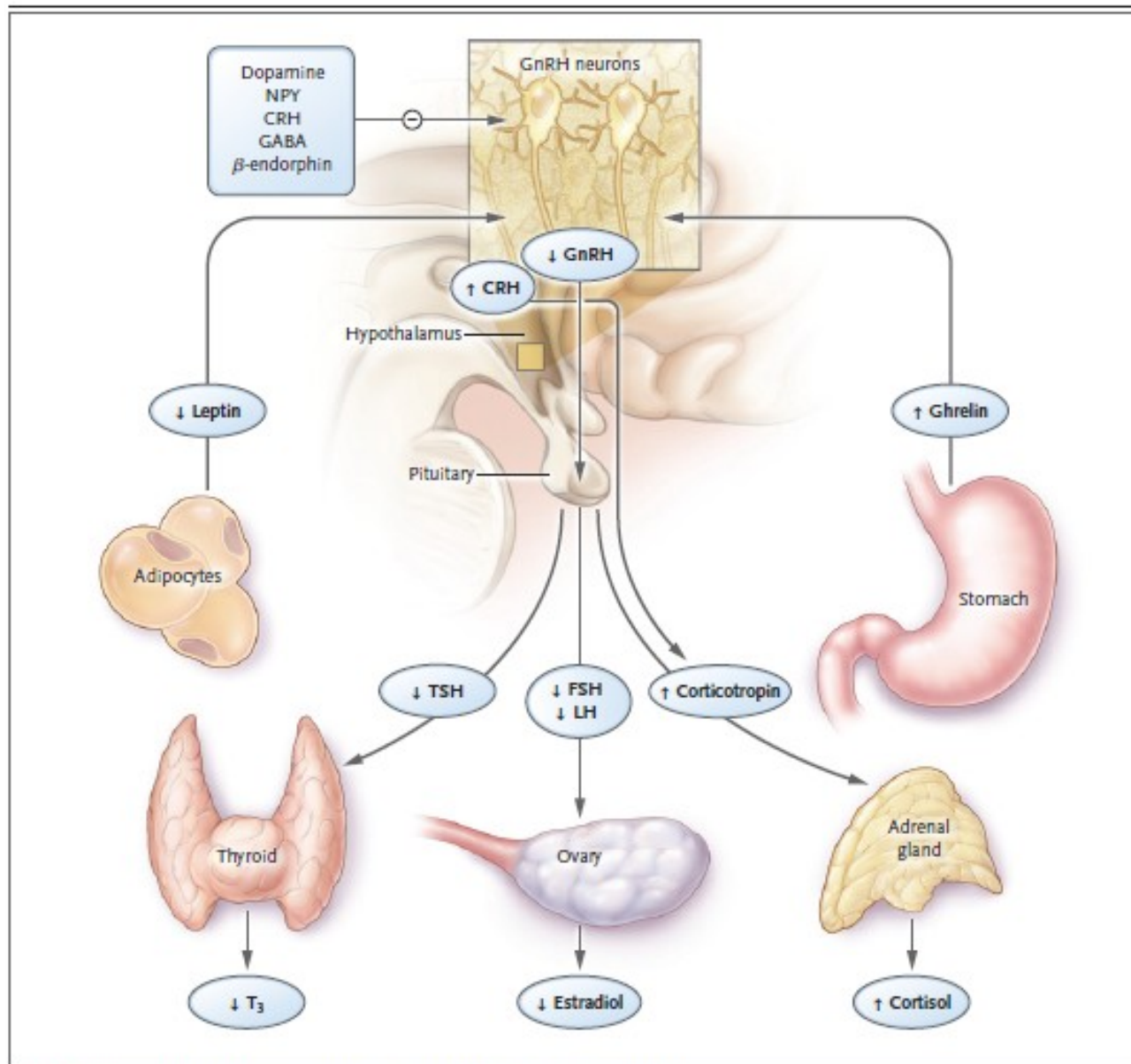


Figure 1. Hormonal and Other Changes in Patients with Hypothalamic Amenorrhea.

Actions de la leptine

- Agit sur les neurones hypothalamiques du noyau arqué (voies orexigènes et anorexigènes) effet net : réduction de la prise alimentaire
- Stimule les voies adrénergiques et augmente la dépense en énergie
- Stimule la satiété (NTS)
- Action sur les réseaux dopaminergiques (récompense)

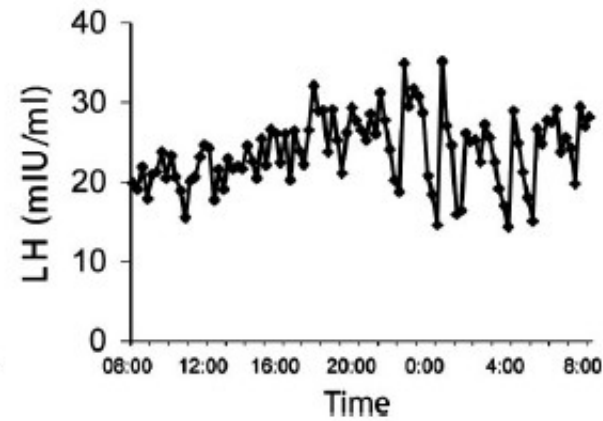
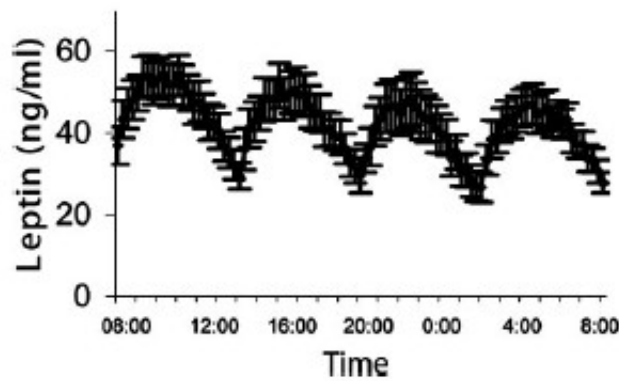
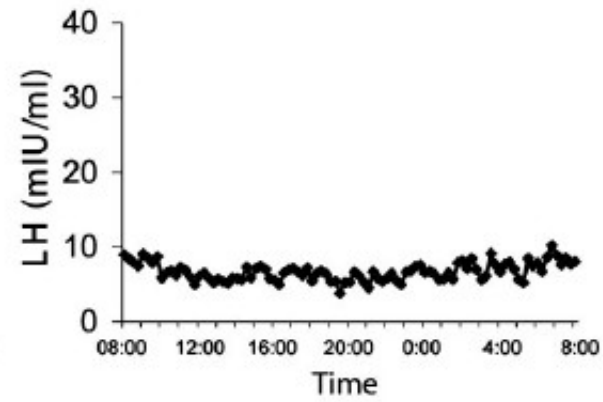
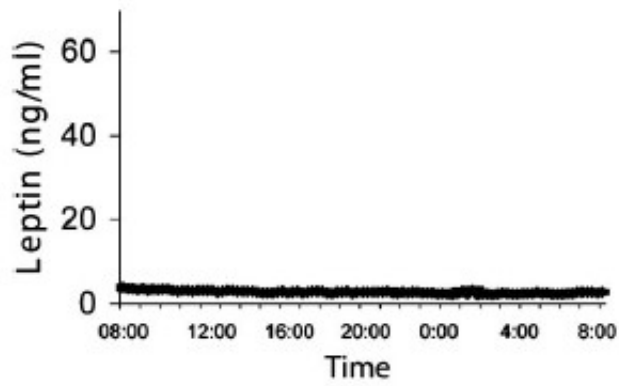
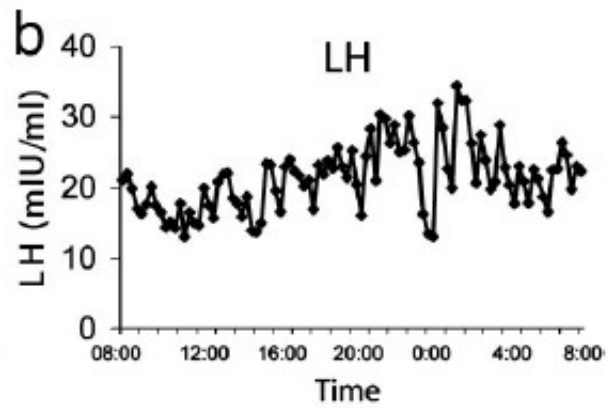
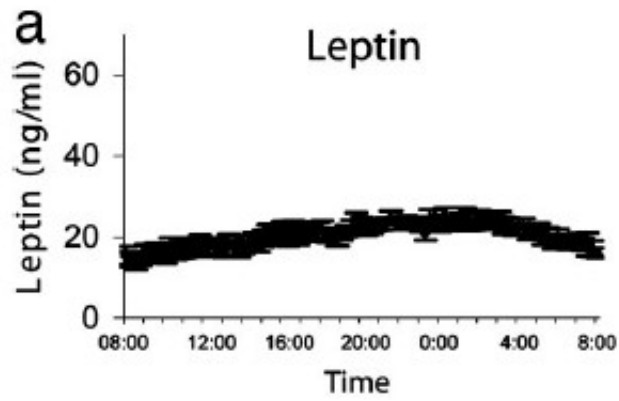
Leptine abaissée

- Diminution +++ en cas de jeune, hors de proportion avec la perte de masse grasse
- Diminue la réponse de LH (pulsatilité)= reproduction
- Diminue la réponse TSH (frein métabolique)
- Augmente la GH (catabolisme)
- Diminue l'IGF1: réponse anabolique (croissance...)

• **Un seuil de 5ng/ml semble séparer**

Table 1. Weight, body composition, resting metabolic rate (RMR), and hormone levels at the beginning (Day 1) and end (Day 4) of a fed state ($n = 7$), 72-h fasting with placebo ($n = 6$), and 72-h fasting with r-metHuLeptin ($n = 7$) mean \pm SE

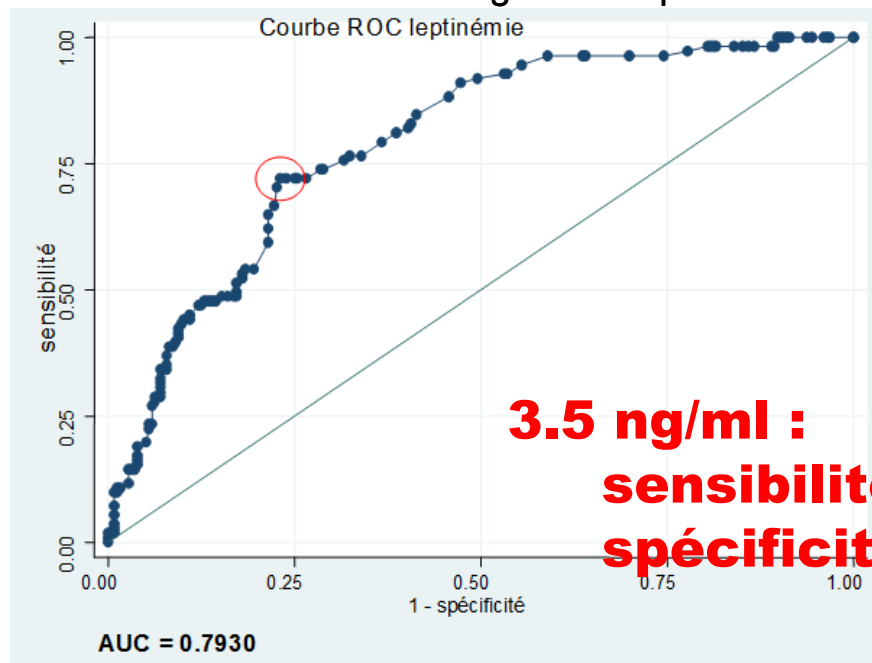
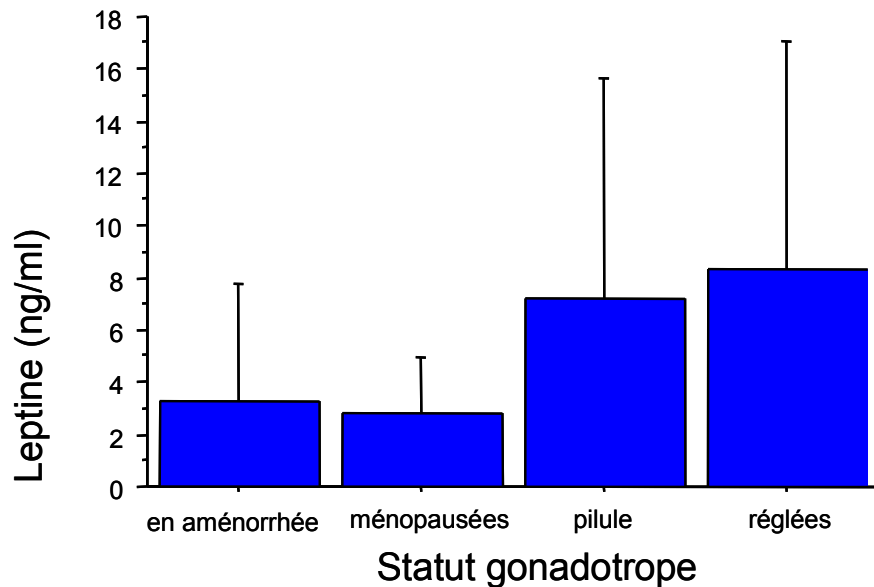
	Baseline fed state ($n = 7$)		Fasting + placebo ($n = 6$)		Fasting + leptin ($n = 7$)		Overall P	Baseline P
	Day 1	Day 4	Day 1	Day 4	Day 1	Day 4		
Weight, kg	57.0 \pm 2.3	58.0 \pm 2.2*	56.9 \pm 3.1	55.4 \pm 2.8*	56.2 \pm 2.2	54.1 \pm 2.0*	0.01 ^{†‡§}	0.61
Fat mass, %	29.9 \pm 1.5	30.0 \pm 1.4	31.2 \pm 1.9	29.3 \pm 2.2*	30.0 \pm 1.6	29.1 \pm 1.9	0.07 ^{†‡}	0.85
Fat mass, kg	17.2 \pm 1.3	17.3 \pm 1.2	18.0 \pm 1.9	16.4 \pm 1.8*	17.0 \pm 1.4	15.9 \pm 1.5*	0.01 ^{†‡§}	0.45
Fat-free mass, kg	39.9 \pm 1.4	40.7 \pm 1.7	38.9 \pm 1.6	39.0 \pm 1.6	39.2 \pm 1.3	38.2 \pm 1.3*	0.03 ^{†‡¶}	0.68
RMR, kcal/d	1,267 \pm 40	1,259 \pm 36	1,285 \pm 82	1,352 \pm 43	1,330 \pm 52	1,344 \pm 34	0.26	0.12
Respiratory quotient	0.87 \pm 0.03	0.91 \pm 0.01	0.88 \pm 0.02	0.74 \pm 0.01*	0.88 \pm 0.03	0.72 \pm 0.01*	0.01 ^{†‡§}	0.83
Leptin, ng/ml	11.4 \pm 1.6	16.7 \pm 1.2*	14.7 \pm 2.6	2.8 \pm 0.3*	12.2 \pm 1.6	28.8 \pm 2.0*	0.002 ^{†‡§¶}	0.85



	Cortisol	PYY	Leptin	Ghrelin
EDE-Q				
Core psychopathology				
Dietary restraint	0.53 ^{‡,§}	0.22*	−0.17	0.04
Eating concern	0.56 ^{‡,§}	0.41 ^{‡,§}	−0.36 [‡]	0.09
Shape concern	0.47 ^{‡,§}	0.26 [†]	−0.05	−0.01
Weight concern	0.43 ^{‡,§}	0.26 [†]	−0.09	0.00
Global concern	0.53 ^{‡,§}	0.30 [†]	−0.17	0.03
Associated behaviors				
Overexercise/month	0.29 ^{†,§}	0.26 [†]	0.01	0.01
EDI-2				
Core psychopathology				
Drive for thinness	0.27 [†]	0.35 ^{‡,§}	−0.22*	0.04
Bulimia	0.08	0.22*	−0.20	0.00
Body dissatisfaction	0.19 [§]	0.13	0.15	−0.08
Associated psychological features				
Ineffectiveness	0.36 [‡]	0.27 [†]	−0.29 [†]	0.10
Perfectionism	0.10	0.14	−0.22	0.01
Interpersonal distrust	0.36 ^{‡,§}	0.26 [†]	−0.27 [†]	0.07
Interoceptive awareness	0.29 [†]	0.17	−0.28 [†]	0.14
Maturity fears	0.19	0.09	−0.24*	0.27 [†]
Asceticism	0.32 [†]	0.35 [‡]	−0.30 [†]	0.09
Impulse regulation	0.27 [†]	0.33 ^{‡,§}	−0.21	0.16
Social insecurity	0.30 [†]	0.40 ^{‡,§}	−0.24*	0.21

Linear regression, multivariate least-square analyses * $P < 0.10$, $^{\dagger}P \leq 0.05$, $^{\ddagger}P \leq 0.01$, $^{\S}P \leq 0.05$ after controlling for BMI.

Analyse 560 anorexies mentales



Mortalité
Fonction cognitive
Reproduction

Masse grasse seule ou hormones?



1. **Guérison**

« **Adaptation santé** »

2. **Cicatrices (obsessions)**

« **Adaptation santé** »
dépassée

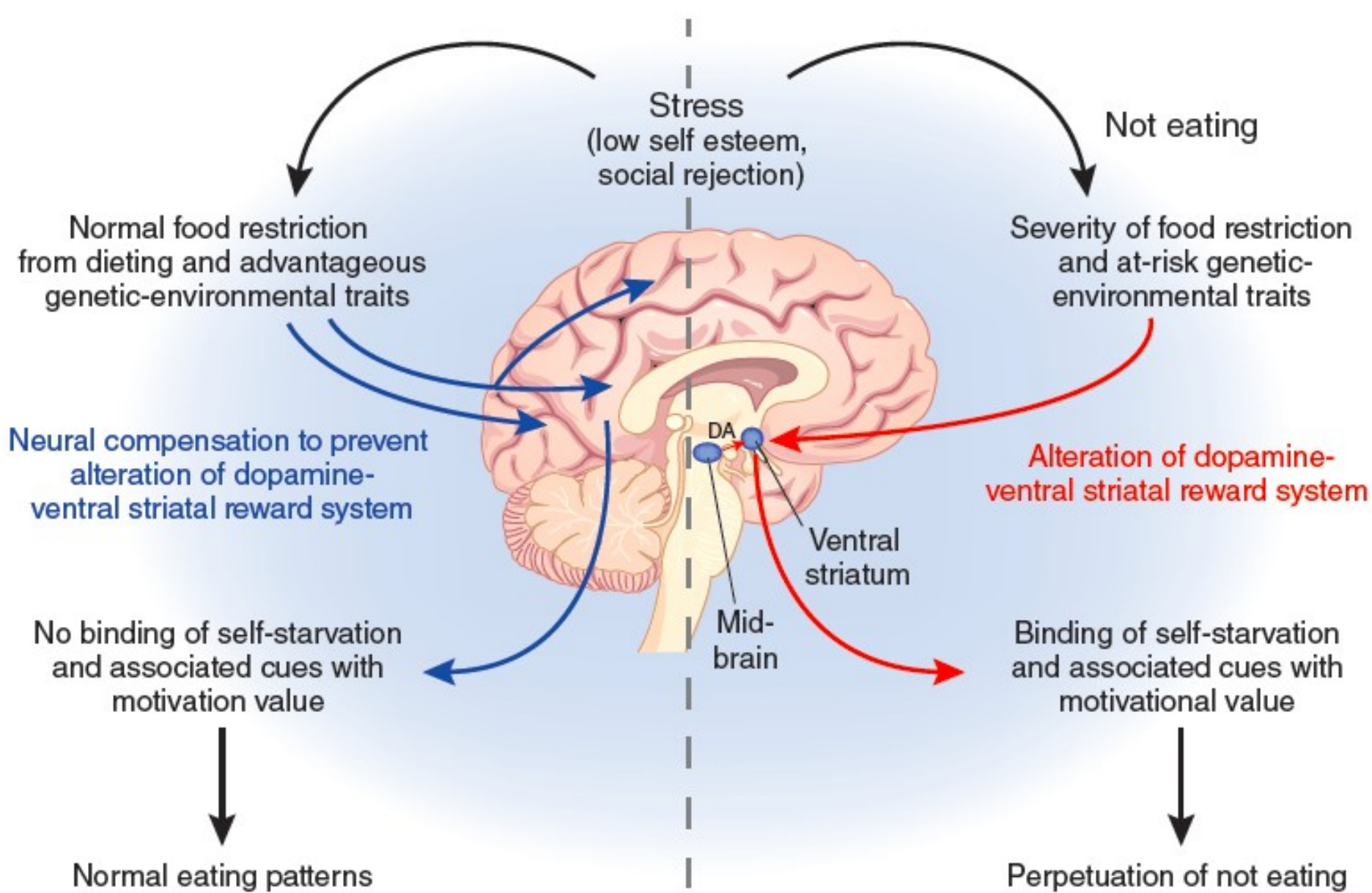
3. **Séquelles (os, dents...)**

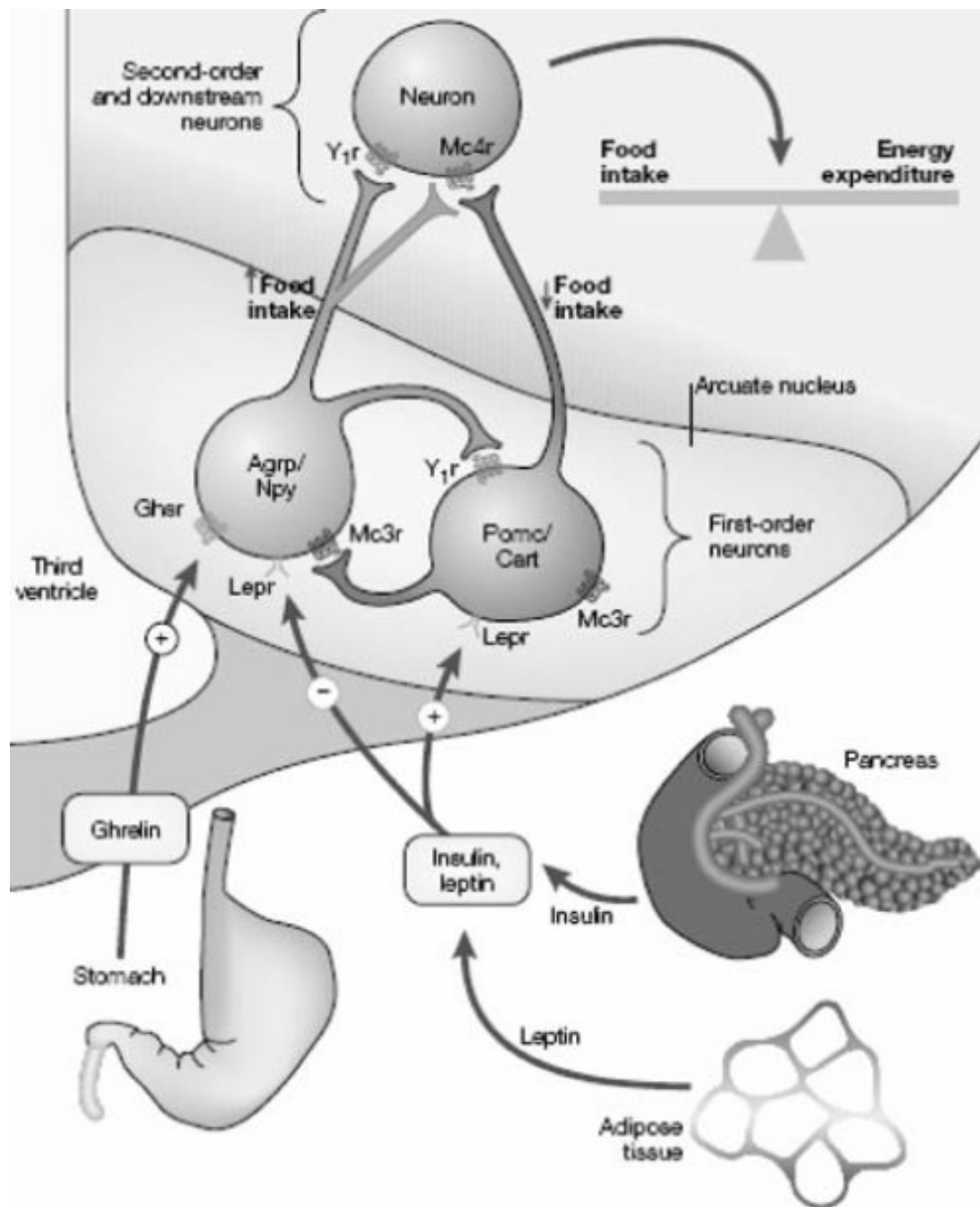
Résultats

Population de l'étude n=186		
Age (années)	26,0 ± 10,0	
Sex ratio Femmes / Hommes (n)	179 / 7	Valeurs minimales et maximales
Durée d'évolution des troubles (années)	6,8 ± 8,1	
AN-R/AN-B/BN (n)	128 / 53 / 5	
Taille (m)	1,64 ± 0,07	
Poids (kg)	43,0 ± 8,3	22,7 - 66,6
IMC (kg/m ²)	16,03 ± 2,82	10,2 - 23,6
Masse grasse (kg)	6,97 ± 5,43	0,9 - 28,6
Masse maigre (kg)	34,89 ± 4,91	22,1 - 49

Comparison between healthy women and women with eating disorders for plasma hormone and glucose concentrations^a

	Healthy women (<i>n</i> = 15)	Women with anorexia nervosa (<i>n</i> = 21)	Women with bulimia nervosa (<i>n</i> = 32)	Women with binge-eating disorder (<i>n</i> = 14)
Body weight (kg)	56.9 ± 6.1	41.9 ± 5.6*	53.6 ± 8.8	82.2 ± 20.2*
Height (cm)	161.7 ± 4.7	162.0 ± 5.0	161.8 ± 7.7	163.5 ± 5.6
Body mass index (kg/m ²)	21.7 ± 2.2	16.0 ± 1.6*	20.5 ± 2.8	30.9 ± 7.9*
Plasma prolactin (ng/ml)	19.0 ± 7.6	7.2 ± 2.7*	9.7 ± 6.5*	9.0 ± 3.9*
Plasma cortisol (nmol/l)	304 ± 107	445 ± 171**	370 ± 238	350 ± 120
Plasma 17β-estradiol (pg/ml)	72.4 ± 59.2	18.7 ± 16.1*	42.0 ± 40.5**	34.0 ± 8.5***
Plasma glucose (mg/dl)	93.6 ± 20.4	82.7 ± 11.5***	84.2 ± 18.4	90.0 ± 15.3





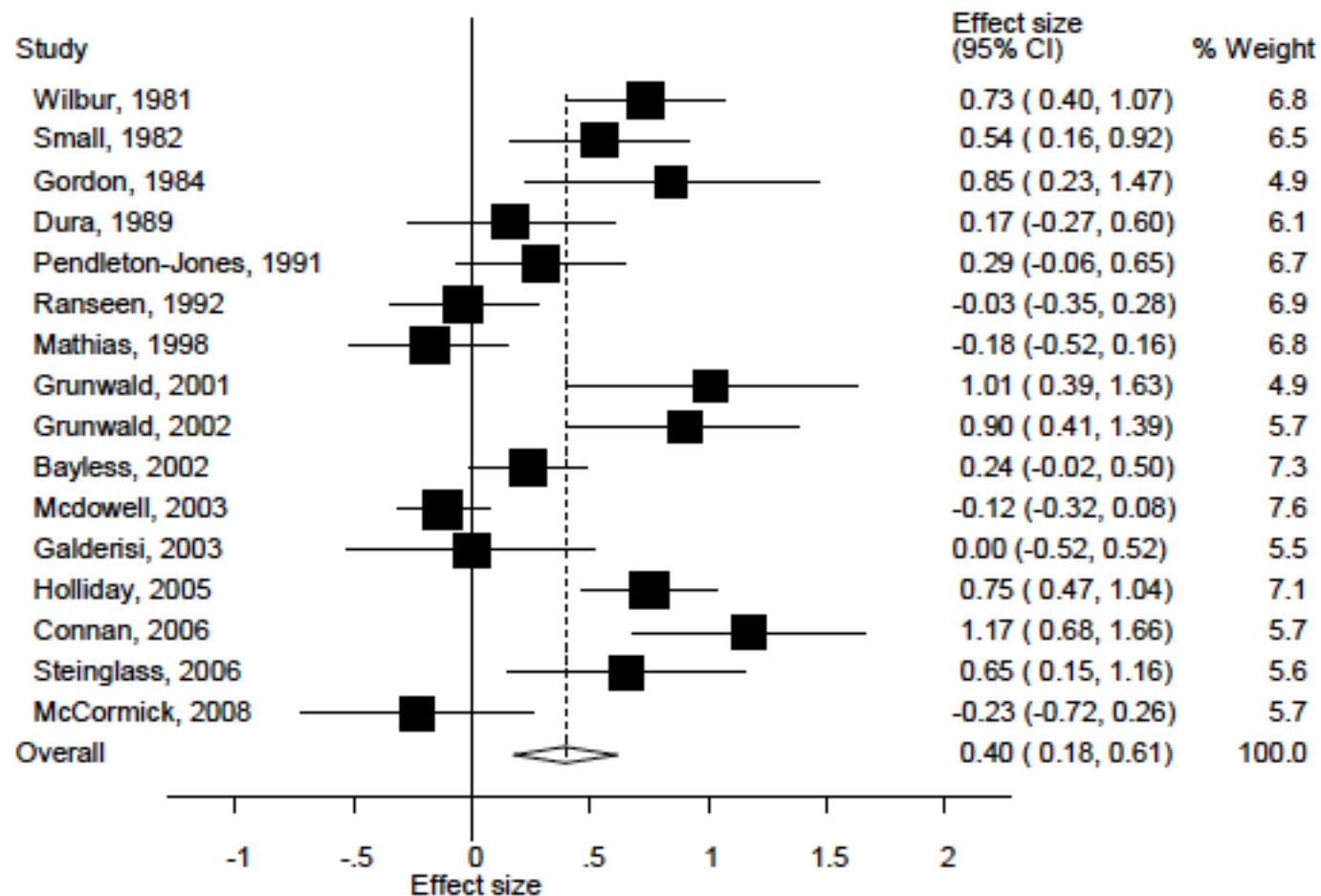


Figure 2 Forest plot for intelligence quotient (IQ) studies using Wechsler's tests: standardised effects for patients with eating disorders (EDs) relative to the normative population (norm) group.

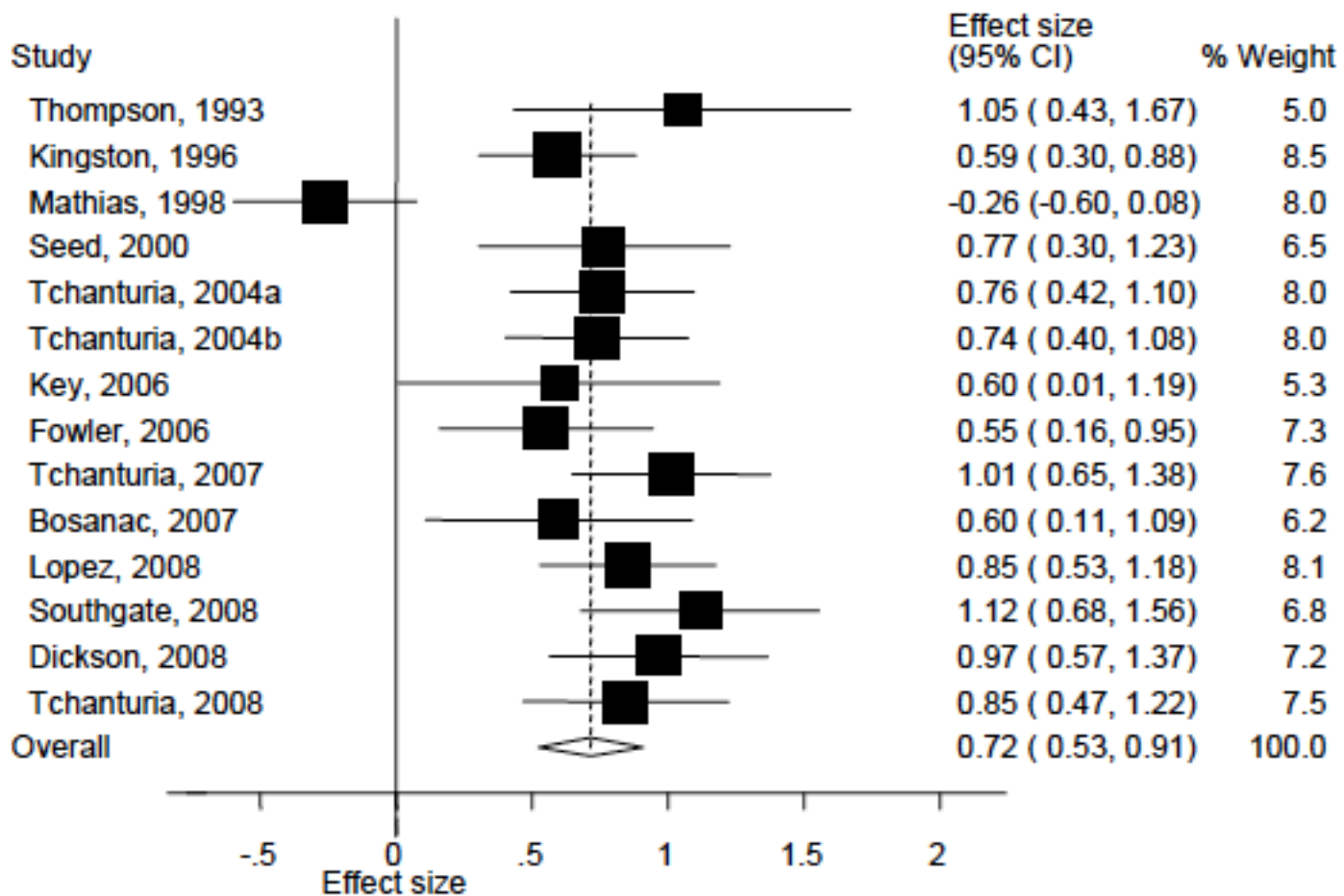
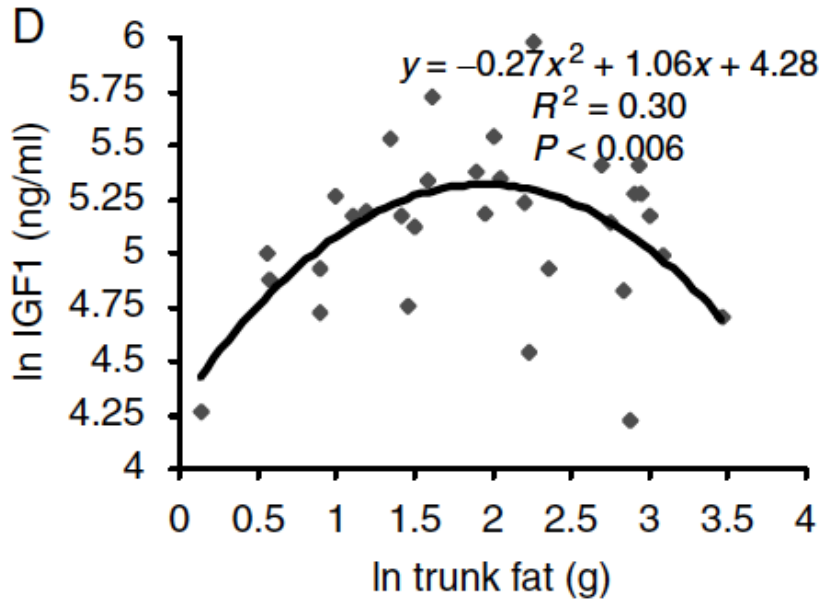
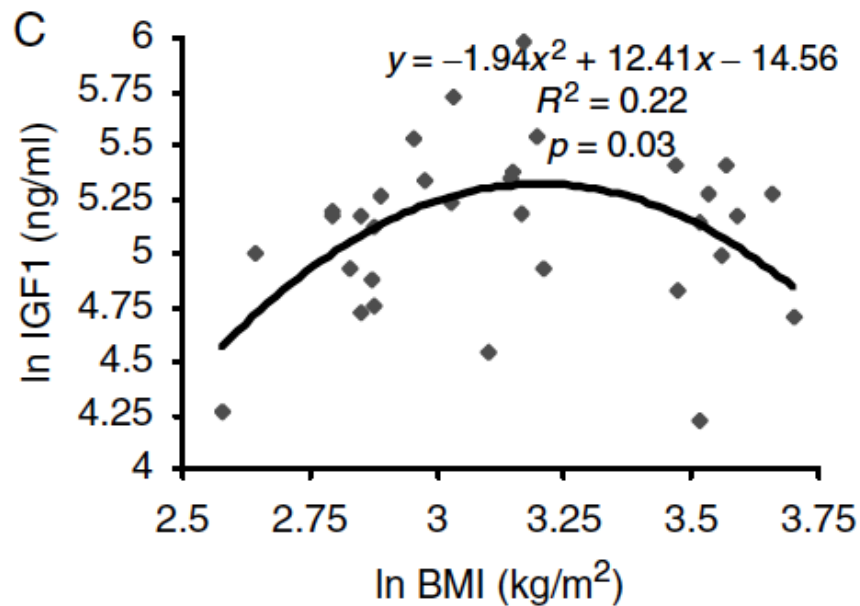
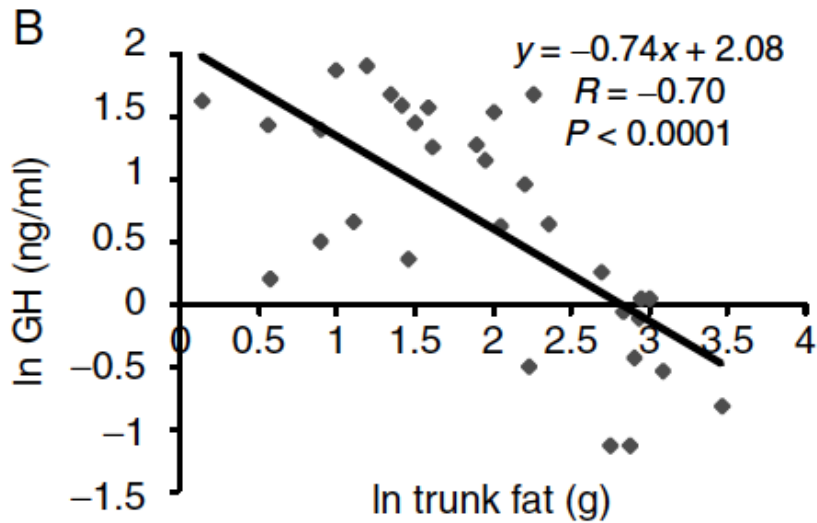
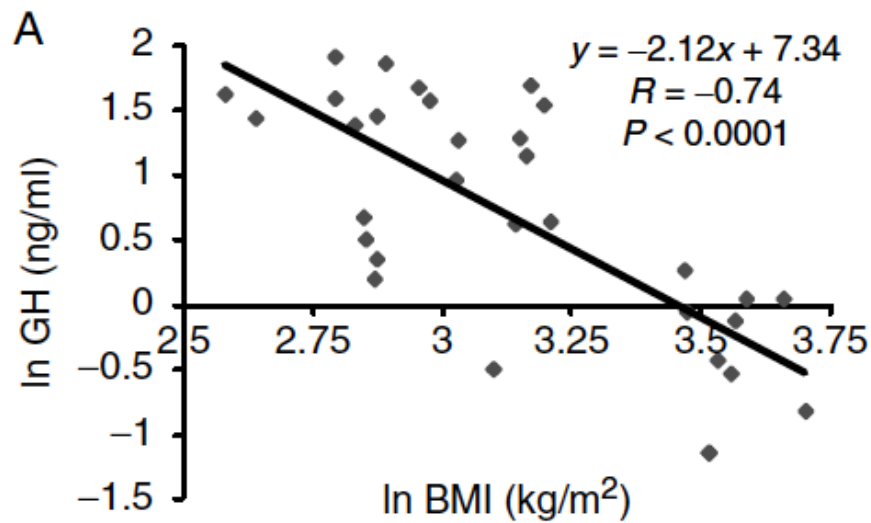


Figure 1 Forest plot for intelligence quotient (IQ) studies using the National Adult Reading Test (NART): standardised effects for patients with eating disorders (EDs) relative to the normative population (norm) group.



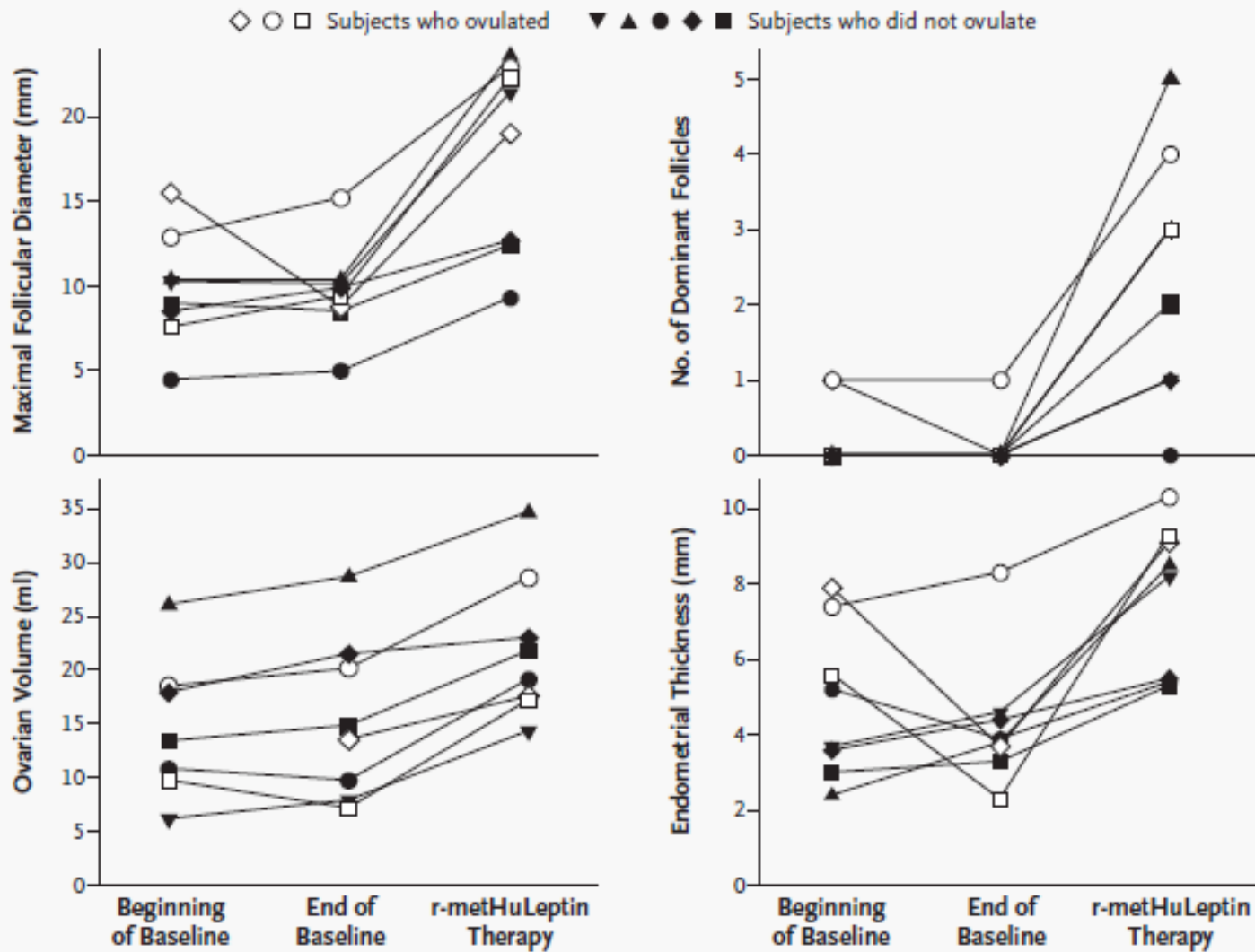


Figure 2. Follicular, Ovarian, and Endometrial Ultrasonographic Measurements at the Beginning and End of the One-Month Baseline Period and at Their Maximum during r-metHuLeptin Treatment.

Each symbol represents one subject.

LEPTIN FOR WOMEN WITH HYPOTHALAMIC AMENORRHEA

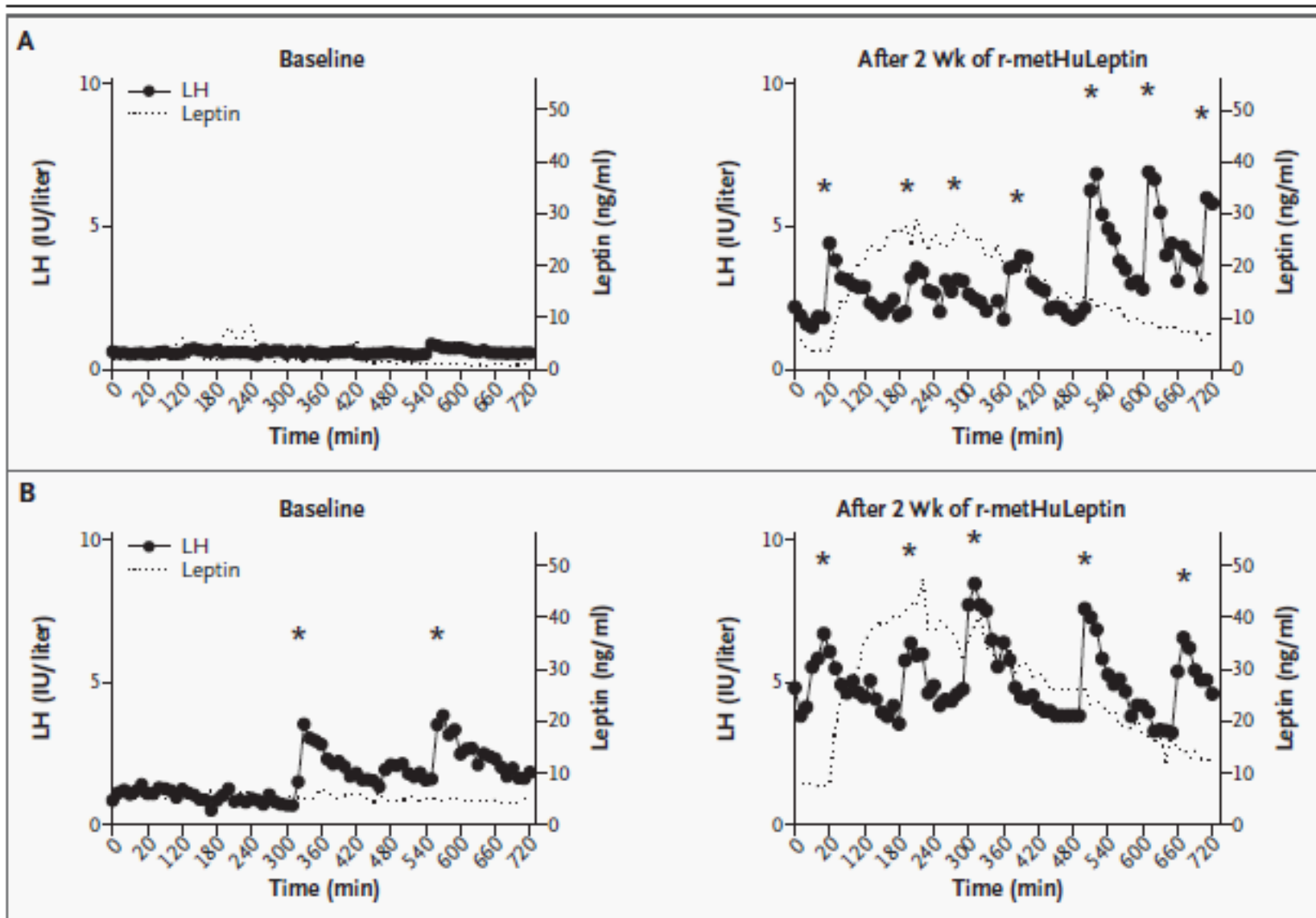


Table 1. Weight, body composition, resting metabolic rate (RMR), and hormone levels at the beginning (Day 1) and end (Day 4) of a fed state ($n = 7$), 72-h fasting with placebo ($n = 6$), and 72-h fasting with r-metHuLeptin ($n = 7$) mean \pm SE

	Baseline fed state ($n = 7$)		Fasting + placebo ($n = 6$)		Fasting + leptin ($n = 7$)		Overall <i>P</i>	Baseline <i>P</i>
	Day 1	Day 4	Day 1	Day 4	Day 1	Day 4		
Insulin, μ U/ml	6.72 \pm 1.21	9.28 \pm 1.51*	6.06 \pm 0.81	1.22 \pm 0.24*	7.91 \pm 1.54	1.23 \pm 0.30*	0.01 ^{†‡§}	0.85
FFA, mmol/l	0.07 \pm 0.01	0.04 \pm 0.00*	0.05 \pm 0.01	0.94 \pm 0.16*	0.04 \pm 0.01	0.83 \pm 0.08*	0.01 ^{†‡§}	0.08
Estradiol, pg/ml	57.0 \pm 12.1	64.5 \pm 11.3	60.9 \pm 13.1	66.1 \pm 27.2	61.2 \pm 11.1	52.8 \pm 10.2	0.31	0.61
FSH, mIU/ml	6.00 \pm 0.61	5.39 \pm 0.90	5.83 \pm 0.47	4.92 \pm 0.51	5.81 \pm 0.44	5.66 \pm 0.69	0.22	0.85
Testosterone, ng/dl	74.6 \pm 11.8	74.2 \pm 10.9	78.5 \pm 11.9	68.5 \pm 9.8	66.4 \pm 8.1	67.6 \pm 7.1	0.85	0.61
ft3, pg/ml	2.81 \pm 0.10	2.60 \pm 0.08	2.98 \pm 0.17	1.66 \pm 0.11*	2.78 \pm 0.16	1.69 \pm 0.08*	0.01 ^{†‡§}	0.68
Reverse T3, ng/dl	15.0 \pm 0.7	12.4 \pm 1.0*	16.9 \pm 2.3	33.5 \pm 3.7*	15.8 \pm 0.9	34.1 \pm 2.0*	0.01 ^{†‡§}	0.61
Free T4, ng/dl	1.19 \pm 0.07	1.12 \pm 0.06	1.22 \pm 0.09	1.18 \pm 0.08	1.17 \pm 0.08	1.17 \pm 0.08	0.83	0.54
IGF-1, ng/ml	265.3 \pm 17.1	346.9 \pm 24.5*	260.8 \pm 19.5	162.2 \pm 12.5*	239.3 \pm 25.3	147.6 \pm 10.7*	0.01 ^{†‡§}	0.31
IGF-BP3, μ g/ml	4.78 \pm 0.11	5.11 \pm 0.22*	4.94 \pm 0.14	4.22 \pm 0.33	4.66 \pm 0.25	4.06 \pm 0.21*	0.04 ^{†‡§}	0.51
Cortisol, μ g/dl	16.9 \pm 3.4	16.7 \pm 3.1	17.5 \pm 0.9	17.6 \pm 3.0	16.9 \pm 1.9	14.5 \pm 2.1	0.51	0.85