SFNEP
Société Francophone Nutrition Clinique et Métabolisme
Nourrir l'Homme malade

JDP SFNEP Journées de Printemps

JDP LIMOGES 2016

BIENVENUE !

Nourrir l'Homme malade

Nutrition et hypermétabolisme lors de la Sclérose Latérale Amyotrophique (SLA)

Jésus P, Fayemendy P, Marin B, Nicol M, Morin B, Deluche E, Sourisseau H, Bonhommo S, Machat S, Lautrette G, Preux PM, Couratier P, Desport JC.

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Sclérose Latérale Amyotrophique (SLA)

- Atteinte du motoneurone
- Formes sporadiques : 90% des cas
- Formes spinale et bulbaire
- Rare : incidence 2 à 3 / 100 000 personnes
- Rapidement létale : médiane survie 17,5 mois

(Chiò A. Neuroepidemiology 2013 ; Marin B. Eur J Neurol 2014 ; Marin B. Neurodegener Dis 2016)

Recommandations

RECOMMANDATIONS PROFESSIONNELLES

Prise en charge des personnes atteintes de sclérose latérale amyotrophique

GUIDE – AFFECTION DE LONGUE DUREE

PROTOCOLE NATIONAL DE DIAGNOSTIC ET DE SOINS (PNDS)
SCLEROSE LATERALE AMYOTROPHIQUE (ALD9)

Good practice in the management of amyotrophic lateral sclerosis: Clinical guidelines. An evidence-based review with good practice points. EALSC Working Group

PETER MUNCH ANDERSEN[1], GIAN DOMENICO BORASIO[2], REINHARD DENGLER[3], ORLA HARDIMAN[4], KATJA KOLLEWE[3], PETER NIGEL LEIGH[5], PIERRE-FRANCOIS PRADAT[6], VINCENZO SILANI[7] & BARBARA TOMIK[8]

Neurology®

Practice Parameter update: The care of the patient with amyotrophic lateral sclerosis: Drug, nutritional, and respiratory therapies (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology
R. G. Miller, C. E. Jackson, E. J. Kasarskis, et al.

European Journal of Neurology 2012, **19:** 360–375 doi:10.1111/j.1468-1331.2011.03501.x

EFNS GUIDELINES

EFNS guidelines on the Clinical Management of Amyotrophic Lateral Sclerosis (MALS) – revised report of an EFNS task force

The EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis: Peter M. Andersen[a], Sharon Abrahams[b], Gian D. Borasio[c], Mamede de Carvalho[d], Adriano Chio[e], Philip Van Damme[f], Orla Hardiman[g], Katja Kollewe[h], Karen E. Morrison[i], Susanne Petri[h], Pierre-Francois Pradat[j], Vincenzo Silani[k], Barbara Tomik[l], Maria Wasner[m] and Markus Weber[n]

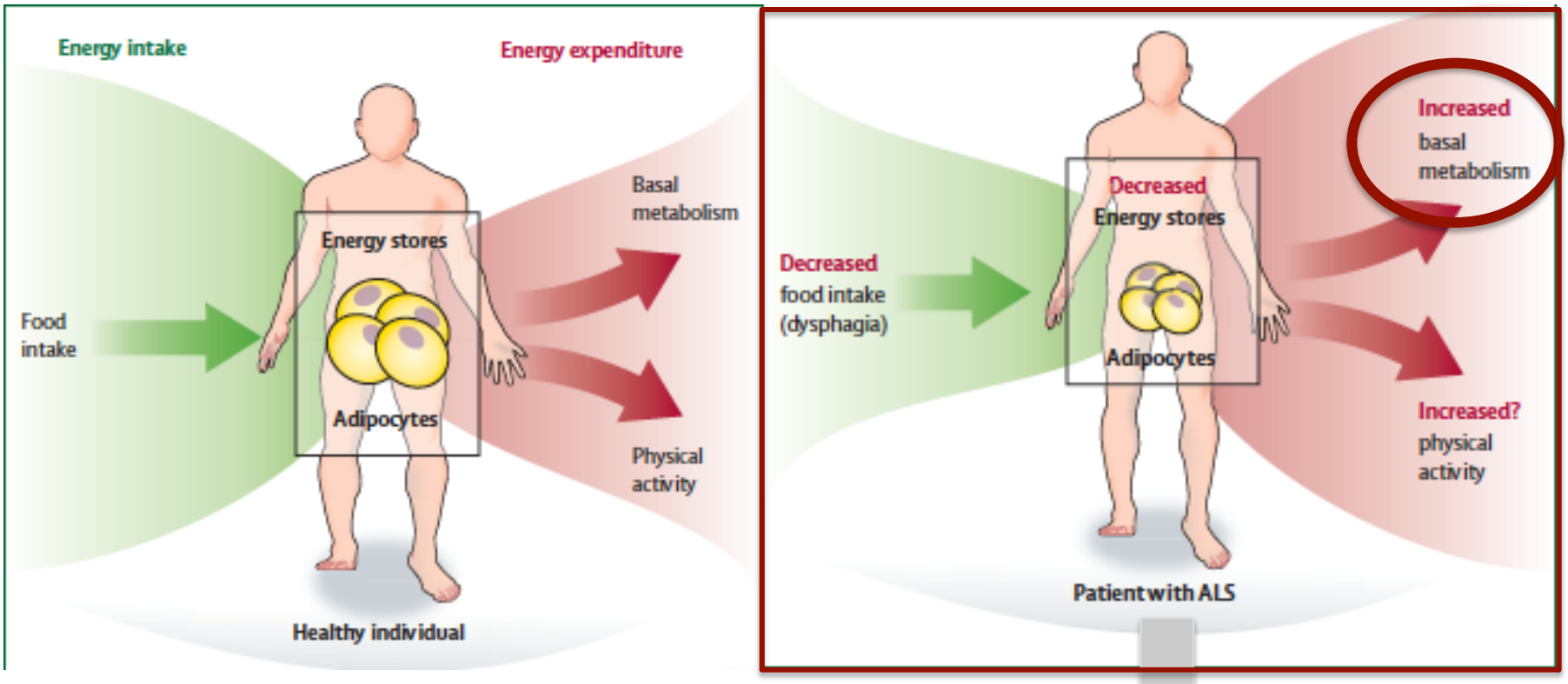
(HAS 2007 ; HAS 2015 ; Miller RG. Neurology 2006 ; Andersen P. ALS 2007 ; Andersen P. Eur J Neurol 2012)

Dénutrition au cours de la SLA

- Dénutrition : 9 à 53% des cas
- Dénutrition = facteur pronostic de survie
- Risque de décéder
  - Perte de poids 5% au diagnostic : ↗ 2 fois
  - Dénutrition au cours de la SLA : ↗ 7 fois
  - Chaque perte pondérale de 5% : ↗ 31%
  - Chaque perte d'un point d'IMC : ↗ 23%

(Desport JC. Neurology 1999 ; Desport JC. ALS 2008 ; Marin B. JNNP 2011 ; Marin B. Neurodegener Dis 2016)

Métabolisme énergétique



Perte pondérale
Risque de dénutrition

(Dupuis L. Lancet Neurol 2011)

L’hypermétabolisme existe t’il?

Comment évaluer l'hypermétabolisme?

- Mesure DER en calorimétrie indirecte

- Variation de la DER : (DERm-DERc)/DERc*100

+ 10% de DER par rapport à la mesure théorique

- **Quelle formule théorique utiliser?**
  - Harris et Benedict 1919 : 72% de bonne prédiction (IMC 18,5-25)

(Jésus P. Clin Nutr 2015)

Quelle formule théorique utiliser?

- Etude en cours (CHU Limoges) n=315

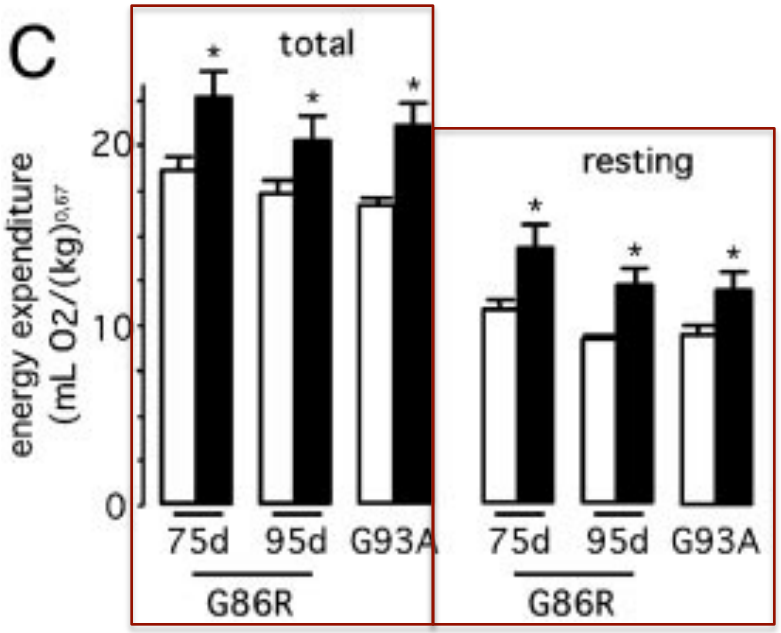
	DER (kcal/j)	hypermétab (%)	Variation de DER (%) moyenne ± ET
Mesurée	15114 ± 298,7	-	-
HB 1919	1355,6 ± 229,2	55,2	11,8 ± 12,5
HB 1984	1377,2 ± 223,3	49,8	9,9 ± 12,1
World Schofield	1385,0 ± 215,3	46,7	9,3 ± 13,1
De Lorenzo	1377,1 ± 235,8	49,2	10,1 ± 12,0
Johnstone	1332,5 ± 235,7	59,9	13,8 ± 12,6

(Jésus P. Clin Nutr 2015 ; Jésus P. données non publiées)

Hypermétabolisme dans les modèles animaux de SLA

Evidence for defective energy homeostasis in amyotrophic lateral sclerosis: Benefit of a high-energy diet in a transgenic mouse model

Luc Dupuis*, Hugues Oudart†, Frédérique René*, Jose-Luis Gonzalez de Aguilar*, and Jean-Philippe Loeffler*‡



(Dupuis L. PNAS 2004)

Hypermétabolisme dans la SLA

Study	Characteristics of subjects	mBEE/cBEE (kcal/d)	Comments on comparison mBEE/cBEE
Kasarskis et al., 1996 [21]	Total *n*: 16, ventilated *n*: NA Age: M:58 ± 18 yrs/F: 58 ± 5 yrs BMI: NA Disease duration:: M: 24 ± 16 mo/F: 31 ± 24 mo ALS-FRS: NA	NA	- Increasing ratio of mBEE/cBEE in proximity to death
Sherman et al., 2004 [10]	Total *n*: 34, ventilated *n*: 18 Age: Ventilated +: 67 ± 3 yrs/Ventilated -: 56 ± 15 yrs BMI: Ventilated+: 25 ± 4 kg/m^2/Ventilated -: 27 ± 9 kg/m^2 Disase duration: NA ALS-FRS: Ventilated+:12 ± 12/Ventilated -: 24 ± 9	Ventilated +: 1655 ± 363/1461 ± NA Ventilated -: 1341 ± 472/1505 ± NA	- *T*-test: $p < 0.05$ between mBBE and cBEE - Simple regression: significant correlation between mBEE and cBEE but poor agreement (slope 0.51, intercept 702 kcal) - Bland-Altman: mBEE minus cBEE ranges from −591 kcal to 677 kcal/d - Prediction error 18.4% - mBEE/cBEE independent of severity, duration of disease and BMI. - mBEE/cBEE higher in ventilated than non ventilated subjects
Desport et al., 2001 [25]	Total *n*: 62, ventilated *n*: NA Age: 63 ± 11yrs BMI: 24.7 ± 5 kg/m^2 Disease duration: 24 ± 26 mo ALS-FRS: 29 ± 7	1562 ± 342/NA	- Hypermetabolism (mBEE/cBEE ≥ 1.1) of 68% of patients - mBEE/cBEE independent of age, sex, FFM, weight, Norris limb score - mBEE/cBEE positively correlated with manual muscular testing score and neutrophil count
Desport et al., 2005 [16]	Total *n*: 168, ventilated *n*: NA Age: NA BMI: 24.4 ± 4.4 kg/m^2 Disase duration: 557 ± 525 d ALS-FRS: 28 ± 7	1521 ± 307/1334 ± 235	- Hypermetabolism (mBEE/cBEE ≥ 1.1) of 14 ± 13% in 62% of patients - Simple regression: mBEE minus cBEE increases in men (vs. women), with higher phase angle (bioimpedance analysis data) and with higher manual muscle testing but was independent of clinical onset (bulbar vs. spinal), BMI and FFM (bioelectrical impedance analysis) and presence of tube feeding.
Vaisman et al., 2009 [15]	Total *n*: 33, ventilated *n*: 0 Age: 59 ± 12 yrs BMI: 23.3 ± 3.3 kg/m^2 Disease duration: 23 ± 14 ALS-FRS: 25 ± 8	1467 ± 218/NA	- mBEE in the normal range ±10% of the cBEE
Funalot et al., 2009 [33]	Total *n*: 44 Age: familial ALS: 60.7 ± 8.8 yrs sporadic ALS: 60.4 ± 8.7 yrs BMI: familial ALS: 27 ± 3.9 kg/m^2 sporadic ALS: 25.5 ± 5.7 kg/m^2 Disease duration: familial ALS: 15.5 ± 10.8 mo sporadic ALS 20.4 ± 21.2 mo ALS-FRS: familial ALS: 27.6 ± 7.3 sporadic ALS: 29.2 ± 6.6		- mBEE/cBEE higher in subjects with familial than sporadic ALS - mBEE/cBEE independent of neurological or respiratory parameters.
Bouteloup et al., 2009 [24]	Total *n* = 61, ventilated *n*: NA Age: 64 ± 10 yrs BMI:24.1 ± 3.8 kg/m^2 Disease duration: 430 ± 301 d ALS-FRS: 31 ± 5	1449 ± 301/1316 ± 242 Bulbar onset: 1402 ± 341/1277 ± 274 Spinal onset: 1492 ± 257/1350 ± 208	- Hypermetabolism (mBEE/cBEE ≥ 1.1) of 10 ± 11% in 48% of patients - mBEE/cBEE independent of BMI, FFM, respiratory function, disease duration, CRP, ALS-FRS, manual muscular testing, smoking, hyperthyroidism - mBEE/cBEE correlates positively with energy and protein intake

(Genton L. Clin Nutr 2011)

Prévalence de l'hypermétabolisme

- Retrouvé dans
  - **25,0%** (n=16) (Kasarskis E. AJCN 1999)
  - **67,7%** (n=62) (Desport JC. AJCN 2001)
  - **62,3%** (n=168) (Desport JC. Neurodegenerative Dis 2005)
  - **47,5%** (n=61) (Bouteloup C. J Neurol 2009)
  - **55,2%** (n=315) (Jésus P. Données non publiées)

- Formes familiales
  - **100%** (n=11) mutation **SOD1** (Funalot B. ALS 2009)
  - **58,1%** (n=31) mutations **C9orf72 : 60%** ; SOD1 : **13,3%** ; SCA2 : 6,7% ; exon 3 FUS/TLR : 13,3% ; TARDBP : 6,7%) (Jésus P. Données non publiées)

Variation de la DER

- Patients SLA
  - **+15,9%** (Desport JC. AJCN 2001)
  - **+13,0%** avec ventilation mécanique (Sherman M. JPEN 2004)
  - **+14,0%** (Desport JC. Neurodegenerative Dis 2005)
  - **+10,5%** (Bouteloup C. J Neurol 2009)
  - **+11,8%** (Jésus P. Données non publiées)

- Patients SLA hypermétaboliques
  - **+19,7%** (Bouteloup C. J Neurol 2009)
  - **+20,6%** (Jésus P. Données non publiées)

SLA versus témoin?

Do patients with amyotrophic lateral sclerosis (ALS) have increased energy needs?

Nachum Vaisman [a,*], Michal Lusaus [a], Beatrice Nefussy [b], Eva Niv [a], Doron Comaneshter [c], Ron Hallack [d], Vivian E. Drory [b]

Parameter	ALS patients $n=33$	Healthy controls $n=33$	*P*-value
Age, years	59.0±12.6 (58.2)	57.8±12.3 (56.0)	0.59
Gender M/F	22/10	22/10	
Weight, kg	65.4±11.0 (65.4)	84.8±15.4 (86.2)	0.0001
Height, m	1.68±0.09 (1.70)	1.72±0.11 (1.74)	0.077
BMI, kg/ht^2	23.3±3.3 (22.0)	28.7±4.8 (27.8)	<0.0001
LBM, kg	41.9±7.2 (42.8)	54.6±12.3 (56.5)	<0.0001
Body fat, %	32.8±9.4 (32.4)	32.7±10.9 (30.2)	0.87
REEm, kcal/d	1467±218 (1486)	1744±367 (1725)	<0.0001
REEPP, %	103.6±11.0 (102.0)	103.8±10.0 (104.1)	0.72
REE/FFM, kcal/kg	35.4±4.3 (35.5)	32.3±3.6 (32.4)	0.001
RQ	0.81±0.06 (0.80)	0.83±0.05 (0.83)	0.24
Daily caloric intake kcal/d	1384±508 (1250)	1912±577 (1822)	0.001
ALSFRS-R	25.25±8.34	48.0±0.0	0.001

(Vaisman N. J Neurol Sci 2009)

SLA versus témoin?

Factors correlated with hypermetabolism in patients with amyotrophic lateral sclerosis[1,2]

Jean C Desport, Pierre M Preux, Laurent Magy, Yves Boirie, Jean M Vallat, Bernard Beaufrère, and Philippe Couratier

Variable	Total ($n = 62$)	Control group ($n = 31$)
Age (y)	63 ± 11	66 ± 3
Weight (kg)	64.8 ± 15.5	70.4 ± 11.3
BMI (kg/m^2)	24.6 ± 5.2	25.1 ± 2.6
Fat-free mass (kg)	46.9 ± 11.6	48.8 ± 9.7
Measured REE		
(kJ/d)	6527.5 ± 1430.8	5926.0 ± 797.1[2]
(kcal/d)	1561.6 ± 342.3	1417.7 ± 190.7[2]
RQ	0.81 ± 0.04	0.79 ± 0.03
REE/FFM (kcal/kg/d)	33,3	29,1

(Desport JC. AJCN 2001)

SLA versus témoin?

- Etude en cours (CHU Limoges)

	ALS (n=315)	Control (n=134)	p
Age (years)	64.4 ± 12.2	70.9 ± 12.2	0.0002
BMI (kg/m^2)	25.0 ± 4.5	25.6 ± 4.8	ns
FFM (kg)	45.1 ± 10.0	43.6 ± 12.1	ns
REEm (kcal/d)	1514.0 ± 298.7	1272.0 ± 260.9	<0.0001
REE variation (%)	11.8 ± 12.5	-0.5 ±12.0	<0.0001
REE/FFM (kcal/kg/d)	34.1 ± 5.1	30.1 ± 5.3	<0.0001

(Jésus P. Données non publiées)

SLA versus témoin?

- Etude en cours (CHU Limoges)

	ALS no hypermetabolism (n=141)	Control no hypermetabolism (n=115)	p
Age (years)	64.2 ± 13.3	70.9 ± 11.9	0.0046
BMI (kg/m^2)	25.3 ± 5.0	25.7 ± 4.9	ns
FFM (kg)	43.9 ± 10.2	43.6 ± 12.5	ns
REEm (kcal/d)	1369.0 ± 267.2	1237.0 ± 242.3	0.0005
REE variation (%)	1.0 ± 6.6	-0.4 ± 8.4	<0.0001
REE/FFM (kcal/kg/d)	31.7 ± 4.4	29.5 ± 5.2	<0.0001

(Jésus P. Données non publiées)

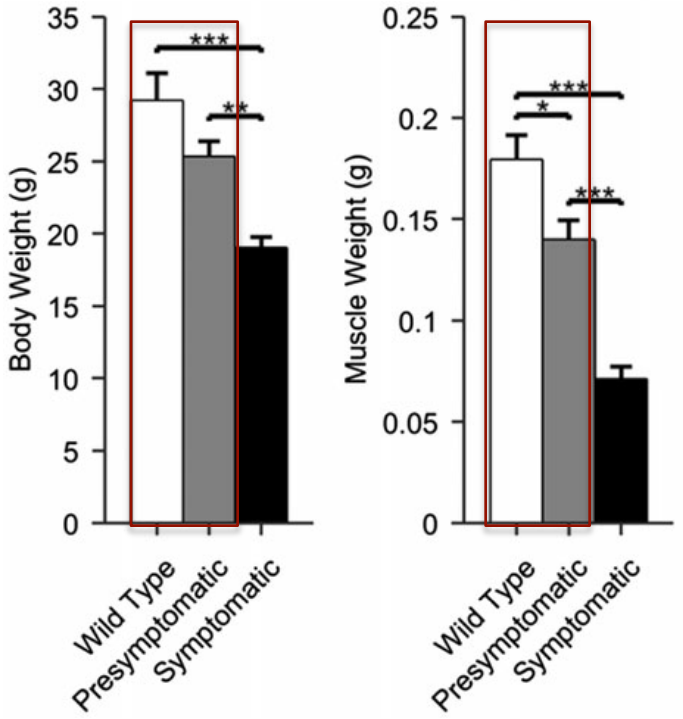
Conclusion 1

- L'hypermétabolisme semble bien exister.
- Repérage simple : DER calo vs H&B.
- DER/MM : SLA vs témoins
  - Toujours hypermétabolisme.
  - Perturbations métaboliques chez tous les patients SLA.

Quand débute l'hypermétabolisme?

Single and modeled multifrequency electrical impedance myography parameters and their relationship to force production in the ALS SOD1G93A mouse

Jia Li, Adam Pacheck, Benjamin Sanchez & Seward B. Rutkove



Possible en présymptomatique

(Li J. ALS 2016)

Quand débute l'hypermétabolisme?

Effect of Presymptomatic Body Mass Index and Consumption of Fat and Alcohol on Amyotrophic Lateral Sclerosis

Mark H. B. Huisman, MD[1]; Meinie Seelen, MD, PhD[1]; Perry T. C. van Doormaal, MD[1]; Sonja W. de Jong, MD, PhD[1]; Jeanne H. M. de Vries, PhD[2]; Anneke J. van der Kooi, MD, PhD[3]; Marianne de Visser, MD, PhD[3]; H. Jurgen Schelhaas, MD, PhD[4]; Leonard H. van den Berg, MD, PhD[1]; Jan H. Veldink, MD, PhD[1]

- **Results** Presymptomatic total daily energy intake in patients, reported as mean (SD), was significantly higher compared with controls (2258 [730] vs 2119 [619] kcal/day; *P* < .01), and **presymptomatic body mass index** (calculated as weight in kilograms divided by height in meters squared) **was significantly lower in patients (25.7 [4.0] vs 26.0 [3.7]; *P* = .02)**…

- **Conclusions and Relevance** The combination of independent positive associations of a low premorbid body mass index and a high fat intake together with prior evidence from ALS mouse models transgenic for *SOD1* and earlier reports on **premorbid body mass index support a role for increased resting energy expenditure before clinical onset of ALS**.

Possible en présymptomatique

(Huisman M. JAMA Neurol. 2015)

Comment évolue le métabolisme énergétique?

Variable	Nb values for ANOVA	M0 n=28	M6	M12	*P* value*
MMT (/150)	27	129.8 ± 19.2	117.5 ± 29.0	103.6 ± 34.1	<0.0001
ALS-FRS (/40)	27	32.2 ± 4.4	26.4 ± 8.3	21.0 ± 9.2	<0.0001
Weight (kg)	28	63.3 ± 12.0	61.8 ± 11.4	60.7 ± 10.4	<0.0001
BMI (kg/m^2)	28	23.6 ± 3.6	22.6 ± 3.2	22.3 ± 3.2	<0.0001
FFM (kg)	22	46.0 ± 10.9	43.9 ± 9.8	41.5 ± 9.1	<0.0001
mREE (kcal/24 h)	20	1484.5 ± 382.1	1424.8 ± 257.4	1457.0 ± 237.5	0.18
cREE (kcal/24 h)	23	1357.5 ± 210.0	1336.6 ± 207.0	1319.8 ± 193.9	0.0001
(mREE–cREE)/cREE (%)	20	9.17 ± 10.90	7.32 ± 9.87	8.78 ± 12.49	0.19
mREE/FFM (kcal/kg day^{-1})	16	32.6 ± 4.1	32.7 ± 4.0	35.3 ± 5.4	0.01
[(mREE–cREE)/cREE]/FFM	16	0.15 ± 0.26	0.11 ± 0.22	0.22 ± 0.30	0.31
FVC (% theoretical)	24	92.1 ± 21.3	81.7 ± 23.9	66.7 ± 27.7	<0.0001
PEFR (% theoretical)	25	78.5 ± 25.5	68.7 ± 21.0	53.6 ± 25.8	<0.0001
Albumin (g/l)	25	40.4 ± 5.7	39.5 ± 5.5	38.9 ± 5.1	0.29

- **77,8%** même statut métabolique

(Bouteloup C. J Neurol 2009)

Comment évolue le métabolisme énergétique?

Do patients with amyotrophic lateral sclerosis (ALS) have increased energy needs?

Nachum Vaisman [a,*], Michal Lusaus [a], Beatrice Nefussy [b], Eva Niv [a], Doron Comaneshter [c], Ron Hallack [d], Vivian E. Drory [b]

n=33 n=10 at 6 months

Parameter	Measurement 1	Measurement 2	*P*-value
Weight, kg	63.5 ± 11.8 (66.5)	60.7 ± 10.2 (65.0)	0.098
BMI, kg/ht^2	23.5 ± 4.3 (22.0)	22.4 ± 3.4 (21.7)	0.074
LBM, kg	39.8 ± 7.9 (39.1)	36.4 ± 7.8 (35.9)	0.002
Body fat, %	34.9 ± 10.5 (34.6)	37.1 ± 10.6 (37.8)	0.13
REEm, kcal/d	1427 ± 219 (1480)	1387 ± 237 (1431)	0.105
REEPP, %	103.9 ± 10.3 (103.4)	103.1 ± 8.4 (102.8)	0.85
REE/LBM (kcal/kg)	36.0 ± 5.3 (35.4)	38.9 ± 5.0 (38.5)	0.02
RQ	0.80 ± 0.06 (0.81)	0.79 ± 0.05 (0.81)	0.53
ALSFRS-R	34.10 ± 6.82 (32.0)	29.1 ± 7.52 (28.5)	0.002

(Vaisman N. J Neurol Sci 2009)

Comment évolue le métabolisme énergétique?

Hypermetabolism in ALS: Correlations with Clinical and Paraclinical Parameters

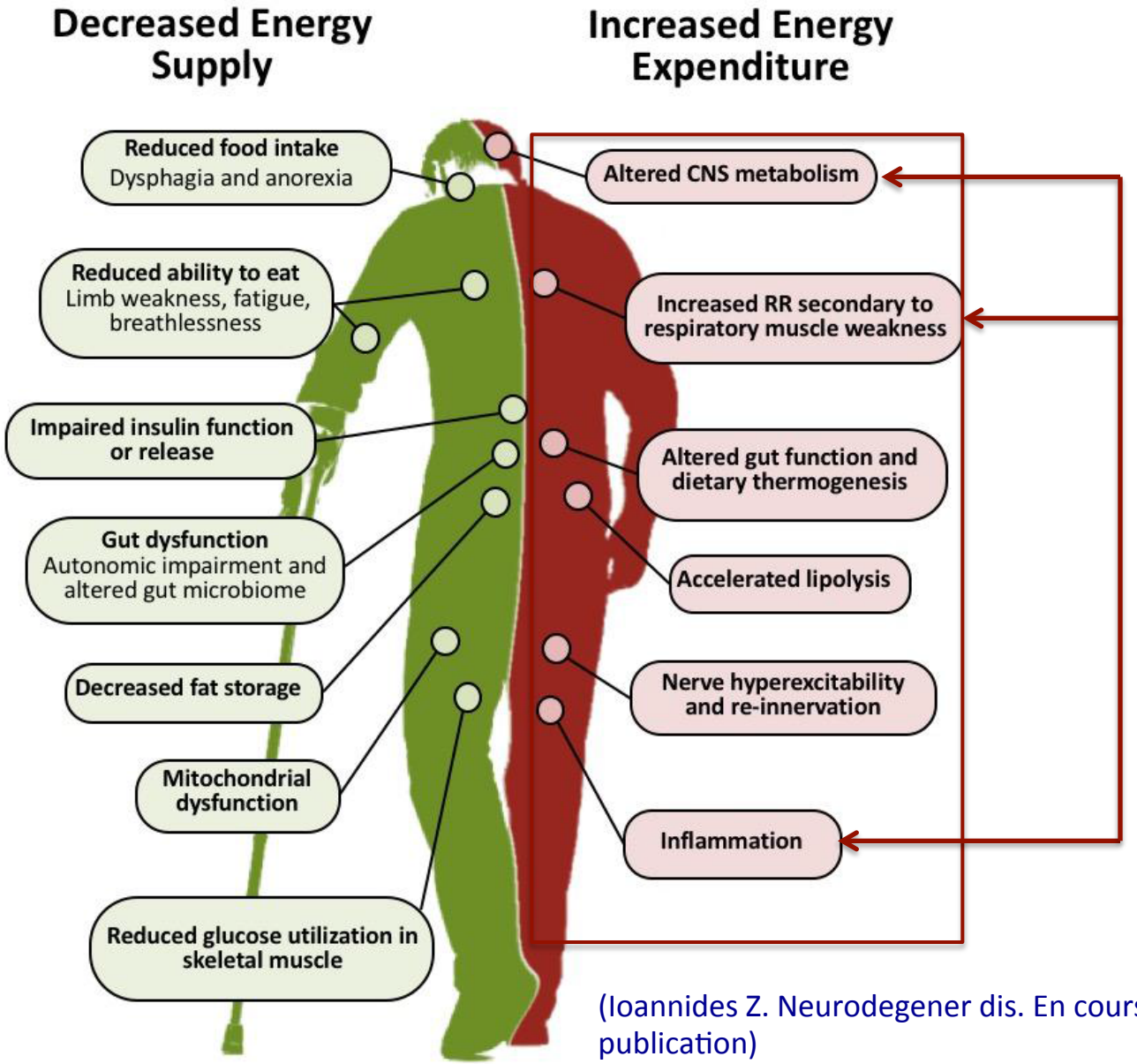
Jean-Claude Desport[a–c] Frédéric Torny[a] Mathieu Lacoste[a]
Pierre-Marie Preux[c] Philippe Couratier[a,c]

Criteria n=44	T_1	T_2 332j	p
MMT/150	121.8	92.8	<0.0001
ALSFRS/40	32.1	22.0	<0.0001
VC, %	87.6	65.1	<0.0001
Weight, kg	65.1	62.8	<0.01
BMI, kg/m^2	24.6	23.7	<0.005
FFM, kg	42.4	41.2	NS
mREE, kcal	1,523.0	1,465.8	<0.01
ΔREE	13.1	12.1	NS
Hypermetabolism, %	56.8	47.7	NS
Respiratory quotient	0.8	0.8	NS
Phase angle, °	3.3	2.7	<0.001

(Desport JC. Neurodegener Dis 2005)

Quels mécanismes en rapport avec l'hypermétabolisme?

- Hypothèses

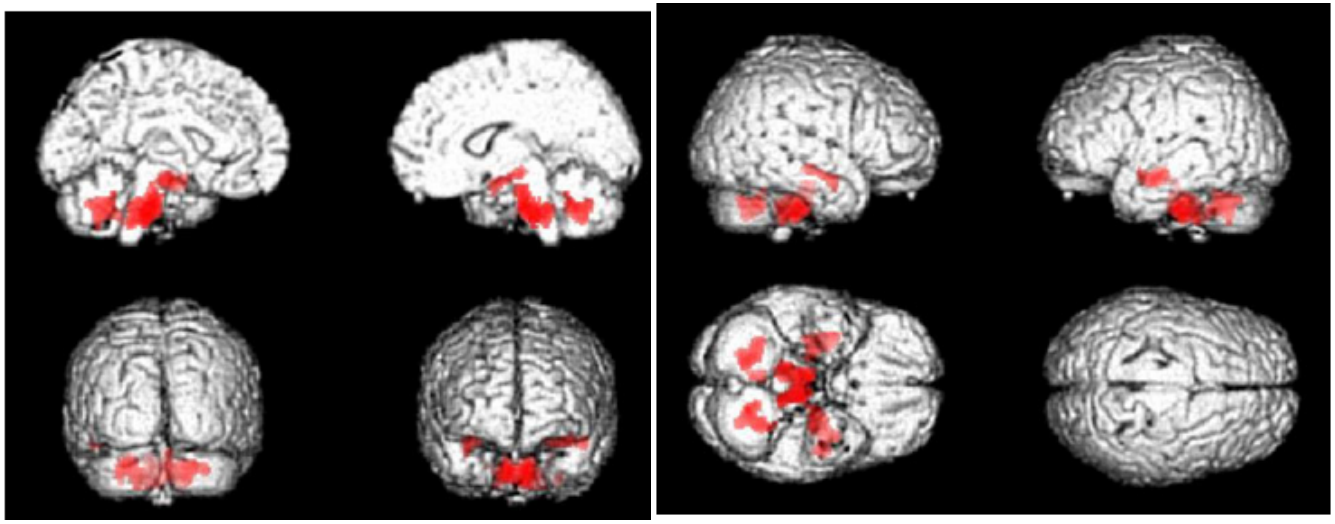


(Ioannides Z. Neurodegener dis. En cours de publication)

- Hypothèse ↗ métabolisme glucidique cérébral

Brain hypermetabolism in amyotrophic lateral sclerosis: a FDG PET study in ALS of spinal and bulbar onset

Angelina Cistaro · Maria Consuelo Valentini · Adriano Chiò · Flavio Nobili · Andrea Calvo · Cristina Moglia · Anna Montuschi · Silvia Morbelli · Dario Salmaso · Piercarlo Fania · Giovanna Carrara · Marco Pagani



Amygdale
Mésencéphale
Pont
Amygdale cérébéleuse
Globus pallidus

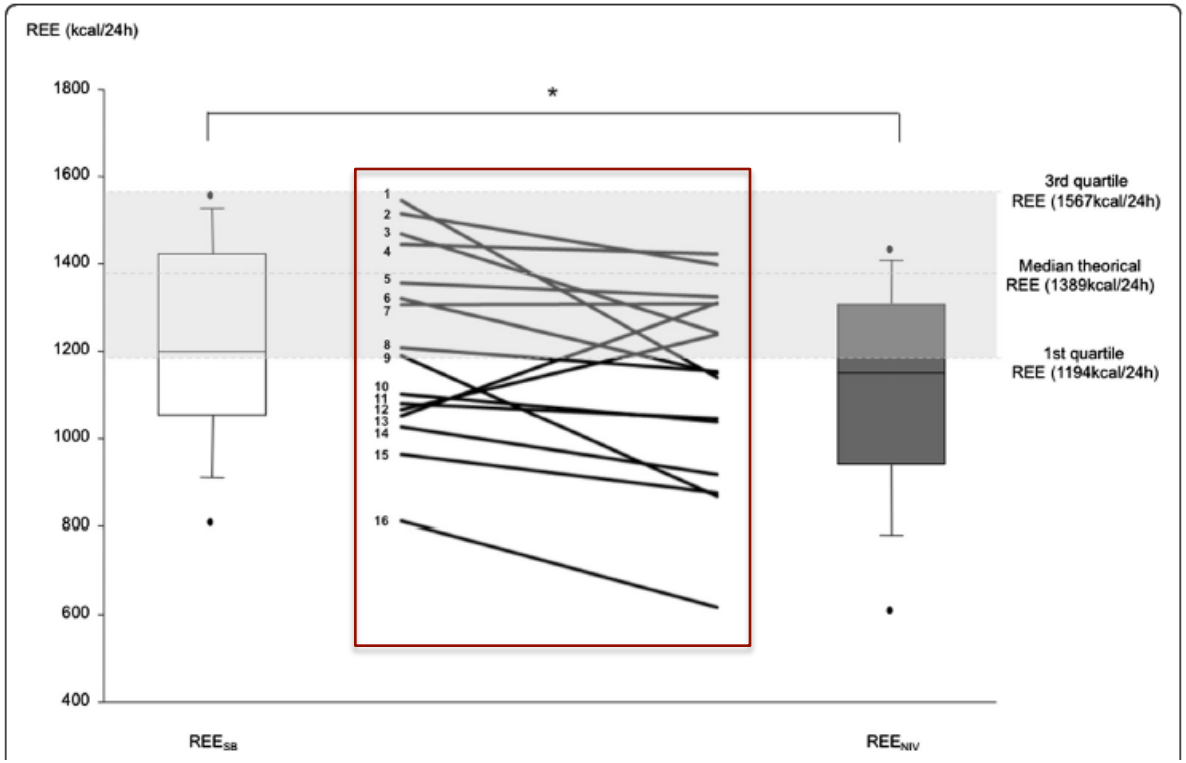
…mais lien incertain avec DER

(Cistaro A. Eur J Nucl Med Mol Imaging 2012)

- Hypothèse respiratoire : ↗ travail resp ⇒↗ DER
  - mais pas de corrélation entre DER et CVF

biais ? ➔ CVF moins sensible que le SNIFF test

➔ diminution de la DER sous VNI



(Desport JC. Neurodegener Dis 2005 ; Bouteloup C. J Neurol 2009 ; Georges M. BMC pulm med. 2014)

- Hypothèses inflammation, adipokines ⇒↗ DER

Altered expression of metabolic proteins and adipokines in patients with amyotrophic lateral sclerosis☆

S.T. Ngo [a,b,c,d,*,1], F.J. Steyn [a,c,1], L. Huang [a], S. Mantovani [a,e], C.M.M. Pfluger [c], T.M. Woodruff [a], J.D. O'Sullivan [d,f], R.D. Henderson [d], P.A. McCombe [c,d,f]

	Control	95% CI (range)	ALS	95% CI (range)	p
Adipokines					
Adiponectin (mg/ml)	26.7 (22.7)	18.7–34.8	40.1 (45.4)	29.1–51.2	<0.05*
HGF (pg/ml)	352.9 (211.3)	279–426	401.0 (260.2)	338–464	0.35
IL-6 (pg/ml)	3.0 (2.4)	2.07–3.81	9.0 (22.4)	3.59–145	<0.05*
IL-8 (pg/ml)	3.1 (2.5)	2.23–3.97	4.6 (2.6)	3.93–5.21	<0.01**
Leptin (ng/ml)	17.2 (27.2)	7.51–26.8	15.0 (27.5)	8.25–21.7	0.71
Lipocalin-2 (ng/ml)	104.3 (40.8)	90.1–119	123.9 (40.9)	114–134	<0.05*
MCP-1 (pg/ml)	161.6 (76.1)	135–188	164.6 (76.8)	146–183	0.83
NGF (pg/ml)	8.0 (4.1)	6.59–9.45	10.3 (21.9)	4.98–15.6	0.55
PAI-1 (ng/ml)	55.5 (39.8)	41.6–69.3	95.9 (60.6)	81.2–111	<0.01**
Resistin (ng/ml)	57.6 (37.0)	44.7–70.5	66.2 (39.3)	56.7–75.7	0.30
TNFα (pg/ml)	3.1 (1.4)	2.59–3.56	3.7 (1.4)	3.40–4.07	<0.01**

(Ngo ST. J Neurol Sci 2015)

Quelles sont les conséquences de l'hypermétabolisme?

- Sur le statut nutritionnel

Hypermetabolism in ALS patients: an early and persistent phenomenon

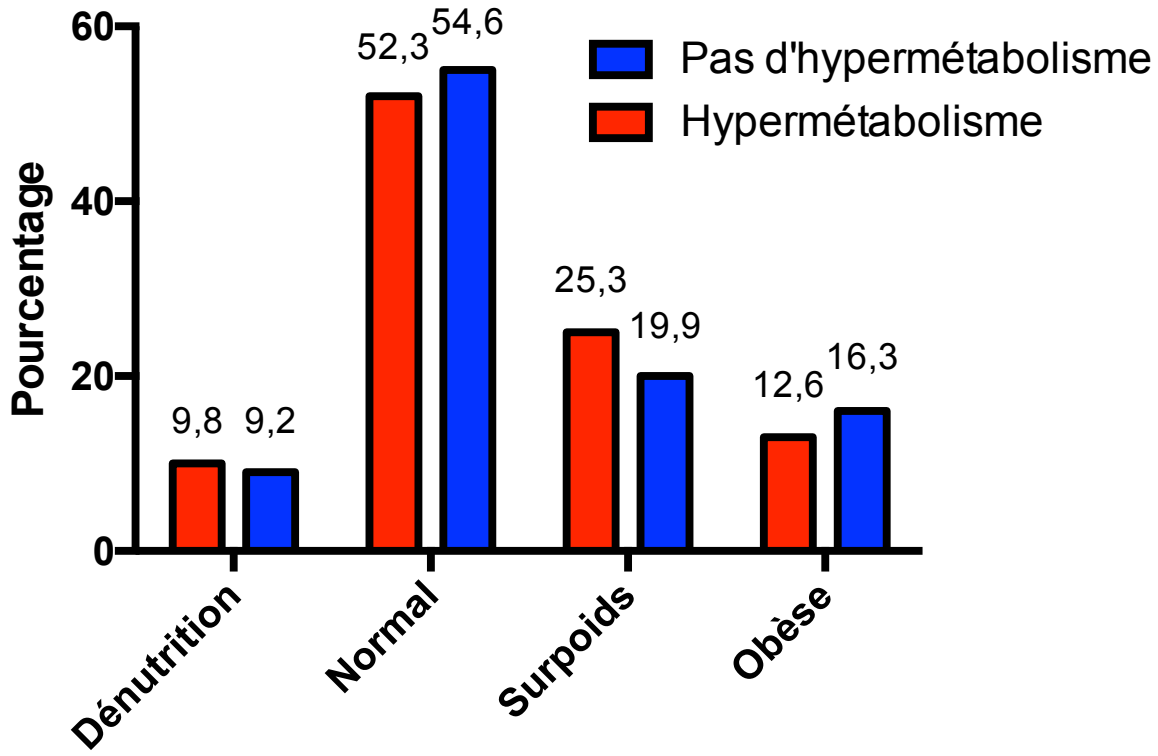
C. Bouteloup · J.-C. Desport · P. Clavelou · N. Guy · H. Derumeaux-Burel · A. Ferrier · P. Couratier

Variable	Normometabolic patients $n = 32$	Hypermetabolic patients $n = 29$	P value*
BMI (kg/m^2)	23.2 ± 3.8	22.2 ± 3.9	NS
Weight variation (%)	−6.9 ± 7.3	−5.9 ± 7.9	NS
FFM (kg)	37.6 ± 12.7	41.7 ± 10.4	NS

(Bouteloup C. J Neurol. 2009)

- Sur le statut nutritionnel

Etude en cours (CHU Limoges) n=315 ; ns



(Jésus P. Données non publiées)

- Sur le statut nutritionnel

Etude en cours (CHU Limoges)

	Hypermetabolism Median (IQR) (n=174)	No hypermetabolism Median (IQR) (n=141)	p
Weight (kg)	64.8 (58.0 – 74.3)	65.4 (57.0 – 74.9)	0.93
BMI (kg/m^2)	24.1 (22.2 – 27.3)	24.4 (21.8 – 27.9)	0.83
Weight loss (%)	-5.3 (-9.9 – 0.4)	-4.9 (-10.9 – -0.1)	0.95
TSF (mm)	12.1 (8.9 – 18.3)	14.4 (10.3 – 19)	0.043
FFM (kg)	45.2 (37.9 – 52.0)	42,5 (36.0 – 51.5)	0.059
FFM (%)	69.3 (62.5 – 77.0)	67.9 (59.3 – 73.9)	0.034
FM (kg)	20.1 (15.2 – 25.0	20.9 15.5 – 26.7)	0.17
FM (%)	30.7 (23.0 – 37.5)	32.1 (26.1 – 40.7)	0.034
PA (°)	3.0 (2.5 – 3.6)	3.0 (2.3 – 3.7)	0.24

Modification composition corporelle

(Jésus P. Données non publiées)

- Sur le statut nutritionnel au cours du suivi (15,4 ± 15,1mois)

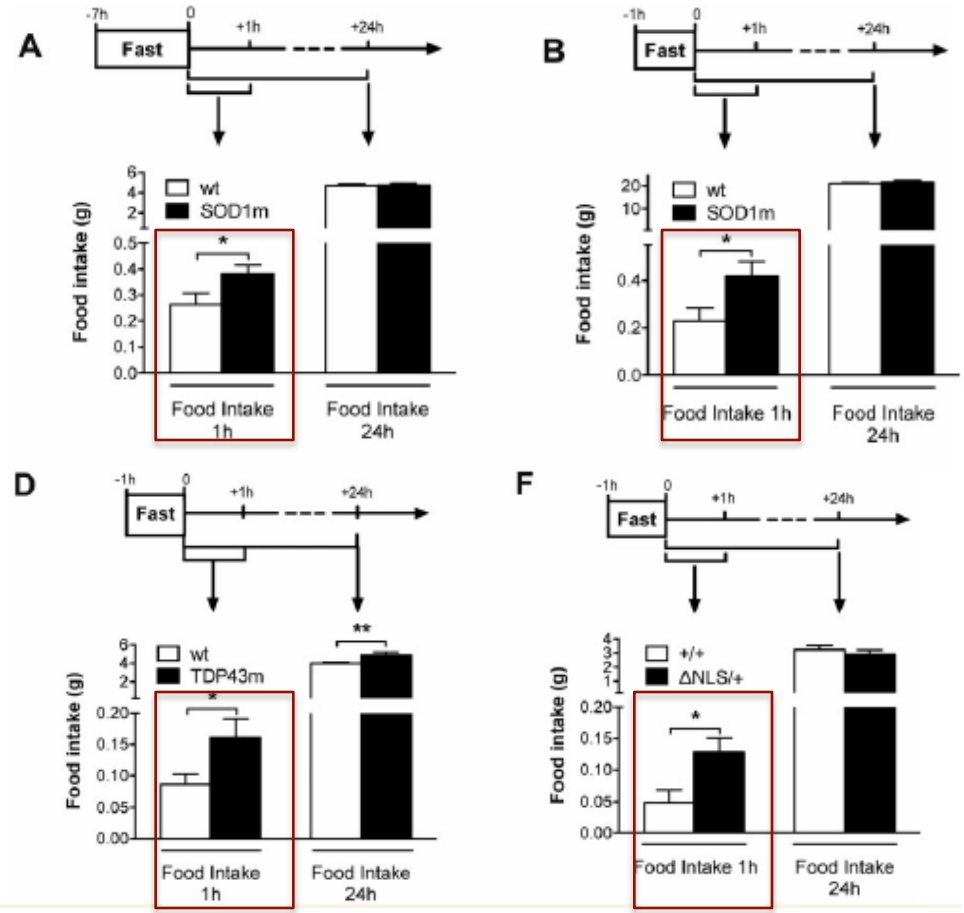
Etude en cours (CHU Limoges)

Variation	Hypermetabolism Median (IQR) (n=174)	No hypermetabolism Median (IQR) (n=141)	p
Weight (%)	-2.5 (-9.7 – 3.7)	-2.1 (-9.4 – 4.1)	0.74
BMI (kg/m^2)	-0.6 (-2.3 – 0.8)	-0.6 (-2.5 – 1.0)	0.78
FFM (kg)	-18.1 (-22.4 – 14.0	-17.0 (-21.5 – 12.6)	0.34
FFM (%)	82.0 (51.9 – 127.3)	69.3 (56.1 – 110.2)	0.38
FM (kg)	16.7 (11.8 – 21.1	14.1 (11.7 – 19.3)	0.45
FM (%)	-40.3 (-43.1 – -36.0)	-38.4 (-41.9 – -33.0)	0.38
PA (°)	-0.7 (-1.6 – -0.2)	-1.0 (-1.3 – -0.4)	0.51

Pas de différence

(Jésus P. Données non publiées)

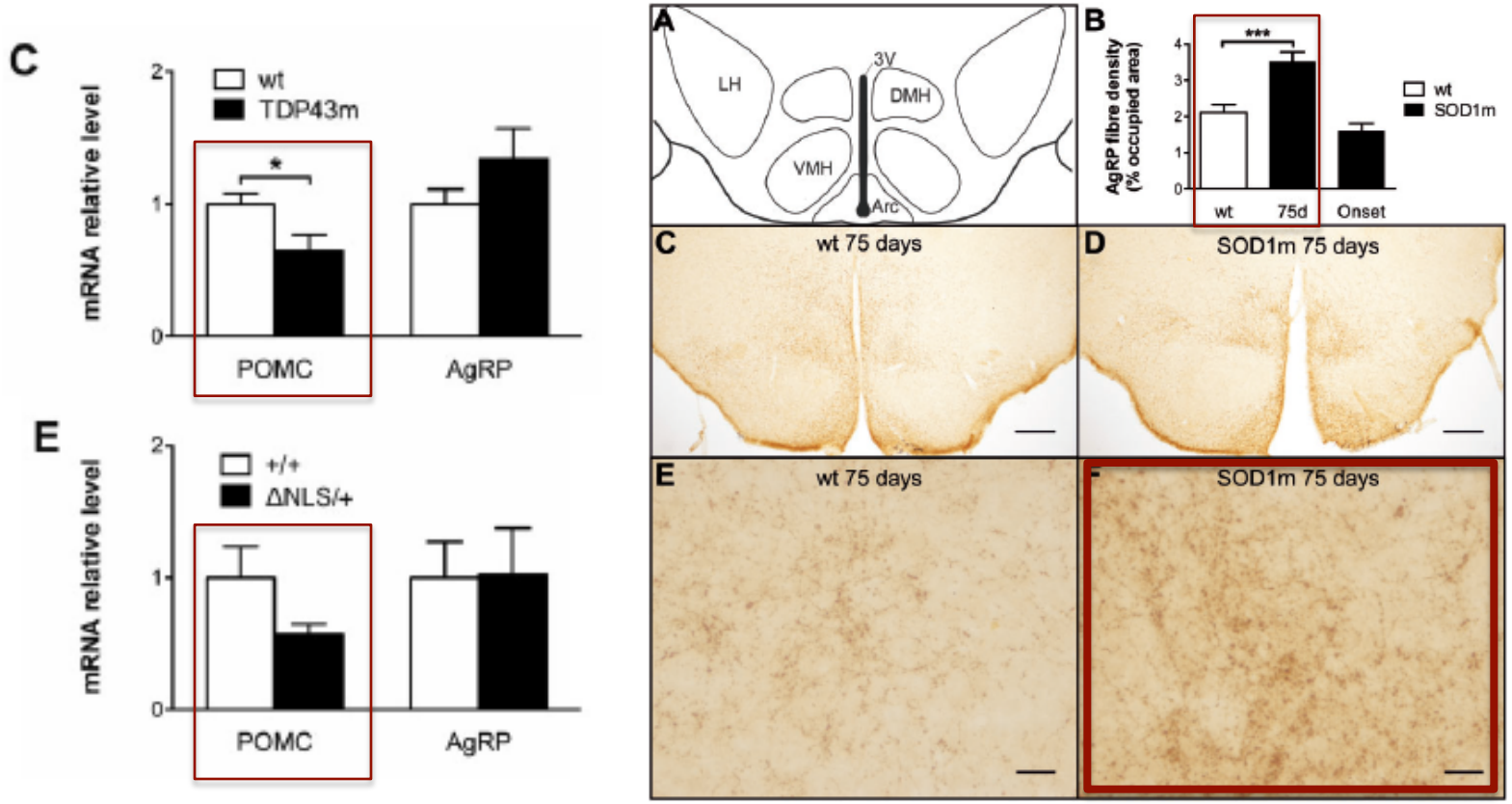
- Sur la prise alimentaire



↗ prise alimentaire après le jeûne

(Vercruysse P. Brain 2016)

- Sur la prise alimentaire



(Vercruysse P. Brain 2016)

- Sur la prise alimentaire

Altered expression of metabolic proteins and adipokines in patients with amyotrophic lateral sclerosis☆

S.T. Ngo [a,b,c,d,*,1], F.J. Steyn [a,c,1], L. Huang [a], S. Mantovani [a,e], C.M.M. Pfluger [c], T.M. Woodruff [a], J.D. O'Sullivan [d,f], R.D. Henderson [d], P.A. McCombe [c,d,f]

	Control	95% CI (range)	ALS	95% CI (range)	p
Metabolic factors					
Amylin (pg/ml)	26.3 (14.4)	21.3–31.4	31.8 (36.3)	23.0–40.6	0.40
c-Peptide (ng/ml)	3.4 (1.9)	2.69–4.05	3.7 (5.5)	2.39–5.05	0.72
Ghrelin (pg/ml)	25.1 (28.2)	15.3–35.0	13.2 (11.2)	10.5–15.9	<0.01**
GIP (ng/ml)	0.4 (0.3)	0.303–0.484	0.3 (0.3)	0.21–0.33	<0.01**
GLP-1 (pg/ml)	30.3 (35.7)	345–627	28.5 (30.7)	230–379	0.80
Glucagon (pg/ml)	44.1 (34.1)	31.6–56.6	37.7 (24.1)	31.8–43.7	0.30
Insulin (pg/ml)	53.4 (46.4)	37.2–69.6	46.6 (51.7)	34.1–59.1	0.52
PP (pg/ml)	485.7 (404.0)	345–627	304.5 (305.5)	231–378	<0.01**
PYY (pg/ml)	172.8 (123.2)	130–216	158.9 (107.3)	133–185	0.56
Leptin (ng/ml)	17.2 (27.2)	7.51–26.8	15.0 (27.5)	8.25–21.7	0.71

(Ngo ST. J Neurol Sci 2015)

• Sur la prise alimentaire

Effect of Presymptomatic Body Mass Index and Consumption of Fat and Alcohol on Amyotrophic Lateral Sclerosis

Mark H. B. Huisman, MD[1]; Meinie Seelen, MD, PhD[1]; Perry T. C. van Doormaal, MD[1]; Sonja W. de Jong, MD, PhD[1]; Jeanne H. M. de Vries, PhD[2]; Anneke J. van der Kooi, MD, PhD[3]; Marianne de Visser, MD, PhD[3]; H. Jurgen Schelhaas, MD, PhD[4]; Leonard H. van den Berg, MD, PhD[1]; Jan H. Veldink, MD, PhD[1]

- **Results** : **Presymptomatic total daily energy intake** in patients, reported as mean (SD), was **significantly higher compared with controls (2258 [730] vs 2119 [619] kcal/day; *P* < . 01**), and presymptomatic body mass index (calculated as weight in kilograms divided by height in meters squared) was significantly lower in patients (25.7 [4.0] vs 26.0 [3.7]; *P* = .02). With values reported as odds ratio (95% CI), higher premorbid intake of total fat (1.14; 1.07-1.23; *P* < .001), saturated fat (1.43; 1.25-1.64; *P* < .001), *trans*-fatty acids (1.03; 1.01-1.05; *P* < .001), and cholesterol (1.08; 1.05-1.12; *P* < .001) was associated with an increased risk of ALS; higher intake of alcohol (0.91; 0.84-0.99; *P* = .03) was associated with a decreased risk of ALS. These associations were independent of total energy intake, age, sex, body mass index, educational level, smoking, and lifetime physical activity. No significant associations between dietary intake and survival were found.

↗ prise alimentaire en présymptomatique

(Huisman MB. JAMA Neurol 2015)

- Sur la prise alimentaire

Hypermetabolism in ALS patients: an early and persistent phenomenon

C. Bouteloup · J.-C. Desport · P. Clavelou · N. Guy · H. Derumeaux-Burel · A. Ferrier · P. Couratier

Variable	Normometabolic patients $n = 32$	Hypermetabolic patients $n = 29$	P value*
Energy intake (kcal/day)	1581.6 ± 539.6	1954.0 ± 511.8	0.02
Protein intake (g/kg day^{-1})	1.26 ± 0.27	1.57 ± 0.46	0.007

↗ prise alimentaire

En cas d'hypermétabolisme

(Bouteloup C. J Neurol 2009)

- Sur la fonction

Hypermetabolism in ALS patients: an early and persistent phenomenon

C. Bouteloup · J.-C. Desport · P. Clavelou · N. Guy · H. Derumeaux-Burel · A. Ferrier · P. Couratier

Variable	Normometabolic patients $n = 32$	Hypermetabolic patients $n = 29$	P value*
MMT (/150)	120.6 ± 17.0	120.2 ± 20.2	NS
ALS-FRS (/40)	28.6 ± 4.9	29.3 ± 4.7	NS
FVC (% theoretical)	71.8 ± 26.9	76.0 ± 22.0	NS
PEFR (% theoretical)	65.3 ± 23.4	74.6 ± 29.6	NS

Pas de différence

(Bouteloup C. J Neurol 2009)

- Sur la fonction

Etude en cours (CHU Limoges)

	Hypermetabolism Median (IQR) (n=174)	No hypermetabolism Median (IQR) (n=141)	p
ALSFRS-R (points)	41.0 (35.0 – 43.0)	38.0 (32.0 – 42.0)	0.013
MMT (points)	137.0 (123.0 – 145.0)	133.0 (116.0 – 143.0)	0,25
SVC (%)	93.0 (71.0 – 111.0)	92.0 (75.0 – 108.0)	0.98
FVC (%)	91.5 (68.0 – 109.0)	89.0 (73.0 – 103.0)	0.58
SNIFF (%)	50.0 (29.0 – 70.0)	54.0 (41.0 – 71.3)	0.089

Interprétation ?

(Jésus P. Données non publiées)

- Sur la fonction au cours du suivi

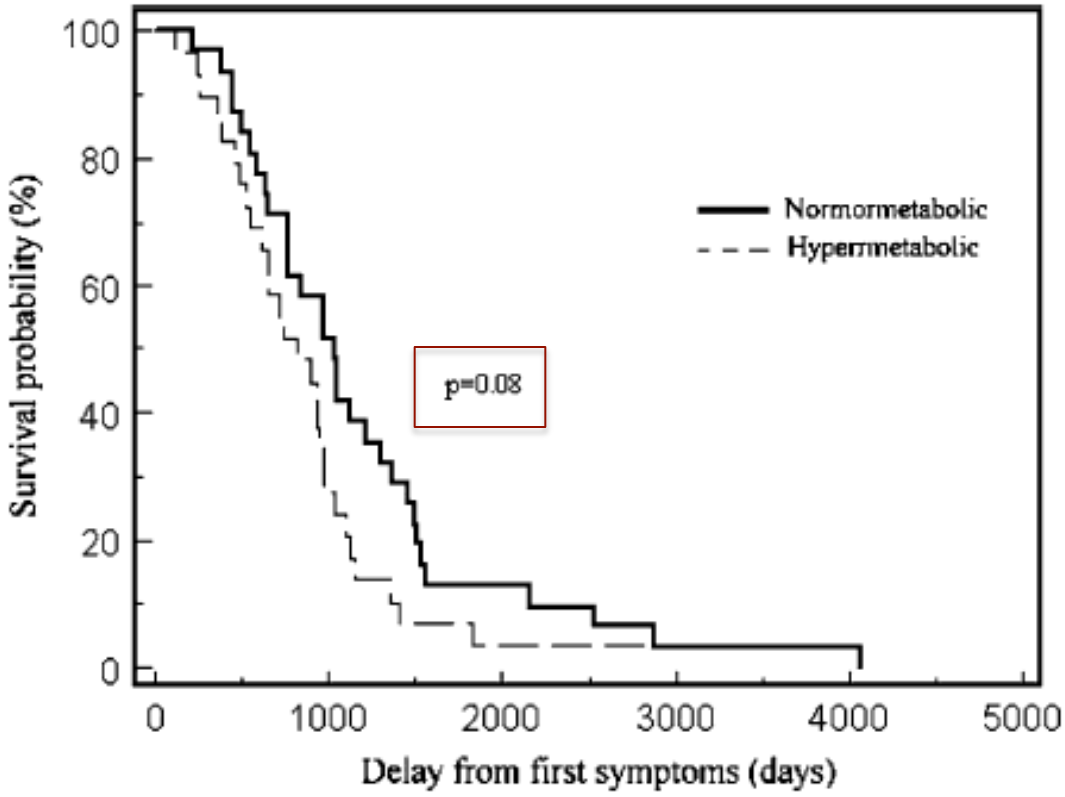
Etude en cours (CHU Limoges)

	Hypermetabolism Median (IQR) (n=174)	No hypermetabolism Median (IQR) (n=141)	p
ALSFRS-R slope (points/month)	-1.3 (-2.0 – -0.7)	-1.0 (-1.6 – -0.5)	0.032
MMT (points)	-35.0 (-55.0 – -17.0)	-39.0 (-55.0 – -22.0)	0.33
SVC (%)	-35.0 (-58.0 – -15.0)	-30.0 (-49.0 – -12.0)	0.11
FVC (%)	-36.0 (-59.0 – -15.0)	-28.0 (-47.0 – -12.0)	0.054
SNIFF (%)	-20.0 (-39.0 – -7.0)	-19.0 (-31.5 – -4.5)	0.25

Altération fonctionnelle

(Jésus P. Données non publiées)

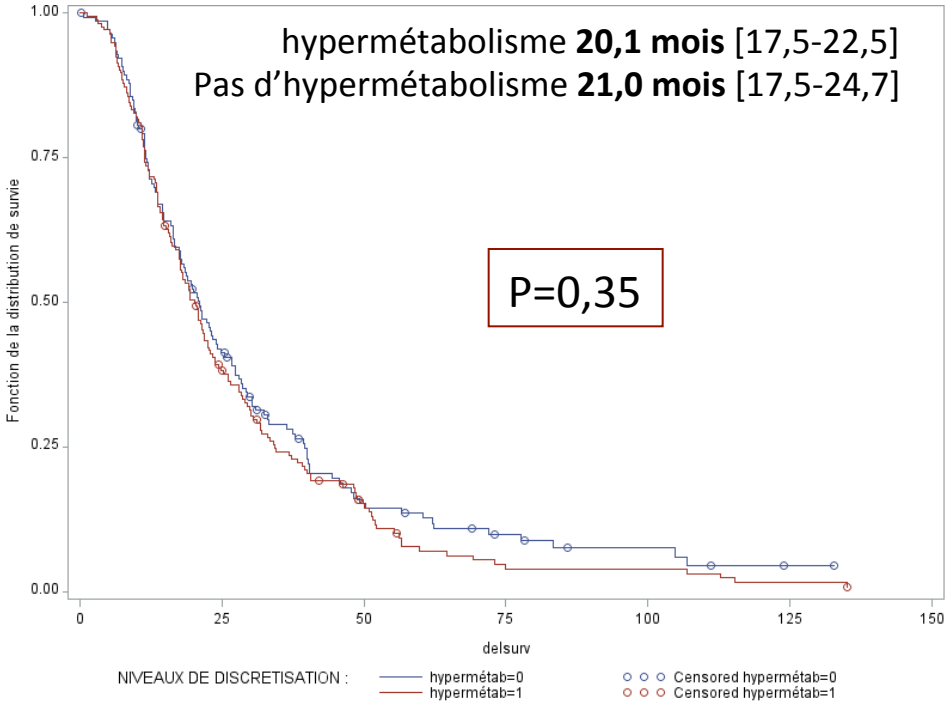
- Sur la survie

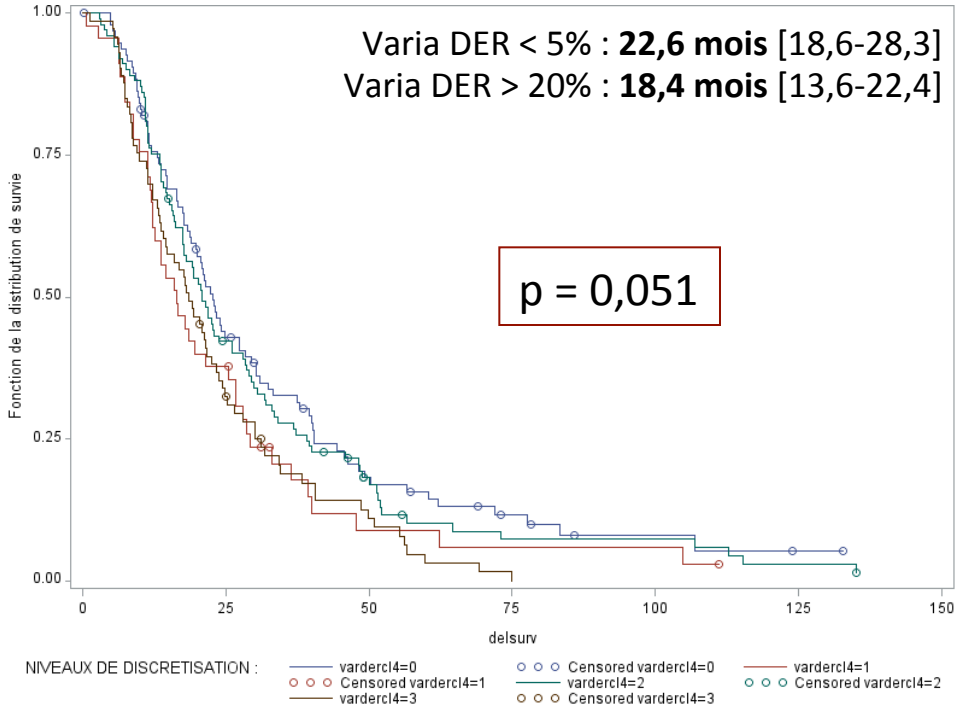


(Bouteloup C. J Neurol 2009)

- Sur la survie

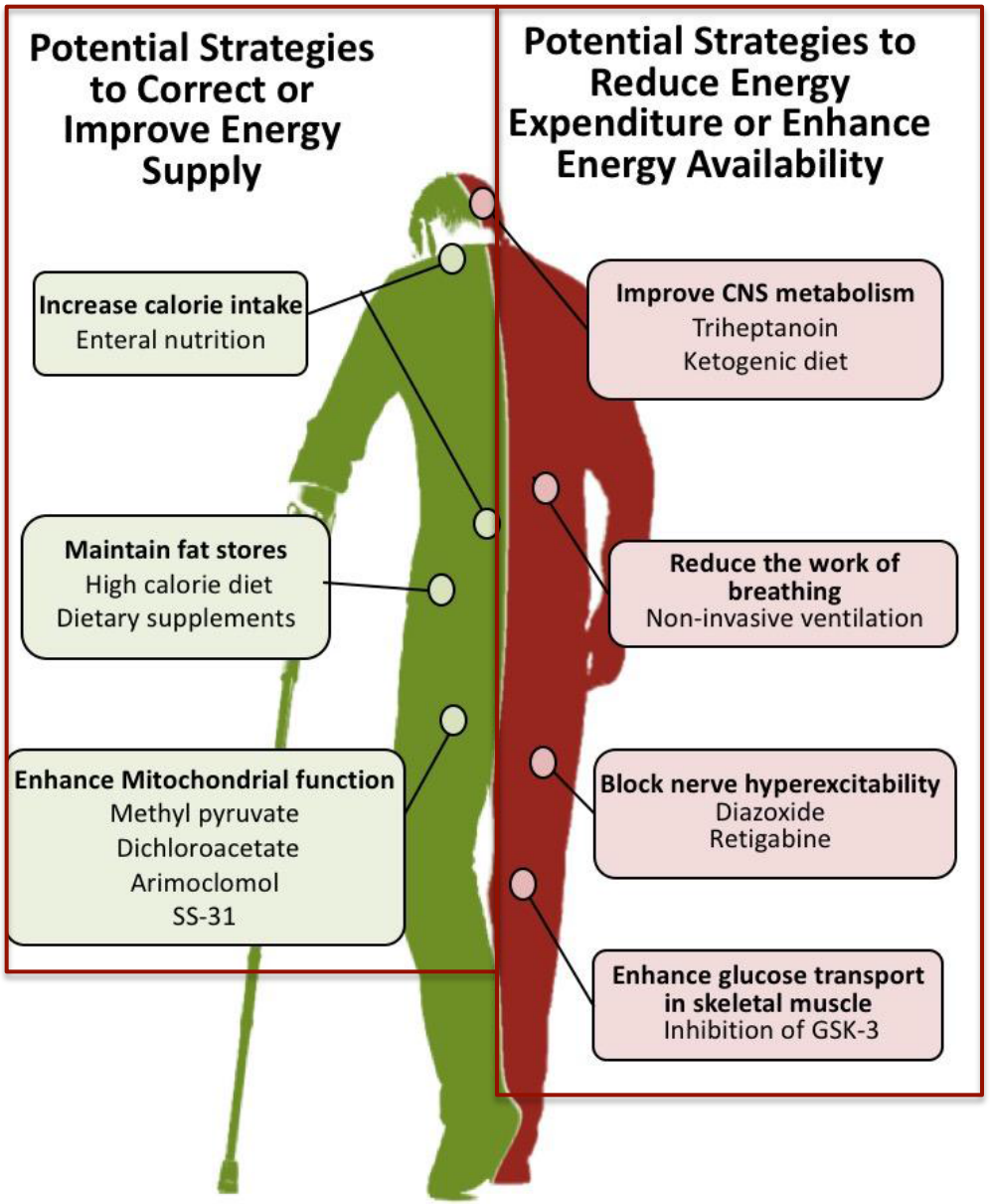
Etude en cours (CHU Limoges)





(Jésus P. Données non publiées)

Quelle prise en charge?



(Ioannides Z. Neurodegener dis. En cours de publication ; recommandations HAS. 2006)

- Augmenter les apports énergétiques et maintenir la masse grasse

- Alimentation hyperénergétique
  (Enrichissement alimentaire, CNO, nutrition entérale)
- Apports énergétiques : **35 kcal/j**

- Clinical trial :
  - Oral nutritional supplementation in als patients (NUTRALS)
  - Efficacy, safety and tolerability of high lipid and calorie supplementation in amyotrophic lateral sclerosis

(Recommandations HAS 2006 ; Kasarskis E. AJCN 2014)

- Améliorer la fonction mitochondriale

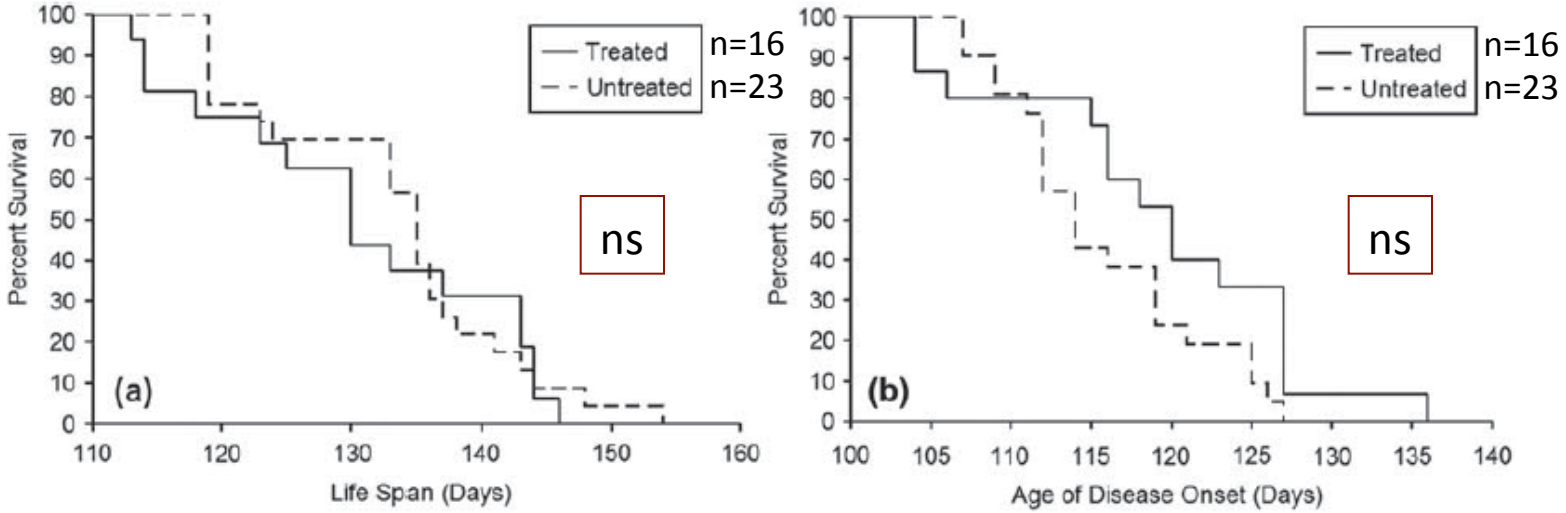
- Phase III : dexpramipexole
- Phase II : Coenzyme Q10
- Etude pilote : Acide tauroursodeoxycholique

➔**PAS DE BENEFICE**

(Mora JS. Lancet Neurol 2013 ; Kaufmann P. Ann Neurol 2009 ; Elia AE. Eur J Neurol 2016)

- Diminuer la dépense énergétique

- Souris SOD1-G93A
- Prise per os méthimazole + sucralose (à 35j)



- T4 libre corrélé à une survie plus longue (r=0,43, p=0,025)

(Li J. ALS 2012)

- Autre substrat énergétique neuronal

- Place de la diète cétogène ?

- Clinical trial : Safety and tolerability of the ketogenic diet in amyotrophic lateral sclerosis

(Zhao W. BMC Neurosci 2006 ; Ari C. PLoS One 2014)

- Diminuer l'hyperexitabilité neuronale

- Phase II : talampanel
- Phase II/III : memantine

➔**PAS DE BENEFICE**

- Phase II : retigabine, en cours
  - ClincalTrials : Clinical trial of ezogabine (retigabine) in als subjects

(Pascuzzi RM. ALS 2010 ; De Carvalho M. ALS 2010)

Conclusion 2

- Hypermétabolisme dans 50%.
- Mais probablement perturbations métaboliques chez tous les patients SLA.
- Impact sur la composition corporelle et l'évolution fonctionnelle mais pas sur la survie.
- Prise en charge…nutritionnelle+++

Remerciements

- Patients atteints de SLA
- Unité de Nutrition (CHU limoges) : Mme Sourisseau
- Centre SLA (CHU de Limoges) : Mme Nicol
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Pr Boirie et Dr Walrand

- Unité de Nutrition (CHU Rouen) : Dr Coëffier