SFRP - Paris, 24 Janvier 2011

Expression de marqueurs de stress dans le cerveau et le sang de rats exposés *in utero* à un signal Wi-Fi

isabelle.lagroye@ims-bordeaux.fr

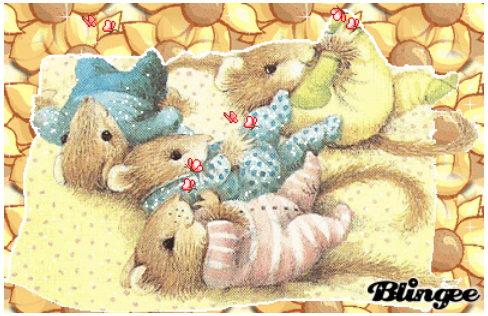
Laboratoire de Bioélectromagnétisme EPHE , Laboratoire IMS - UMR 5218

ENSCBP Pessac, France

Question

LES ENFANTS: Population à risque plus élevé ?

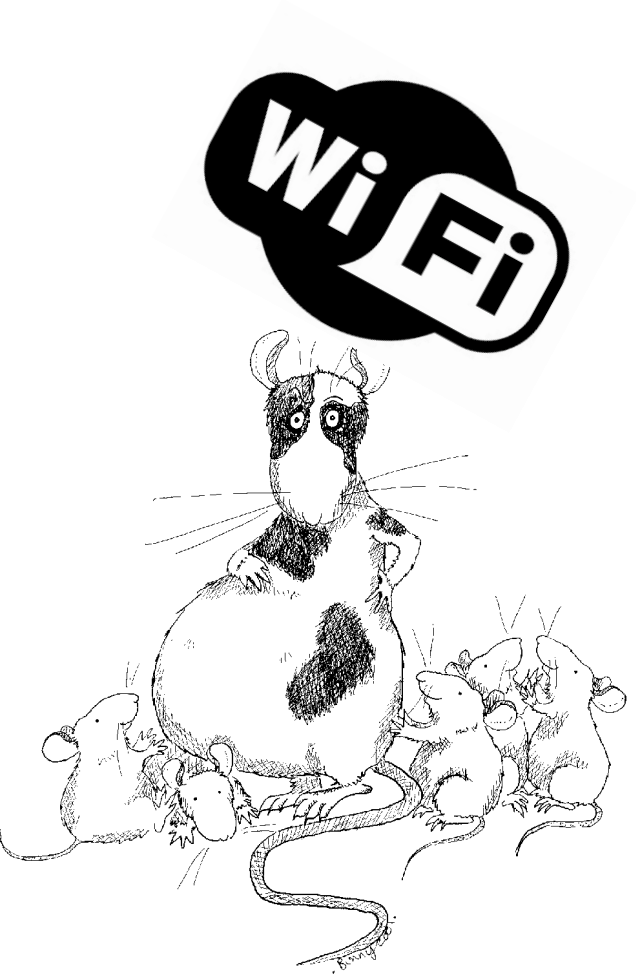
Faits



Peu d'études sur les organismes immatures

- Base de données limitée sauf pour la tératologie
- Effets tératogènes documentés pour exposition aiguë (effets thermiques)

Objectifs



- Approche expérimentale
- Exposition *in utero* à un signal Wi-Fi
- Marqueurs toxicologiques chez les ratons

Protocole

EXPOSITION *IN UTERO*

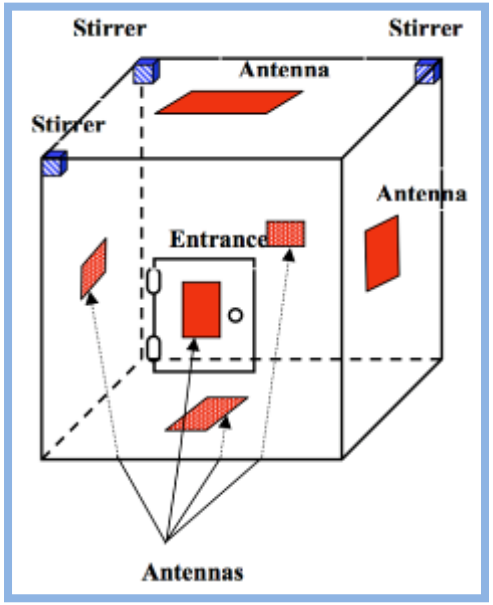
SUIVI DES PORTEES

G3 **G20** **P2** **P30** **P60** **P90**

2 h / jour; 6 jours / sem
0 ; 0,08 ; 0,4 and 4 W/kg
chez les mères

Toxicologie, n= 6-10

Système d'exposition



Chambre Réverbérante (Satimo®)

2450 MHz, Wi-Fi

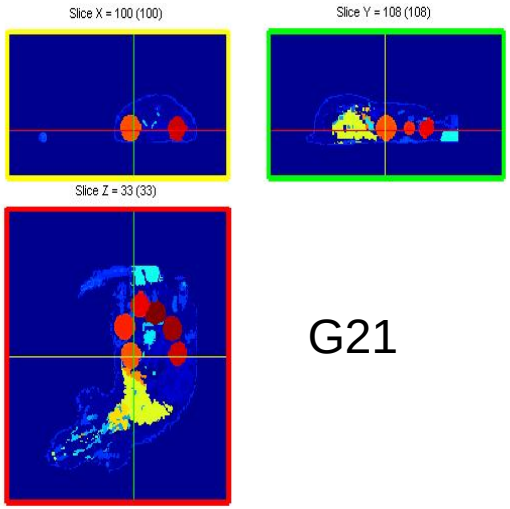
Exposition en aveugle

Exposition corps entier
Liberté de mouvement

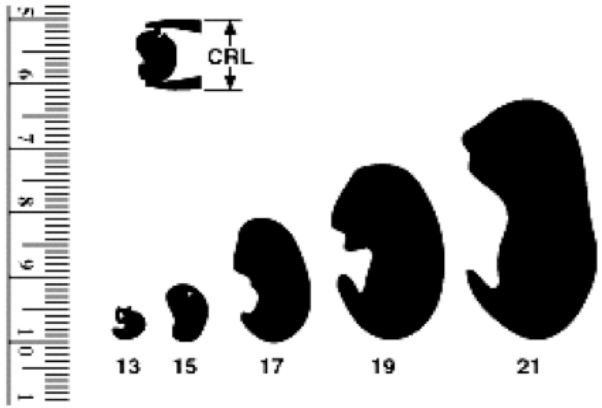
Orange labs, J. Wiart, T. Wu
T. Wu et al., Phys. Med. Biol, 2010

Dosimétrie

- **Modèles numériques**



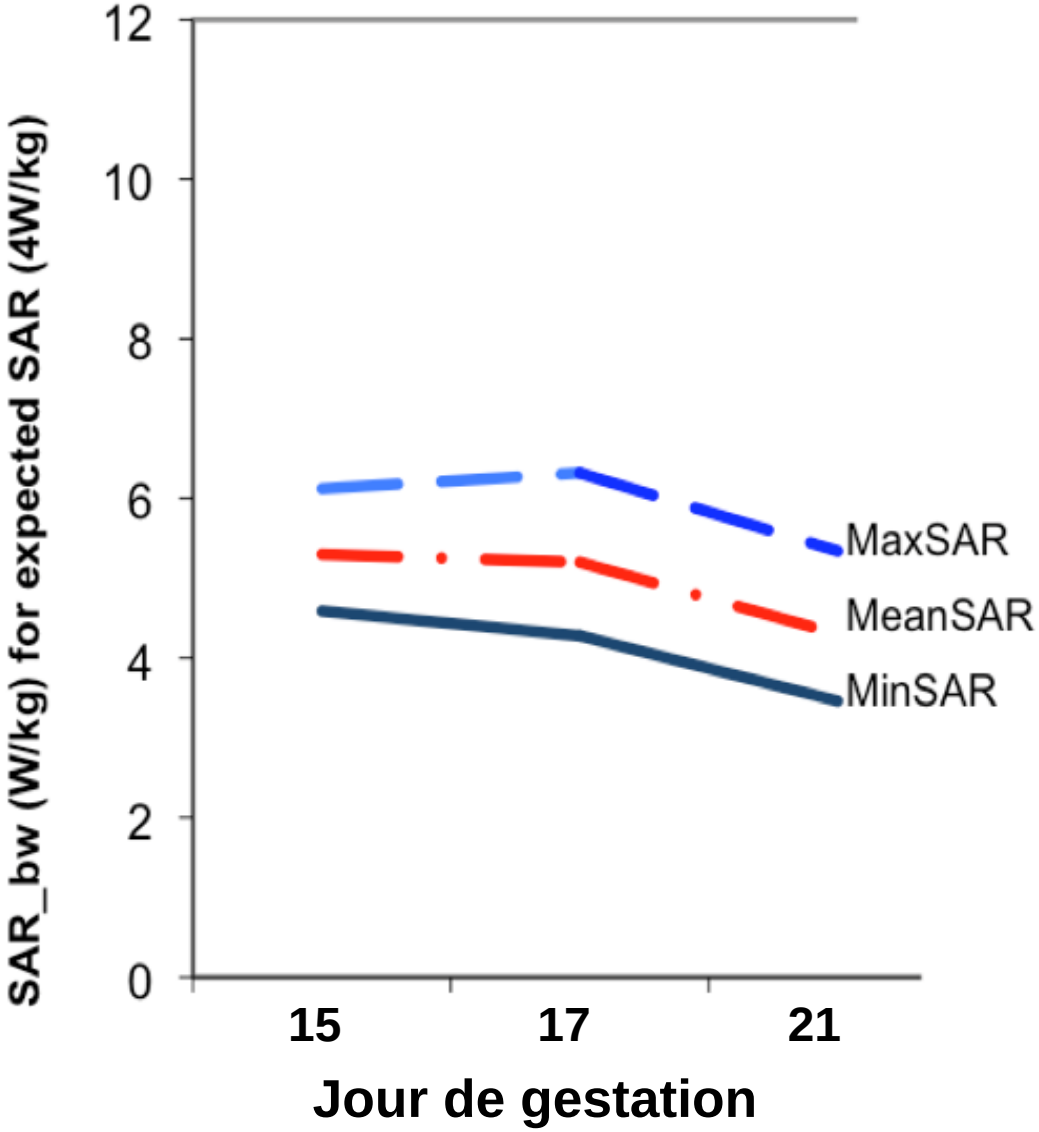
G21



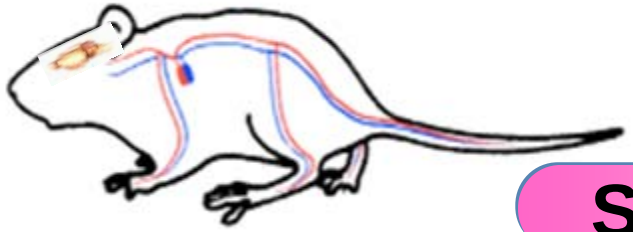
Jour de gestation

Orange labs, J. Wiart, T. Wu
T. Wu et al., Phys. Med. Biol, 2010

- **DAS corps entier**



Marqueurs toxicologiques



CERVEAU

- Cytométrie en Flux
- Apoptose
- Protéines de Stress Hsp25, Hsp70
- Astrogliose
- Activation microgliale

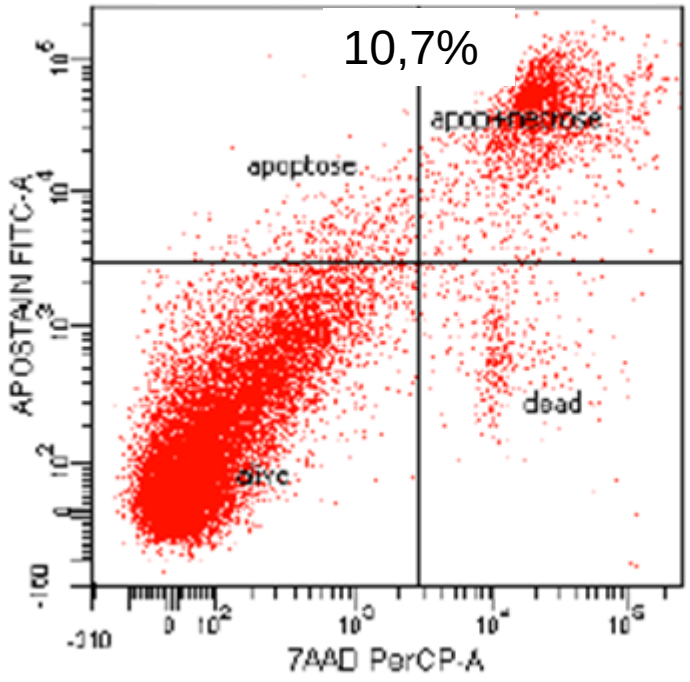
SANG/ SERUM

- Cytométrie en Flux
- Micronoyaux
- ELISA
- 14 néoantigènes Hsp70

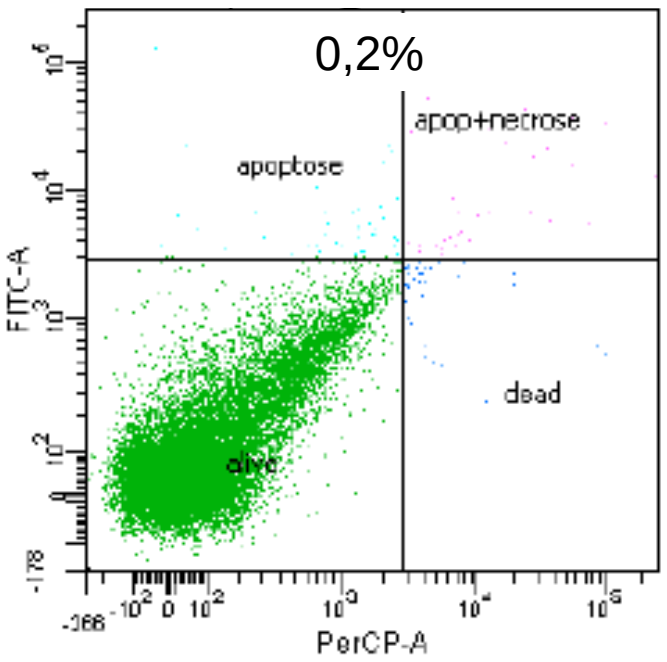
Cerveau- Apoptose

Dissociation du tissu cérébral, kit Apostain®

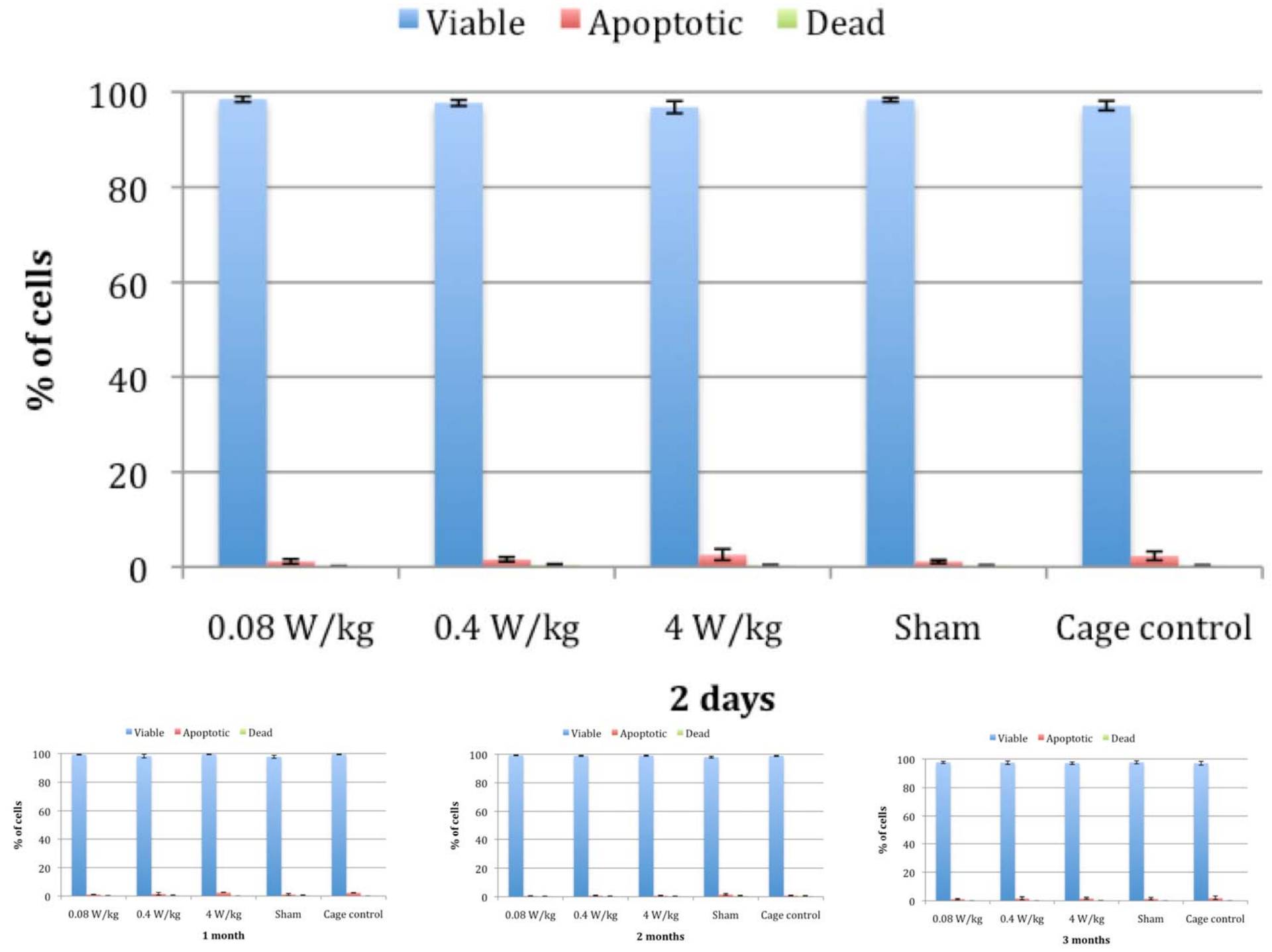
CONTRÔLE POSITIF



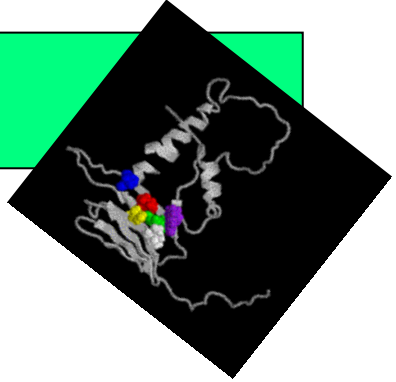
GROUPE EXPERIMENTAL



Methanol ex vivo, 4 jours

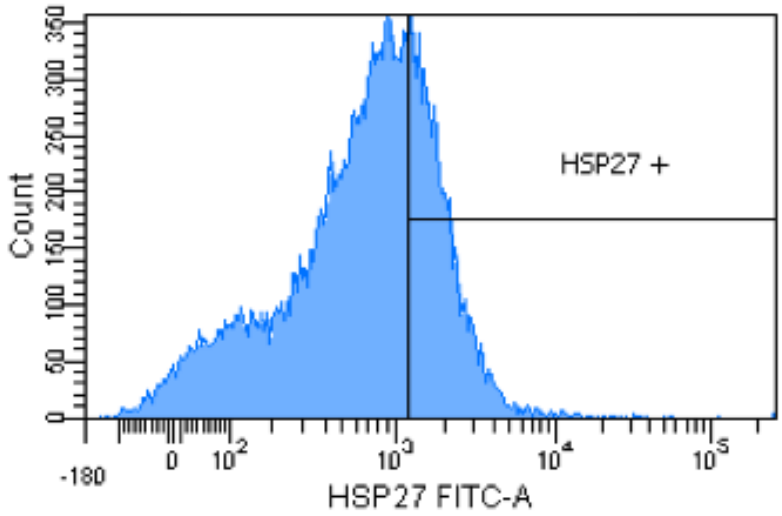

Viable
Apoptotic
Dead
% of cells
100
80
60
40
20
0
0.08 W/kg
0.4 W/kg
4 W/kg
Sham
Cage control
2 days
1 month
2 months
3 months

Cerveau- Hsp 27

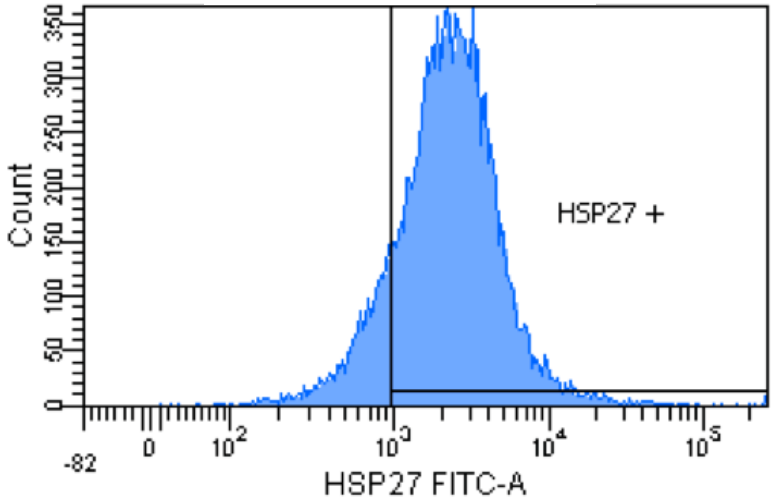


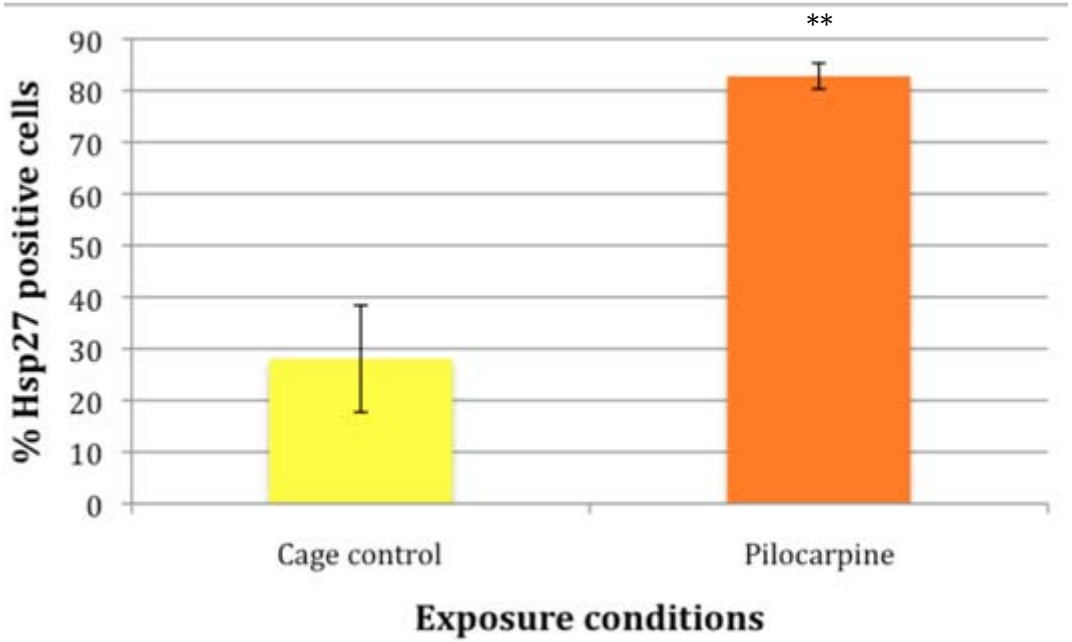
Dissociation tissu cérébral , anti-Hsp27

CONTRÔLE CAGE

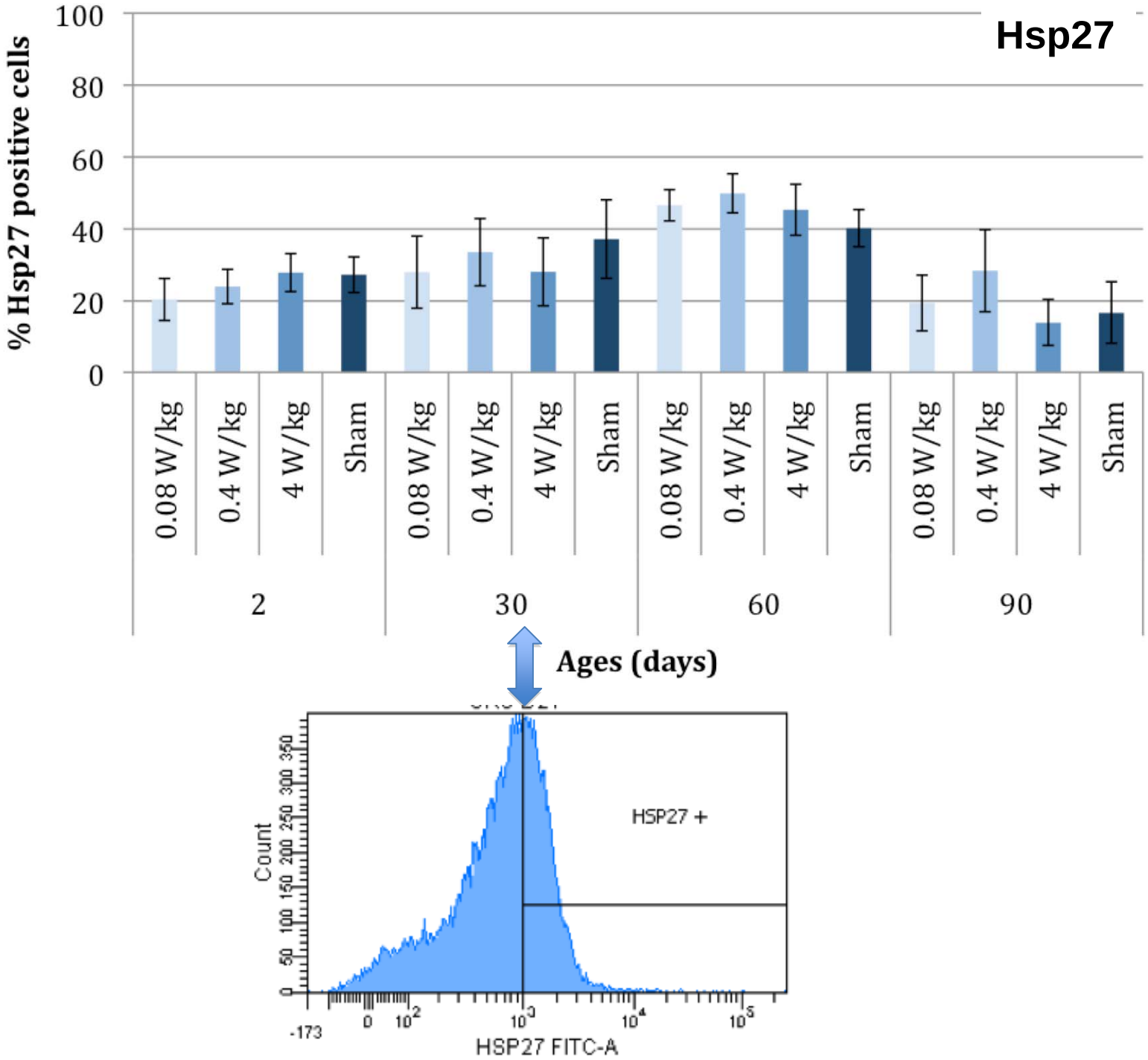


PILOCARPINE

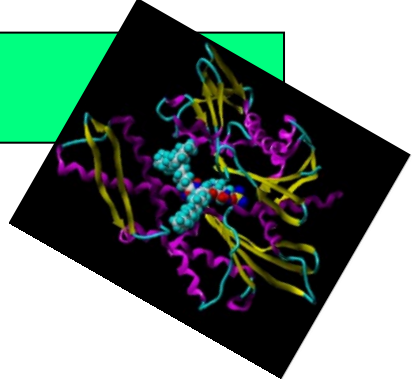




Pilocarpine: 400 mg/kg, sc, 48 hr
* p<0,01, StatXact®

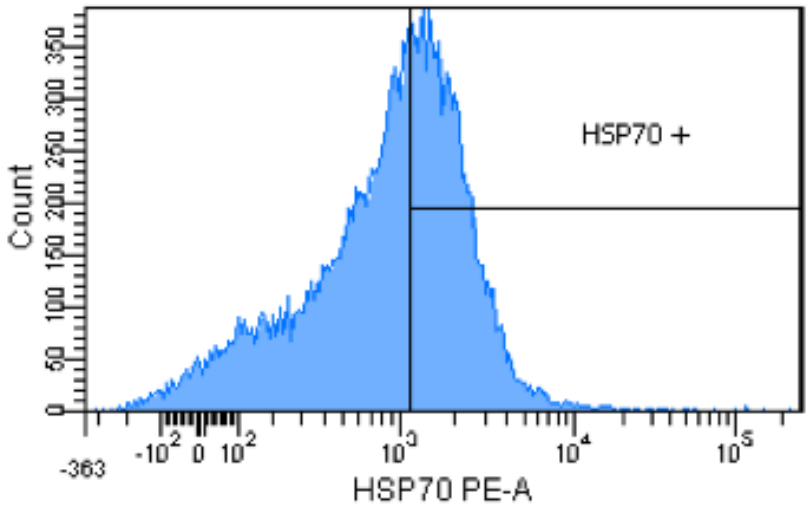

Hsp27
% Hsp27 positive cells
100
80
60
40
20
0
0.08 W/kg
0.4 W/kg
4 W/kg
Sham
2
30
60
90
Ages (days)
Count
HSP27 +
HSP27 FITC-A
-173
0
10^2
10^3
10^4
10^5

Cerveau- Hsp 70

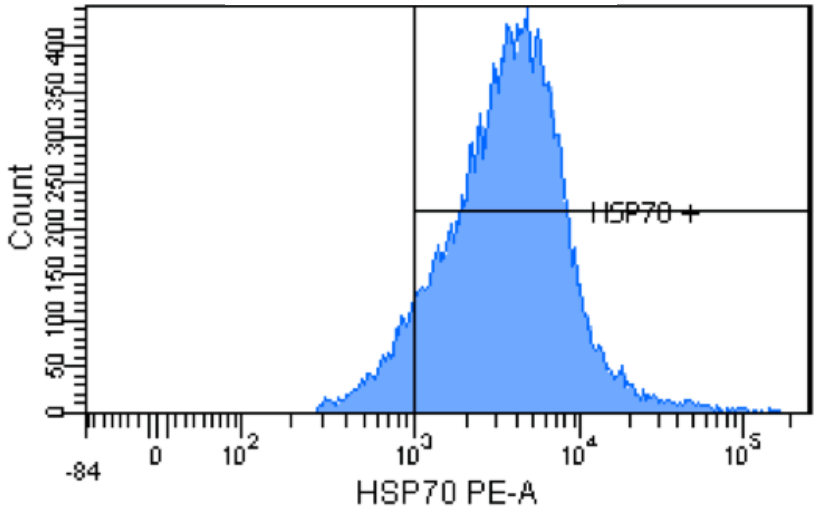


Dissociation tissu cérébral, anti-Hsp70

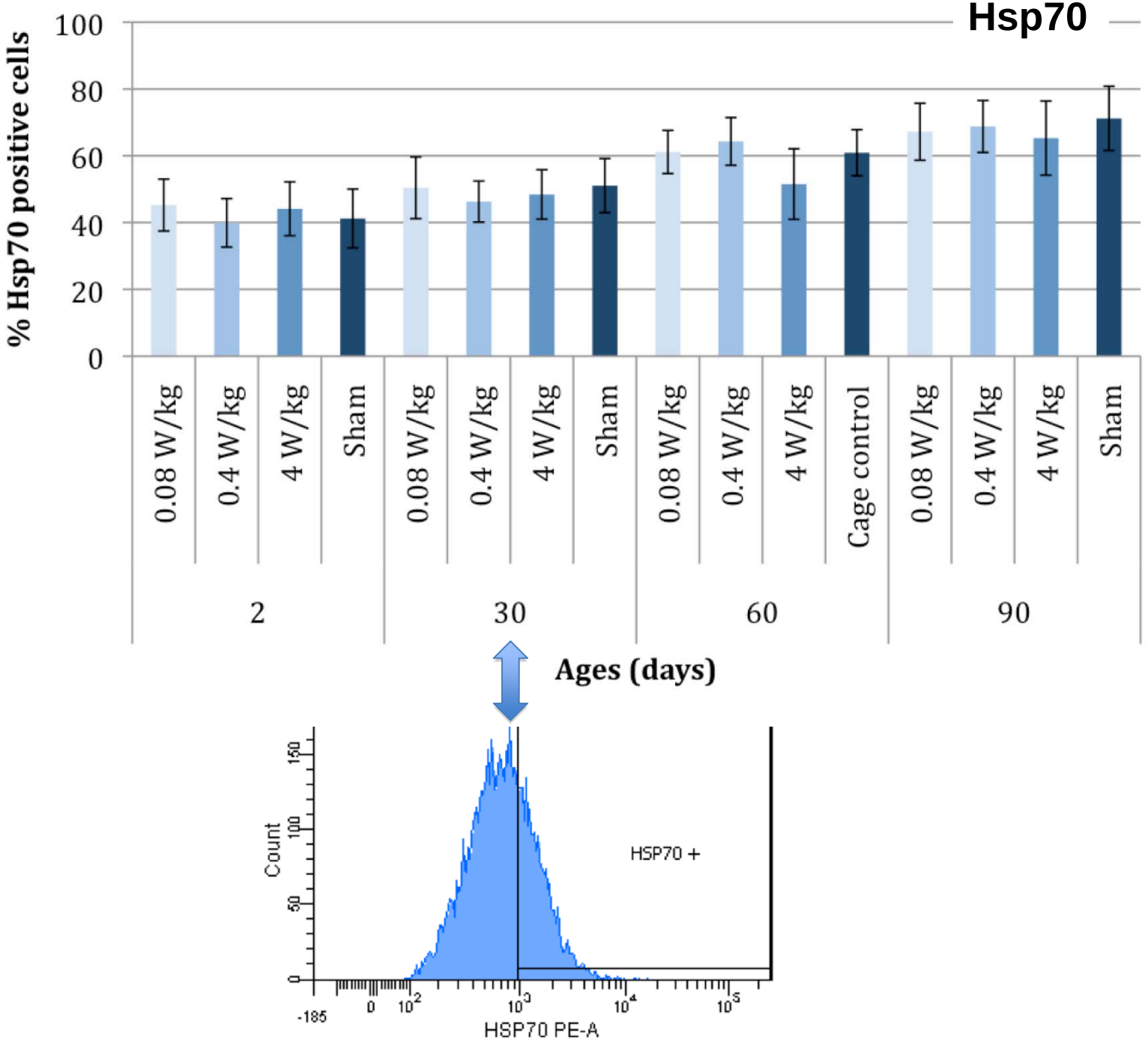
CAGE CONTROL



PILOCARPINE



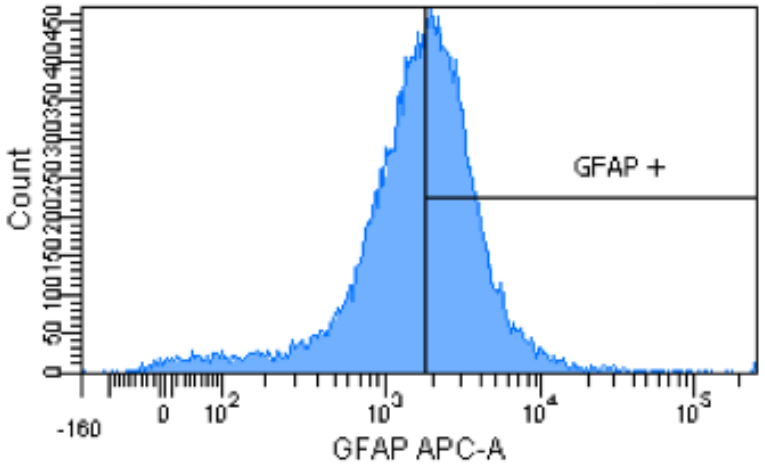
Expression augmentée mais non significative statistiquement


Hsp70
% Hsp70 positive cells
100
80
60
40
20
0
0.08 W/kg
0.4 W/kg
4 W/kg
Sham
0.08 W/kg
0.4 W/kg
4 W/kg
Sham
0.08 W/kg
0.4 W/kg
4 W/kg
Cage control
0.08 W/kg
0.4 W/kg
4 W/kg
Sham
2
30
60
90
Ages (days)
Count
150
100
50
0
HSP70 +
-185
0
10^2
10^3
10^4
10^5
HSP70 PE-A

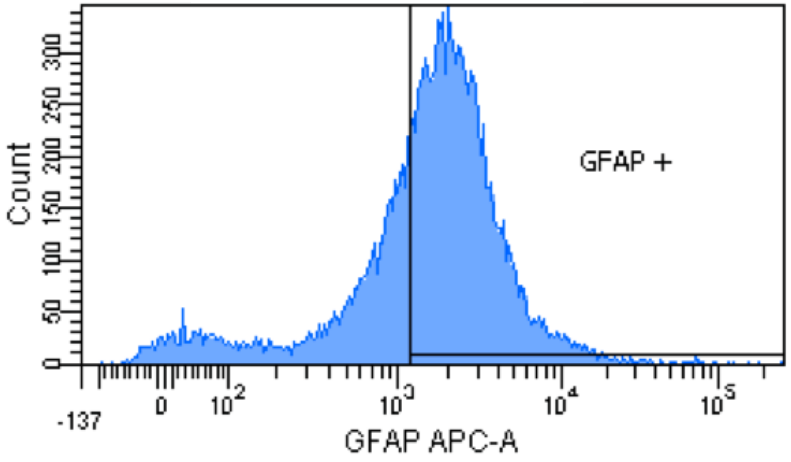
Cerveau- Gliose

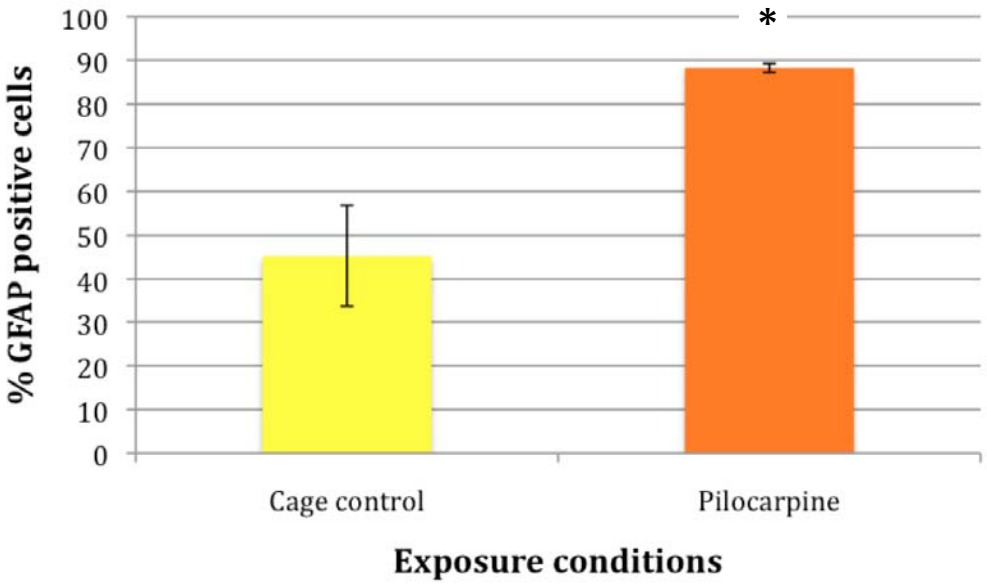
Dissociation tissu cérébral, anti-GFAP

CONTRÔLE CAGE

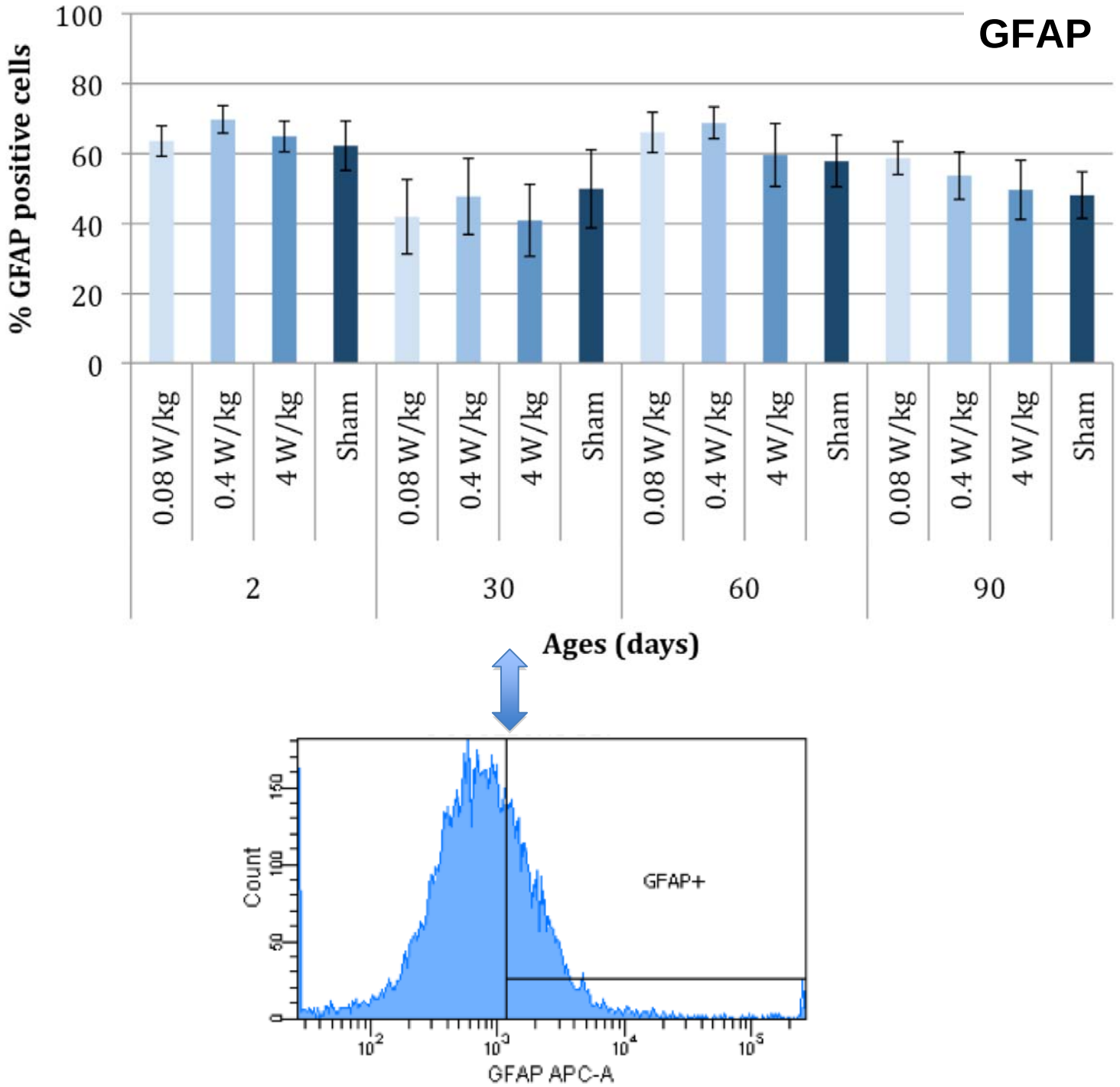


PILOCARPINE





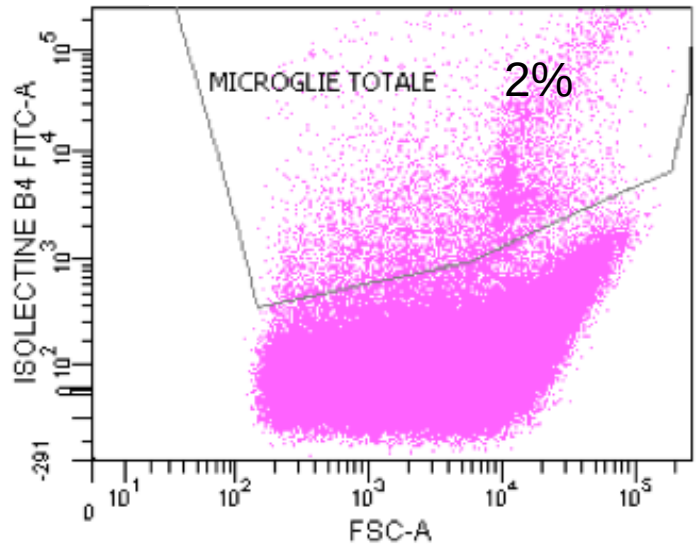
Pilocarpine: 400 mg/kg, sc, 48 heures
* p<0,05, StatXact®

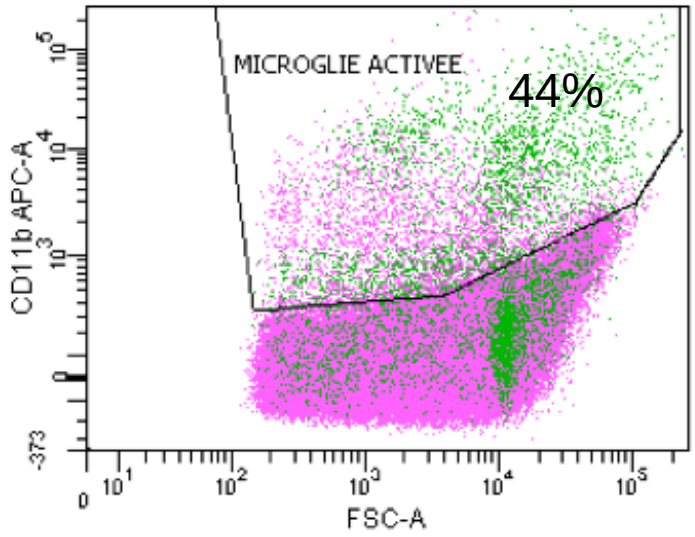

GFAP
% GFAP positive cells
100
80
60
40
20
0
0.08 W/kg
0.4 W/kg
4 W/kg
Sham
2
30
60
90
Ages (days)
Count
150
100
50
0
GFAP+
10^2
10^3
10^4
10^5
GFAP APC-A

Cerveau- Activation microgliale

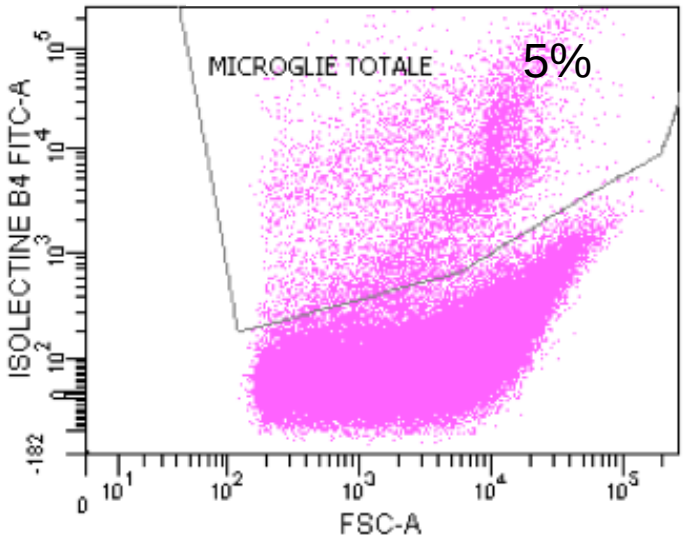
Dissociation tissu cérébral, β4 Isolectine et CD11b

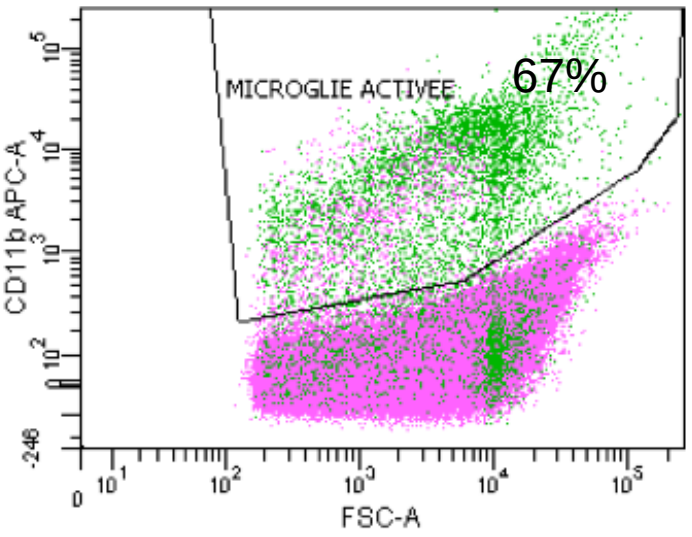
CONTRÔLE CAGE



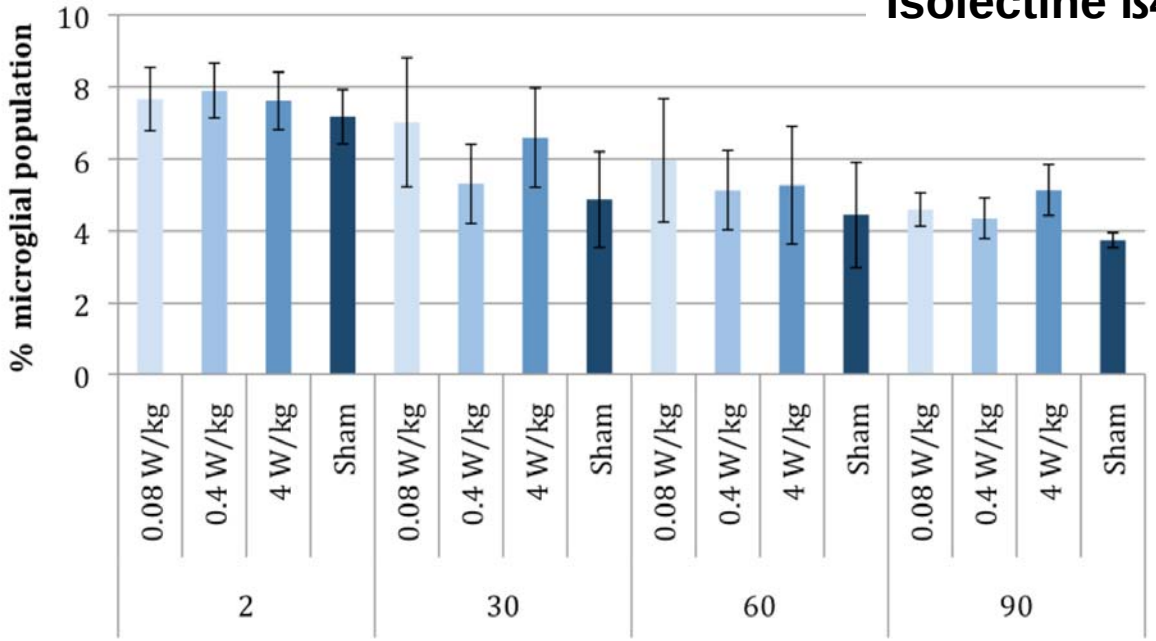


PILOCARPINE

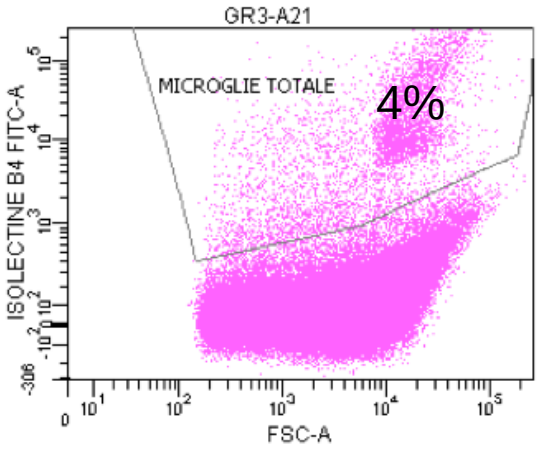




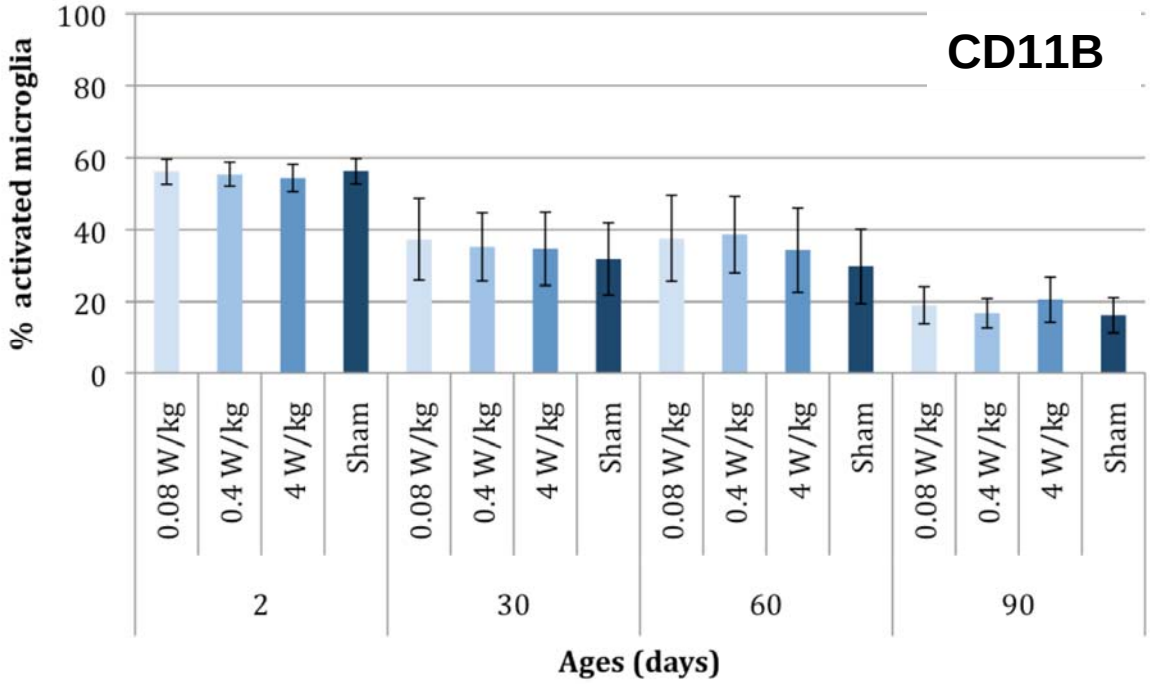
Isolectine ß4

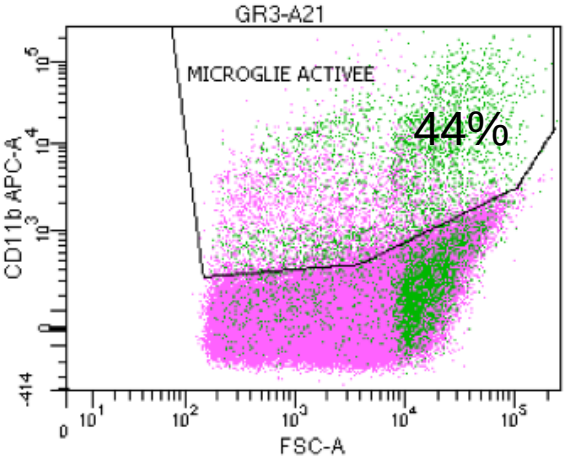


Group A, 1 mois

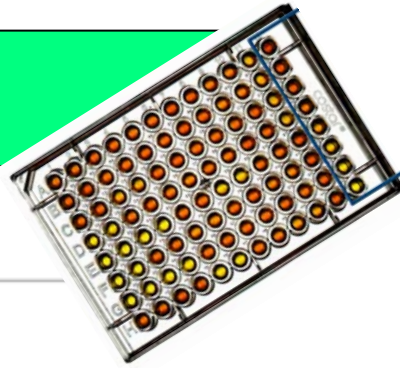


CD11B

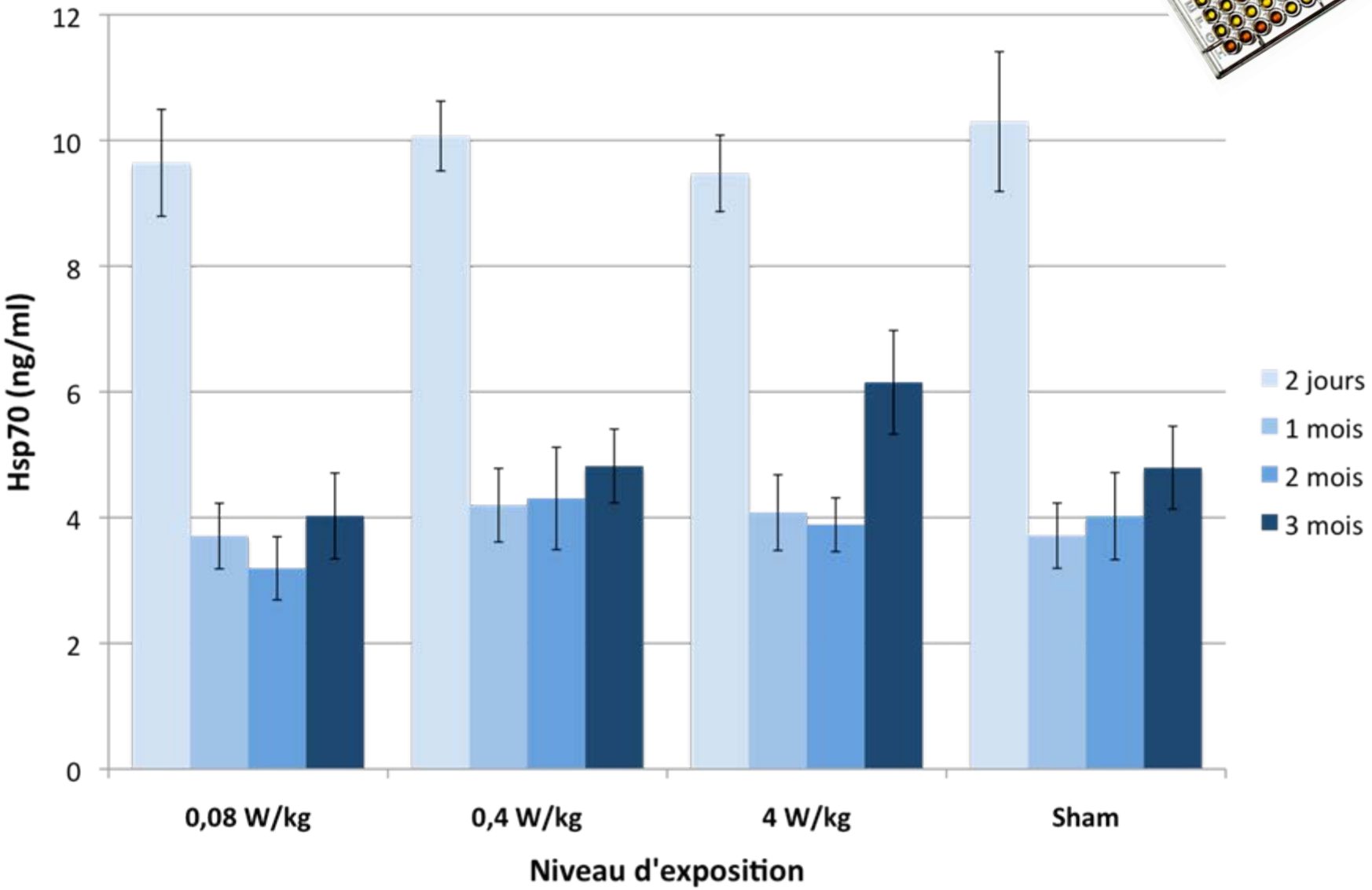




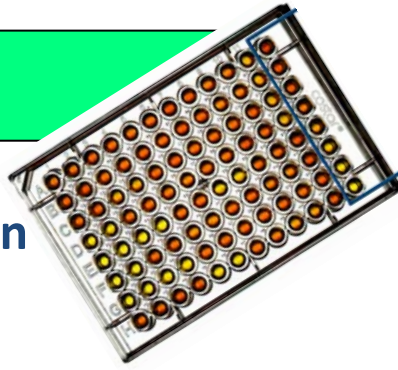
Serum- Hsp 70



Serum, kit HSP70 ELISA (USCN®)



Serum- Néo-antigènes



Serum, kit ELISA IgM (IDRPHT)

Principe

Recherche d'anticorps circulants dirigés contre des néo-antigènes révélés au cours de phénomènes physio-pathologiques

Stress radicalaire, inflammation

NO-Cys/NO-BSA

NO-Tyr/NO-Trp

NO_2-Tyr

NO-Arg

NO-Phe

Neurodégénérescence

NAC-Catécholamines

Neurotoxicité

Quin-a

Kyn/3OH Kyn

Acides gras et leurs altérations

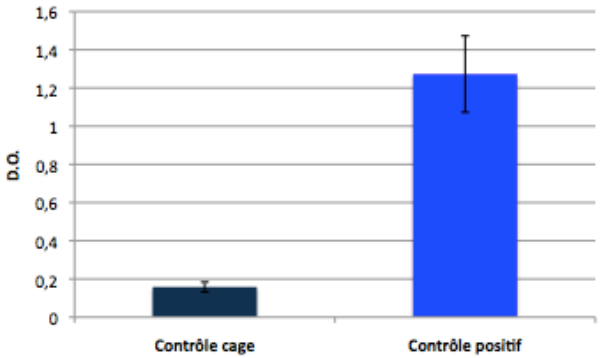
Pal/Myr/Ole/Palmi

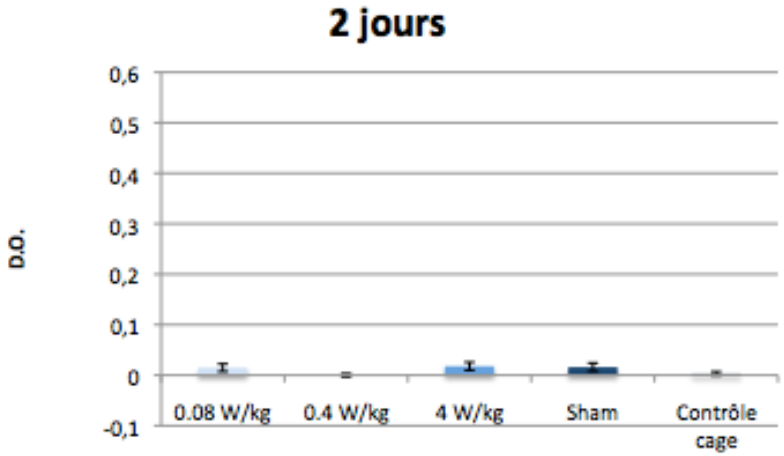
Phosphatidyl-Inositol

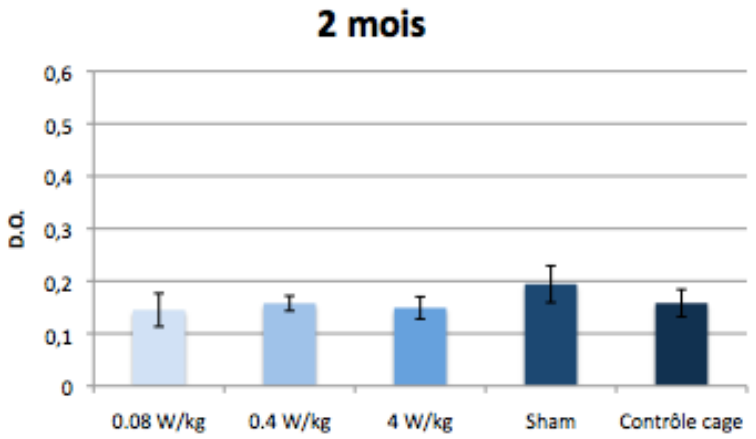
Lipoperoxydation

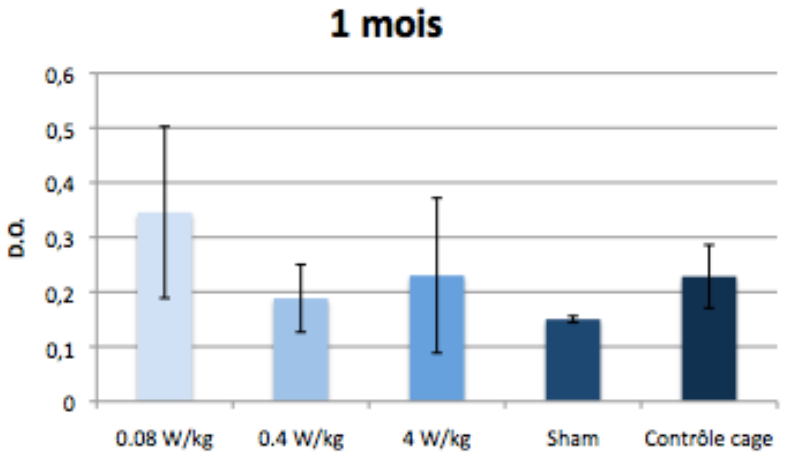
MDA/4HNE

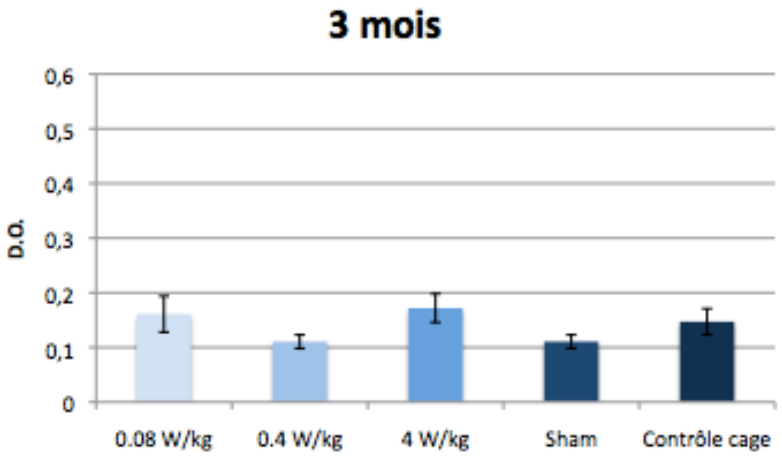
NO-Tyr/NO-Tryp



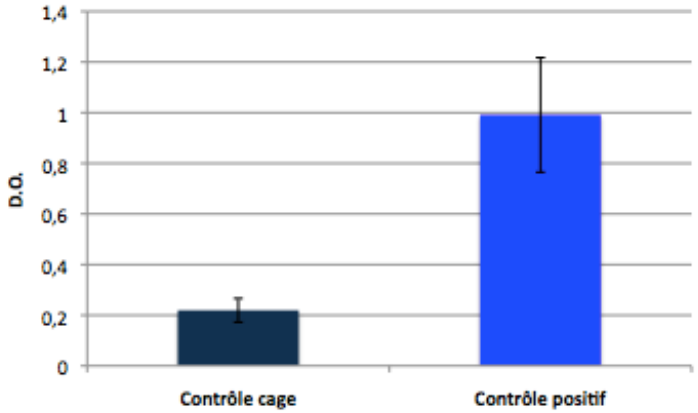




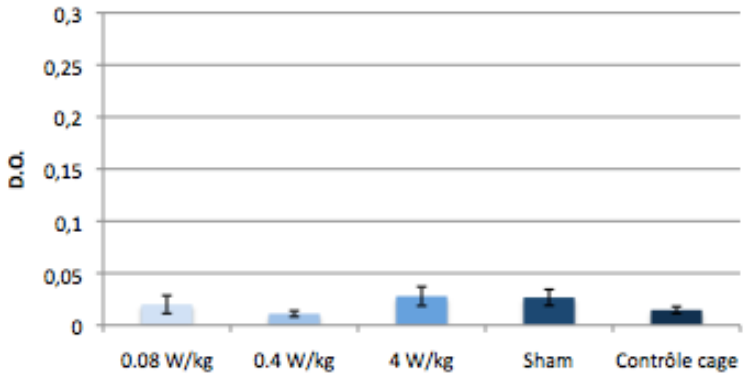




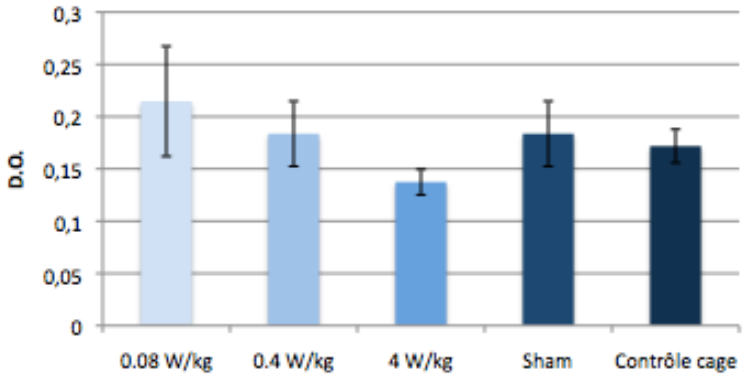
NO_2-Tyr



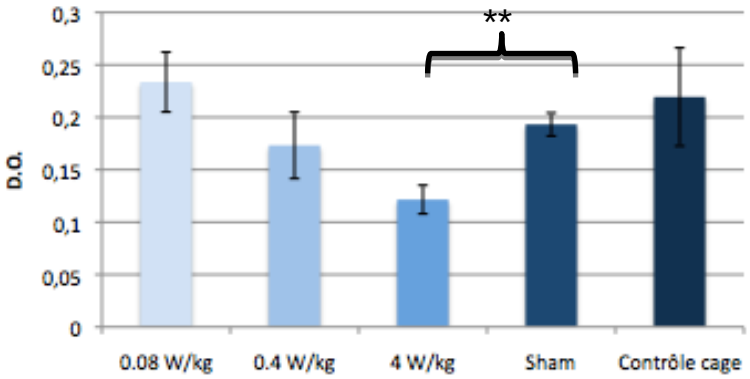
2 jours



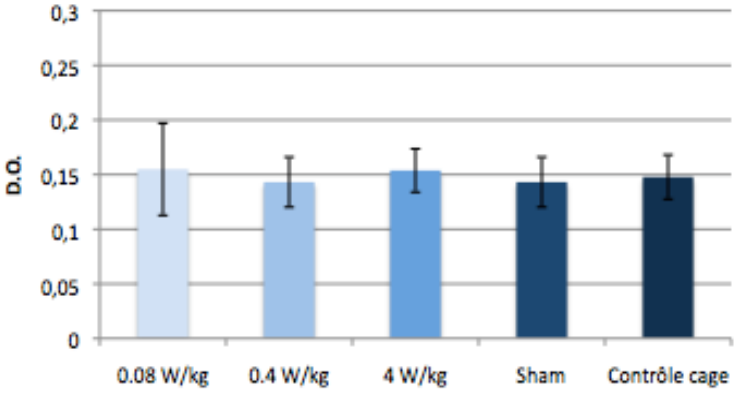
2 mois



1 mois



3 mois



Serum- Néo-antigènes

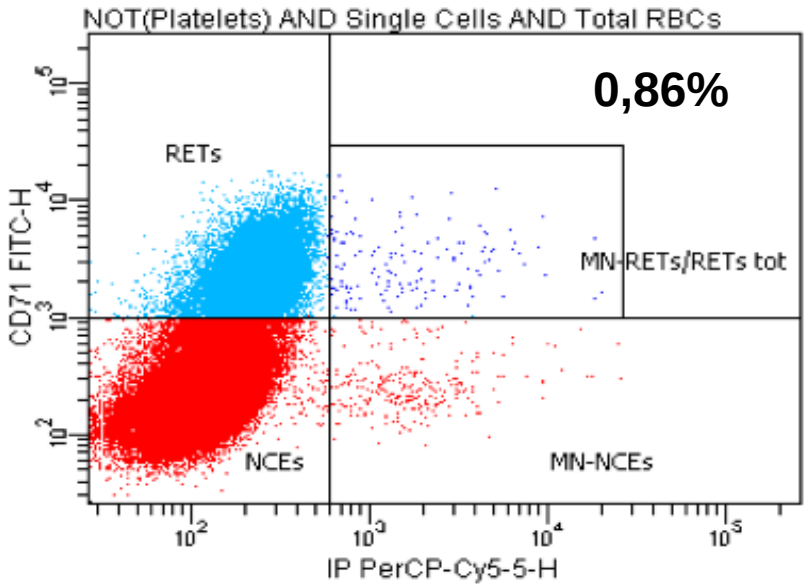
4 antigènes significativement diminués à 4 W/kg versus sham

NO_2-TYR	MDA-4HNE	QUIN-A	3OH-KYN
* *	* *	* *	*

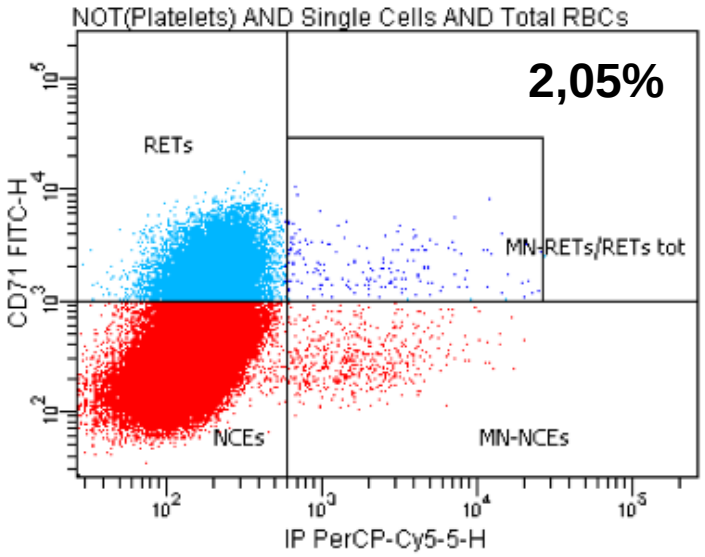
Sang: Micronoyaux

Sang total, kit MicroFlow® Animaux de 2 jours, n=10

Contrôle Cage

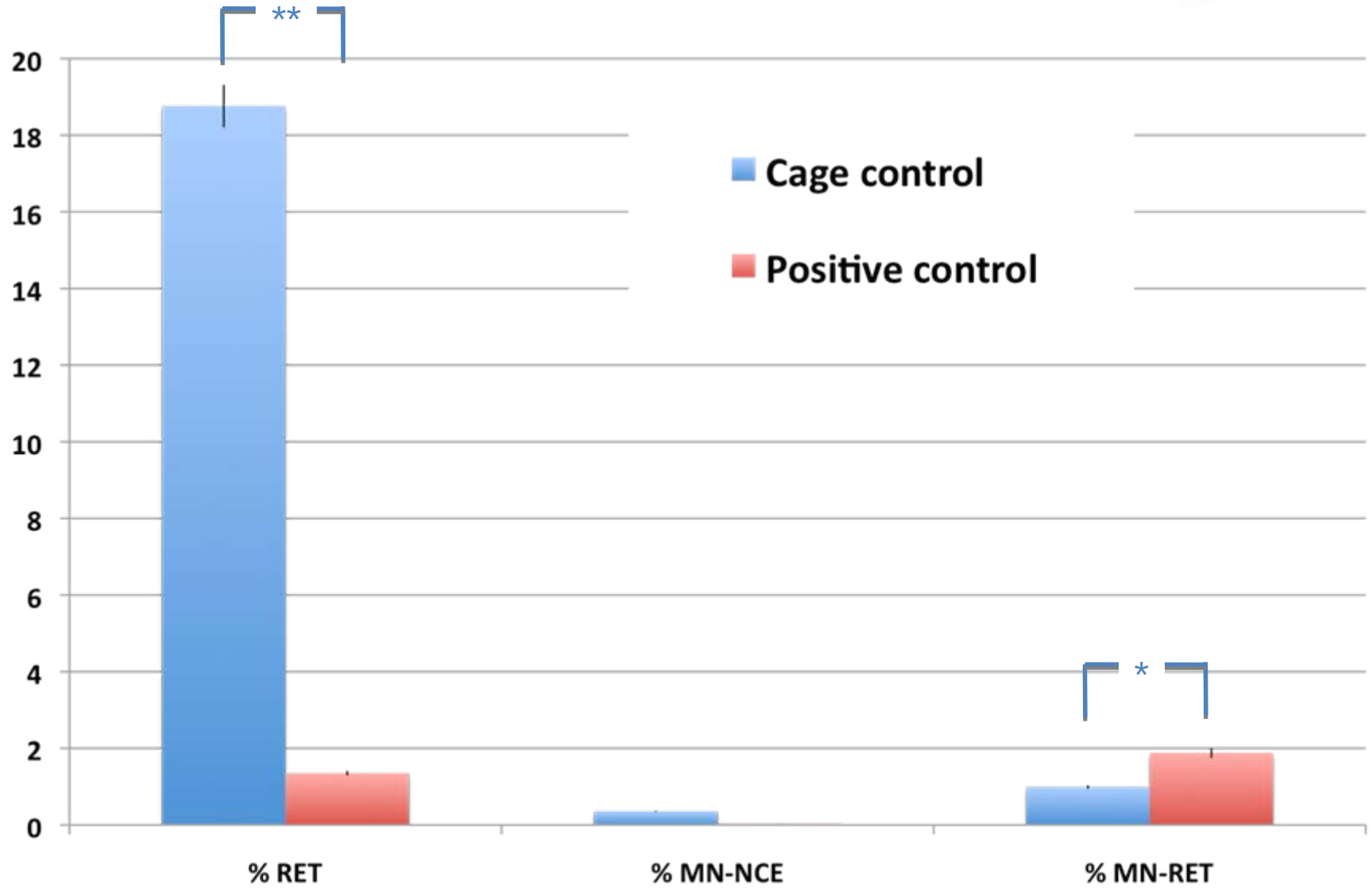


Contrôle positif (Kit)

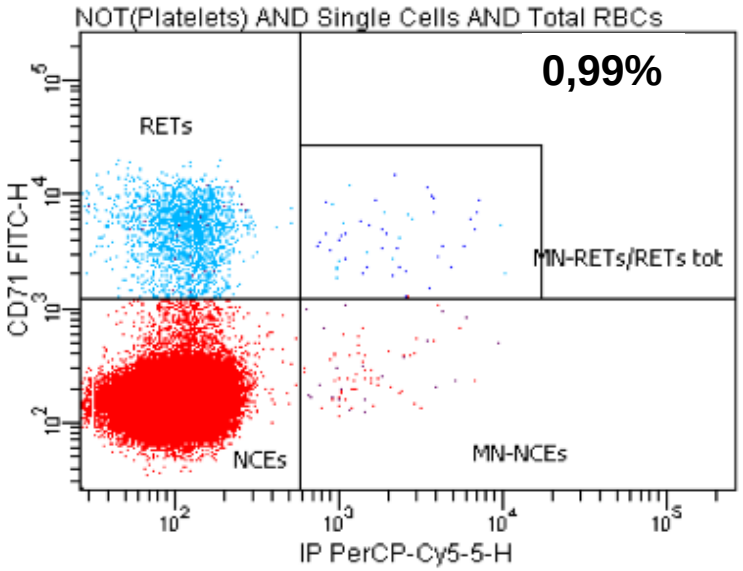


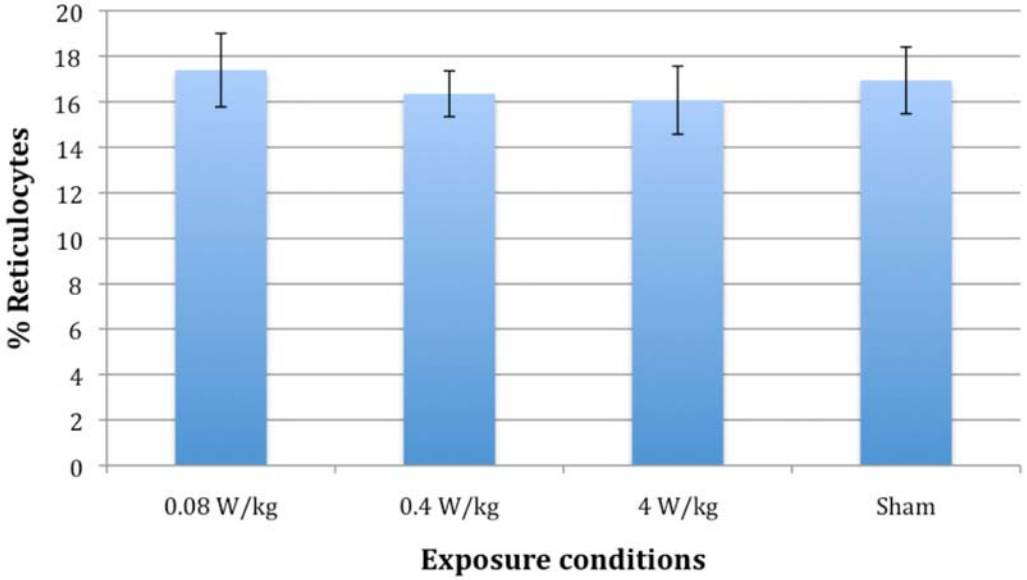
RET: PolyChromatic erythrocytes
NCE: NormoChromatic Erythrocytes
MN: micronucleated

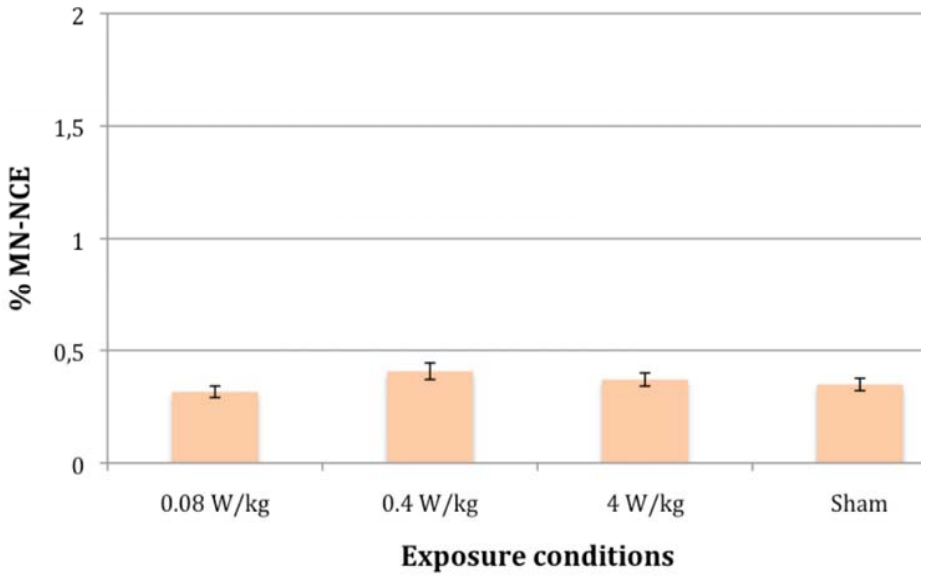
Sang: Micronoyaux

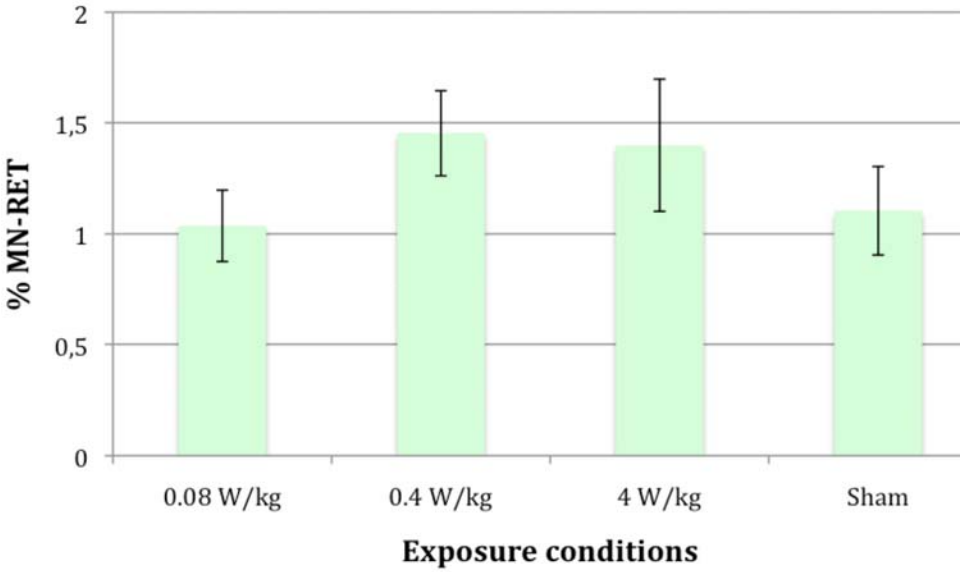


Expérimental (A42)









Conclusions - 1

- Jusqu'à 3 mois après une exposition *in utero* à un signal Wi-Fi, les rats :

  - n'expriment pas de marqueurs toxicologiques dans le cerveau

  - ne présentent pas d'augmentation de micronoyaux dans le sang, ni d'HSP70 dans le sérum

Conclusions - 2

La diminution du taux d'anticorps dirigés contre certains néo-antigènes (1 mois, 4 W/kg) suggère:

- Un impact sur le stade le plus dynamique de la maturation du système immunitaire

- Plus qu'un effet protecteur, une perturbation transitoire (retard) de la réponse cellulaire spécifique serait à privilégier

- Le seuil de l'effet correspond au seuil critique défini par l'ICNIRP

Merci

FONDATION SANTÉ ET RADIOFRÉQUENCES

ANR AGENCE NATIONALE DE LA RECHERCHE

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ims TRANSFERT

Gilles Ruffié
Fabrice Bonnaudin

Labo BioEM :

Florence Poulletier de Gannes
Bernard Billaudel
Michel Geffard
Bernard Veyret
Murielle Taxile
Annabelle Hurtier
Emmanuelle Haro
Saliha Aït Aïssa

Whist Lab
Laboratoire commun de l'Institut Télécom et de Orange Labs

Joe Wiart
Tongning Wu

L'I.D.R.P.H.T.

Sébastien Duleu