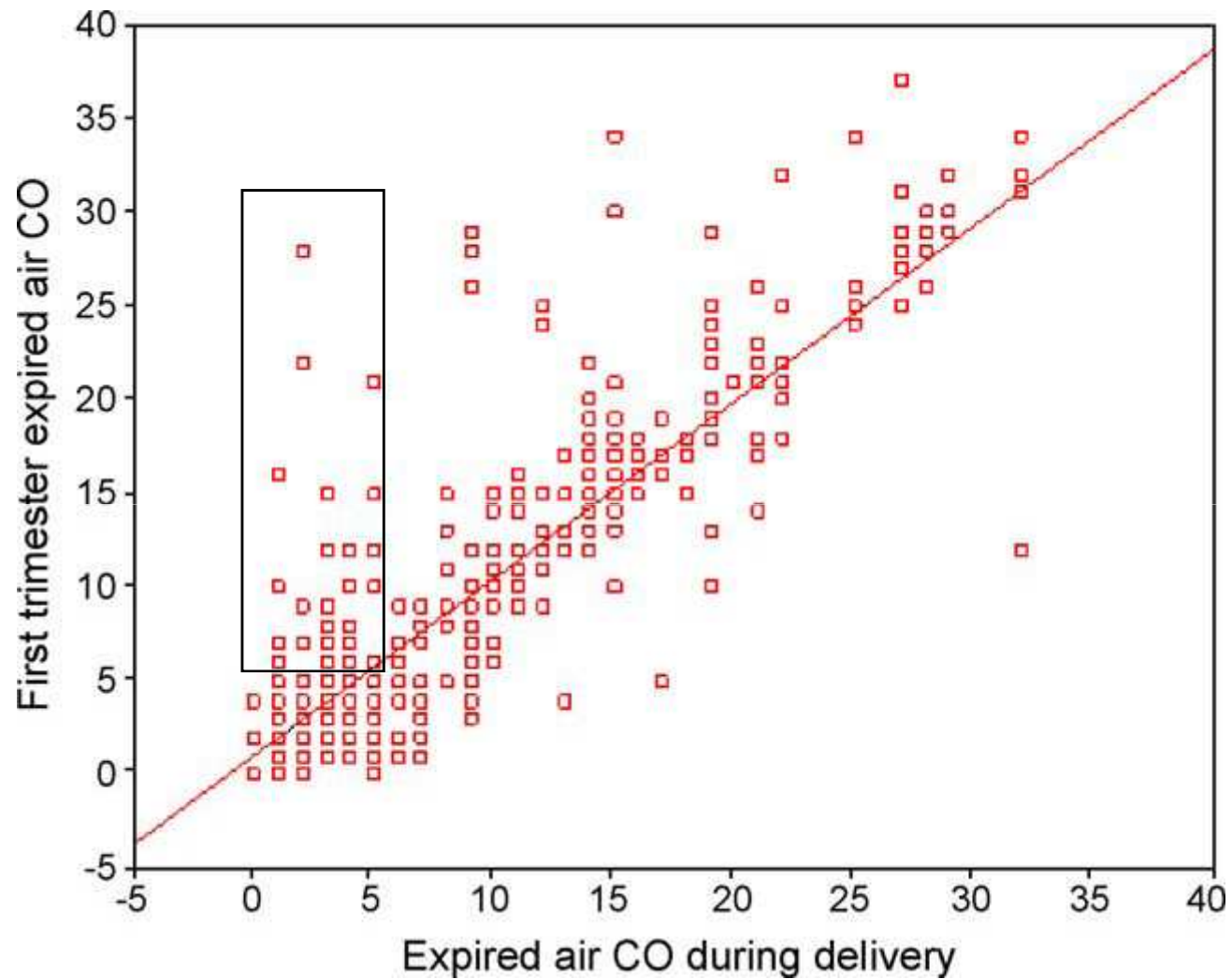


Inhibition de la monoamine oxidase A chez la femme enceinte et son retentissement chez le nouveau-né

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Le nombre de FE dont le CO dans l'air expirer diminue est faible



Tabagisme maternel - exposition *in utero* et troubles du comportement

- 9 - 30 jours: hypertonicité, excitation (Freid et al. 1987)
- Adolescence: initiation plus fréquente (OR: 2.58, Porath & Fried 2005)
- 9 -12 ans: relation inverse dose-dépendante avec l'intelligence globale (Fried et al. 1998)
- Progression vers dépendance nicotinique/tabagisme quotidien (Buka et al. 2003)

Risque accru de

- Comportement violent (Räsänen et al. 1999)
- Trouble du comportement antisocial (Maughan et al. 2004, Weissman et al. 1999)
- Survenu de dépendance aux drogues à adolescence (Weissman et al. 1999)

Morbidité psychiatrique suivi jusqu'à 20 ans (n=175 869) (Ekblad et al. Arch Gen Psychiatry 2010):

≤10 cpj: OR=1.53 (95%CI: 1.47-1.6)

>10 cpj: OR= 1.85 (95%CI: 1.74-1.96)

Mortalité: OR=1.69 (95%CI: 1.31-2.19)

Inhibiton de la MAO A pendant la grossesse.

Reduced Monoamine Oxidase A Activity in Pregnant Smokers and in Their Newborns

Ivan Berlin, Claire Heilbronner, Sabine Georgieu, Cathy Meier, Jean-Marie Launay, and Odile Spreux-Varoquaux
BIOL PSYCHIATRY 2009;66:728–733

ClinicalTrials.gov Identifier: NCT00169390.

Funding: MILDT A02287KS and MGEN RPN04001DD1A grants, France

Activité MAO & comportement

Etudes chez l'homme

Inhibition MAO B

Instabilité émotionnelle, insécurité, relations sociales instables (Castrogiovanni et al. 1990)

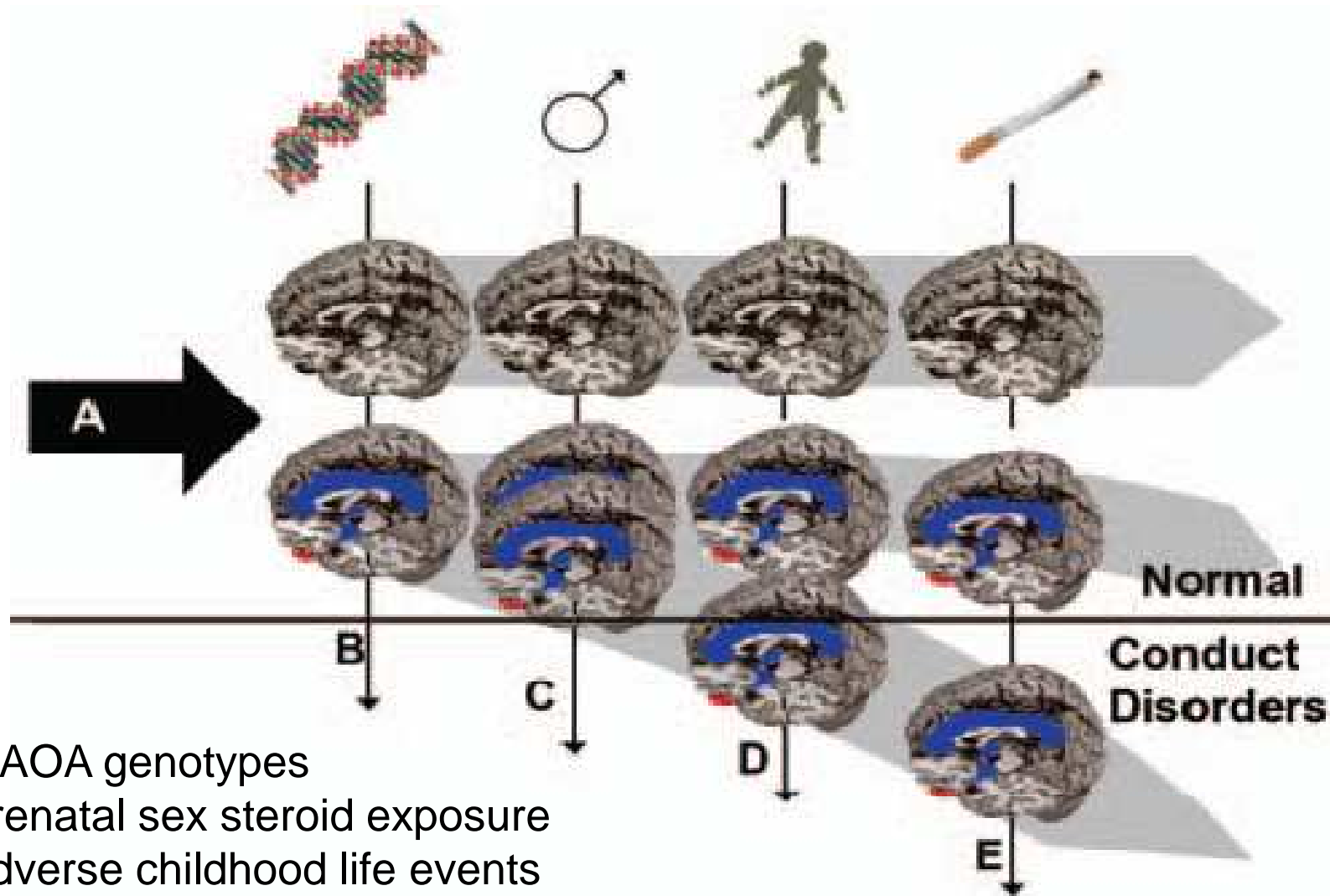
Désinhibition motrice accrue (Klinteberg et al. 1990)

NN avec MAO B activité basse (sang du cordon): inconsolables, pleurs, dorment moins (Sostek et al. 1981)

MAO A

Point mutation exon 8 gène MAO A : déficit complet MAO A: extrêmement impulsifs, agressifs (Brunner et al. 1993)

Hypothetical model: risk factors for developing conduct disorder
Baler, Volkow, Fowler, Benveniste, J Psychiatry Neurosci
2008;33:187-95.



- B: MAOA genotypes
- C: prenatal sex steroid exposure
- D: adverse childhood life events
- E: smoking

Hypothèses

Fumeuses: activité MAO réduite par rapport aux non-fumeuses

NN des mères fumeuses: idem

Retentissement clinique: moins de “bien-être”

Inclusion criteria

- FE 20 - 26 SA
- Non-fumeuses: tabagisme vie entière < 100 cig., pas d'intention de commencer à fumer pendant la grossesse
- Fumeuses: ≥ 10 cpj, pas d'intention d'arrêter ou prendre un TSN

Non-inclusion criteria

- Maladie chronique, pré-éclampsie, médicaments psychotropes, ECHO anormale
- Consommation de cannabis dernier mois, de cocaïne, opioïdes derniers 6 mois
- Abus d'alcool derniers 6 mois ou ≥ 1 verre/j dernier mois
- TSN, tabac oral, cigare, pipe

Evaluations

* **Biologiques**

- Métabolites plasmatiques dépendant de la MAO A

NA: DHPG

DA: HVA, DOPAC,

Sérotonine (5HT): 5HIAA

- Plasma cotinine

Prélèvements

- Fin 2e trimestre
- A l'accouchement
- A la naissance: sang artériel du cordon

* **Comportemental**

- Comportement du NN (Questionnaire EDIN)
Toutes les 8 h pendant 48 h

DHPG: dihydroxyphenylglycol, HVA: homovanillic acid,
DOPAC: dihydroxyphenylacetic acid, NE: norepinephrine,
5HIAA: 5-hydroxyindolacetic acid

Questionnaire of newborns' pain and discomfort (EDIN) (Debillon et al. 2001)

- **Face:** relaxed; rare grimaces; frequent grimaces; continuous twitch
- **Body:** relaxed; agitated transitorily; frequently; permanently
- **Sleep:** falls asleep easily; with difficulty; frequent awakenings; does not sleep
- **Relationship:** smiles; apprehension if contact; cries if contact; no contact possible
- **Comfort:** does not need comforting; calms down if cherished; difficult to calm him/her down; inconsolability

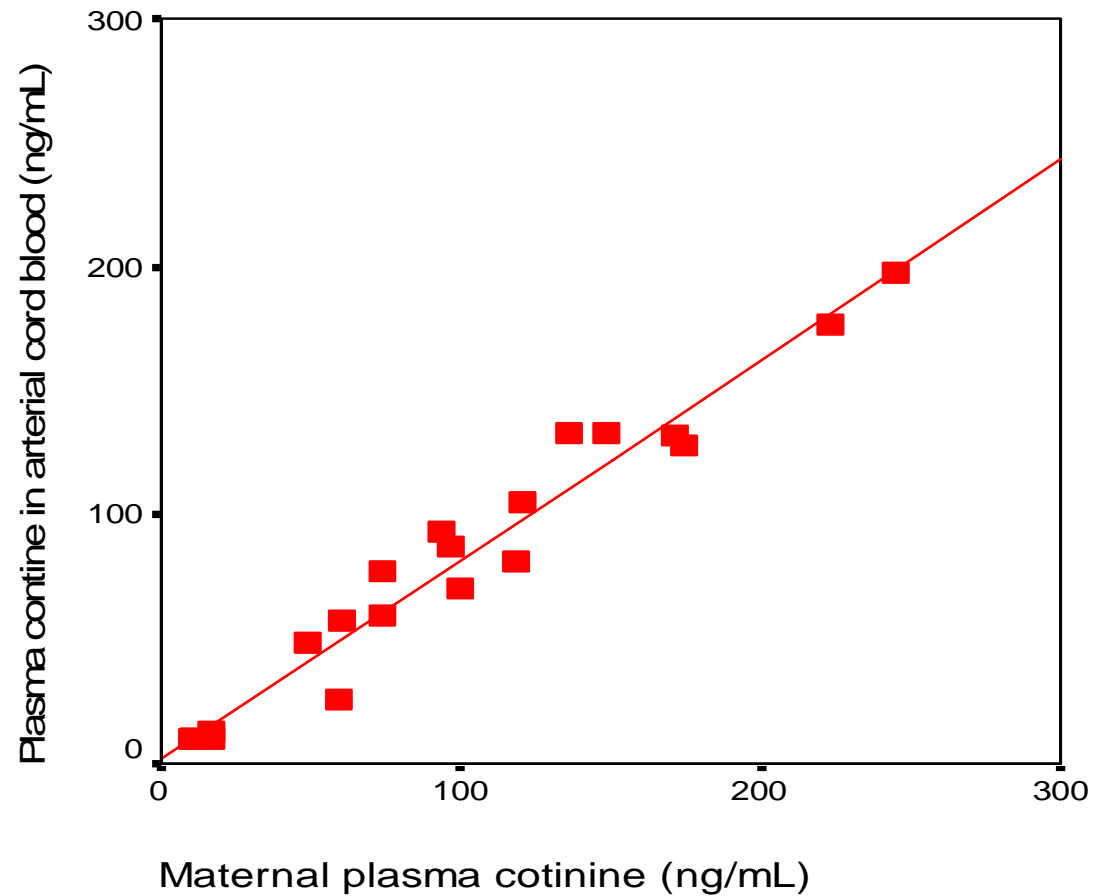
Quotation: 0 to 3

	Smoking pregnant women N=30	Non-smoking pregnant women N=29	P value
Age (years)*	30 (5.9)	31 (4.9)	0.53
Ethnicity, N (%)			0.321
White	29 (97)	29 (100)	
Black	0	0	
Asiatic	0	0	
Other	1 (3)	0	
Spouse smokes, N (%)	22 (76)	7 (25)	<0.001
Smoke exposure inside home	8 (28)	0	0.003
High school completed, N (%)	11 (38)	25 (89)	<0.001
Previous number of pregnancies, N (%)			0.144
0	8 (27)	11 (39)	
1	6 (20)	10 (39)	
2	6 (20)	10 (11)	
3	3 (10)	4 (14)	
4	3 (10)	0	
5	3 (10)	0	
6	1 (3)	0	
Gestational age at inclusion (weeks of amenorrhea)*	26.6 (4.6)	28.3 (4.2)	0.139

*Mean (SD)

	Smoking pregnant women	Non-Smoking pregnant women	P value
Number of cigarettes smoked during the last 7 days			
End of 2nd trimester	73.4 (49.7) median: 70, range: 10-270	NA	
At delivery	79.7 (83) median: 60, range: 5-420	NA	
Plasma cotinine (ng/mL)			
End of 2nd trimester	84 (49)	<10	<0.001
Labor	104 (63)	<10	<0.001
Cord blood	91 (52)	<10	<0.001
Expired air CO (ppm)			
End of 2nd trimester	16.8 (8)	3.2 (2)	<0.001
Labor	13.7 (7)	3.7 (2)	<0.001

Mean (SD)

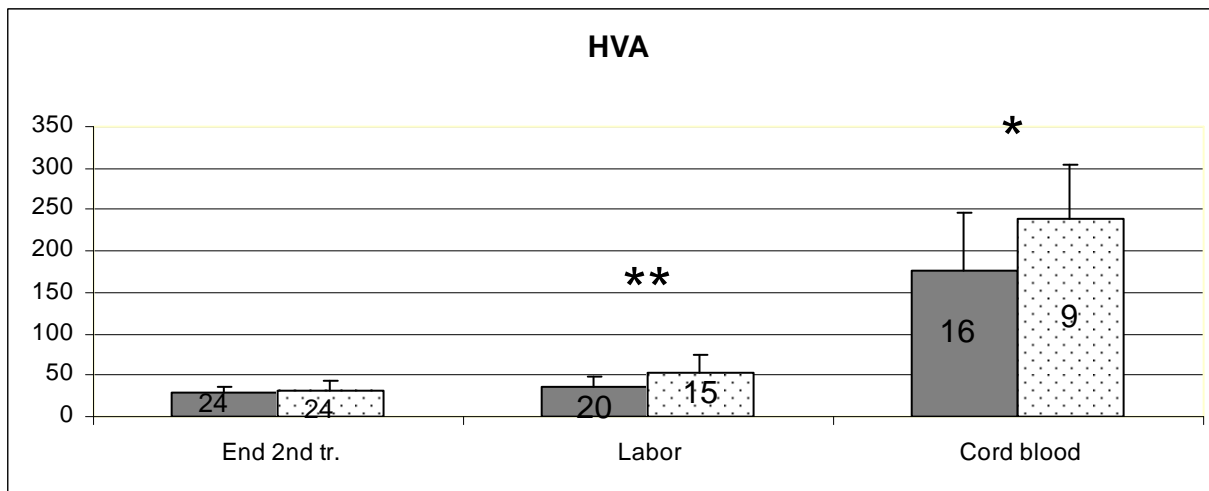
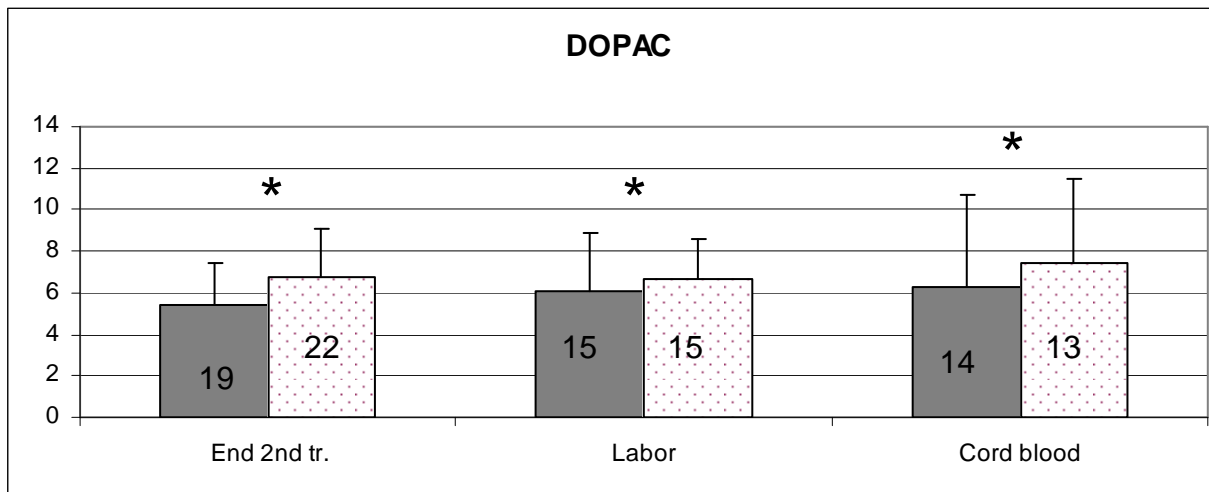


Venous plasma cotinine concentration at the time of labor in smoking mothers plotted against plasma cotinine concentration in arterial cord blood of their newborns. $y=0.79x+0.97$, $Rsq=0.95$, $P < 0.001$

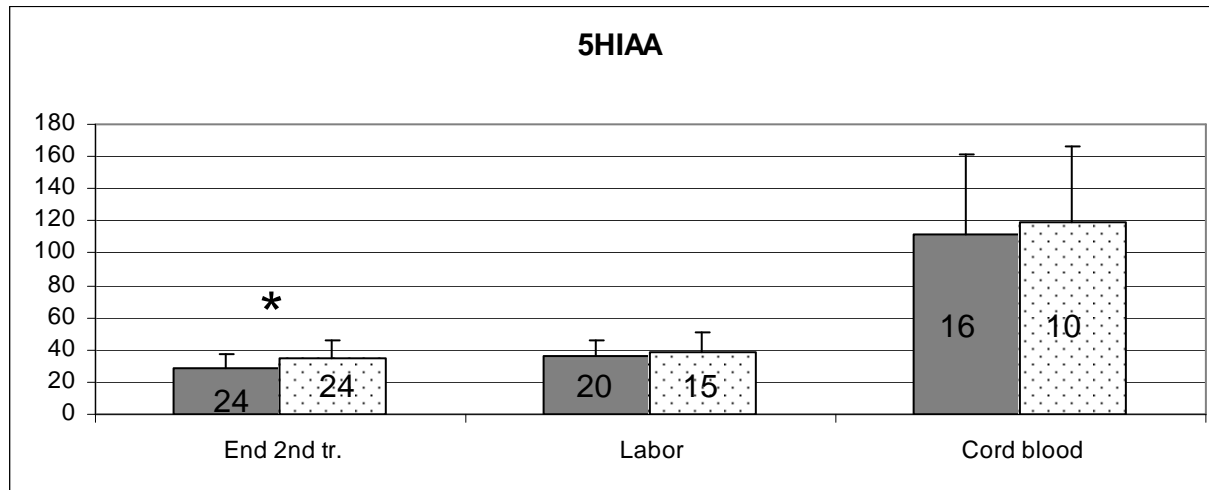
Newborns' birth characteristics	Smoking mothers	Non-Smoking mothers	P value
Sex, N (%)			0.17
Male	11 (39)	15 (58)	
Female	17 (61)	11 (42)	
Birth weight (g)	3038 (433)	3399 (440)	0.004
Height (cm)	48.7 (2.1)	50.5 (1.7)	0.001
Head circumference at birth (cm)	33.5 (1.7)	34.5 (1.4)	0.025
Head circumference at age 48 hours (cm)	33.8 (1.6)	34.7 (1.4)	0.062
Apgar 1 min.	9.6 (1.4)	9.5 (1.2)	0.844
Apgar 5 min.	10 (0)	9.9 (0.4)	0.163

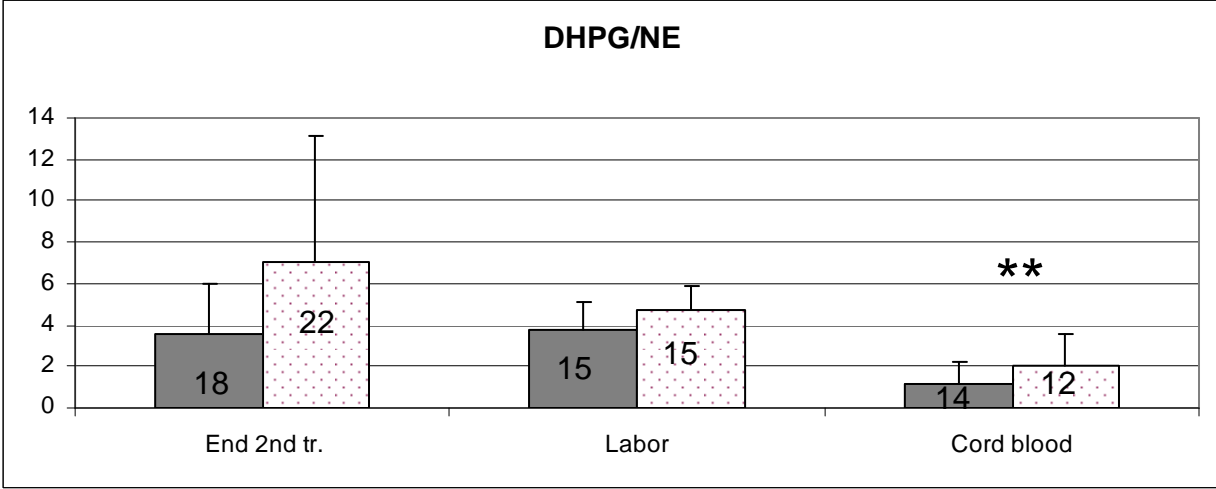
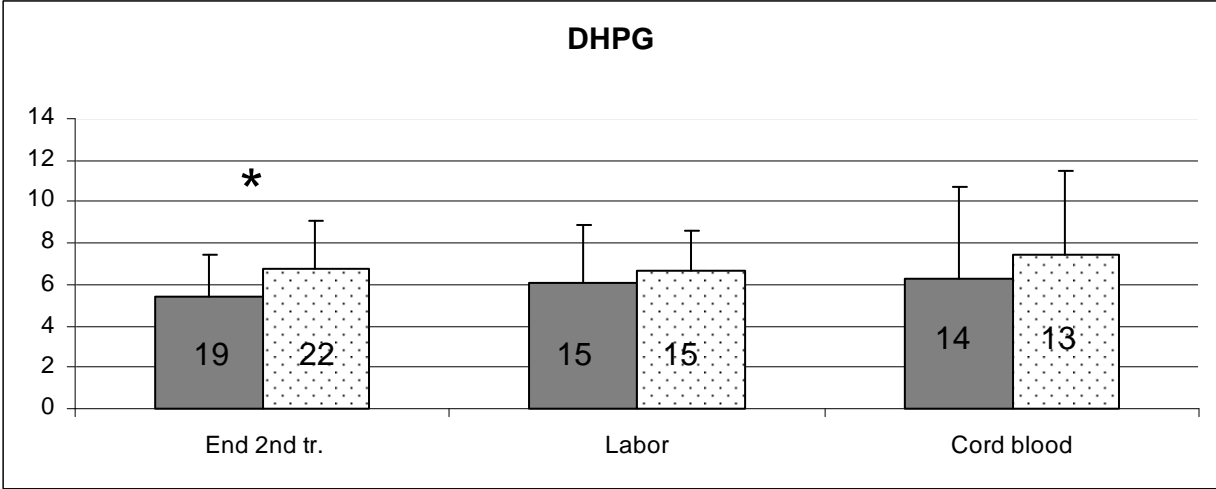
Mean (SD)

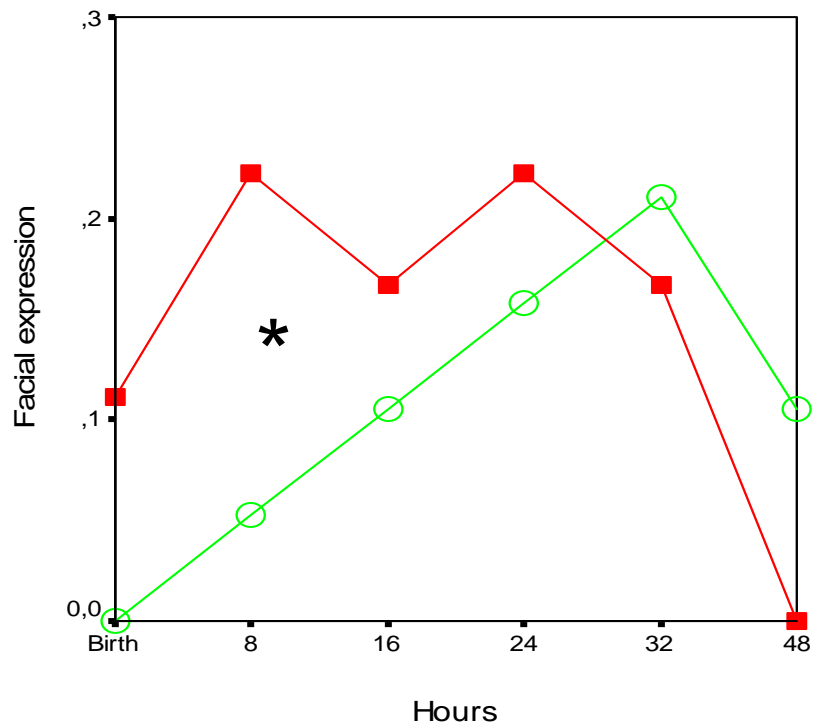
	Repeated measure ANOVA
DOPAC	Main effect of smoking status: F _{1,21} =9.75, p=0.005
HVA	Main effect of smoking status: F _{1,21} =4.37, p=0.028 Time by smoking status interaction F _{1,21} =4.5, p=0.04
5HIAA	Time by smoking status interaction F _{1,23} =3.15, p=0.089
DHPG	Main effect of smoking status F _{1,21} =2.23, p=0.15



Gris: fumeuses

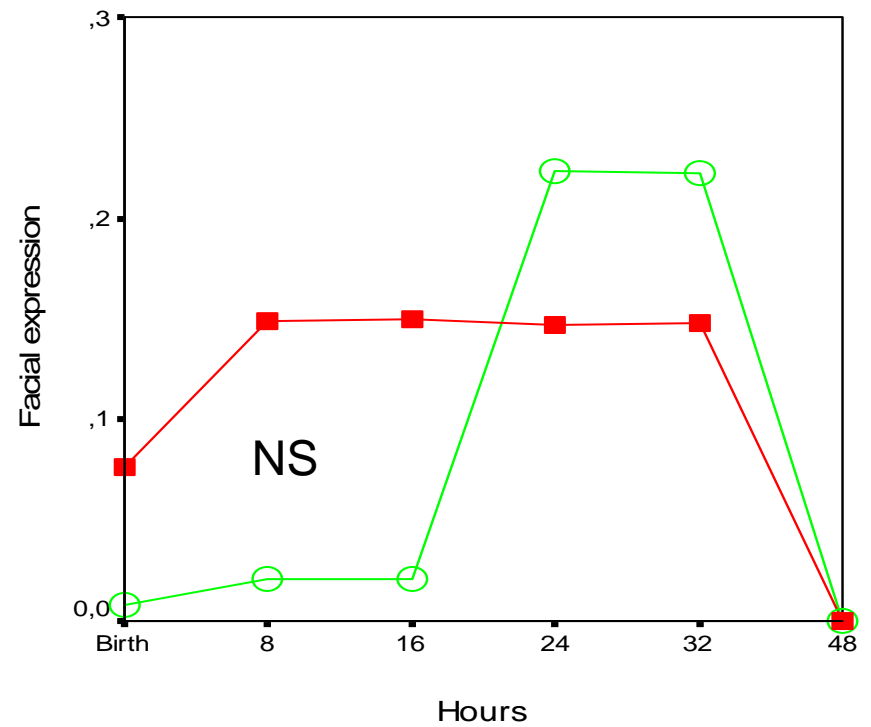






Time by maternal smoking status interaction ($F=5.47$, $p=0.025$)

Rouge: fumeuses



With covariate DHPG/norepinephrine ratio this interaction became non-significant ($F=1.53$, $p=0.23$)

Conclusions

- **Malgré le nombre faible de participants: l'effet foetotoxique des cigarettes peut être démontré - une toxicité hors du commun**
- **Cotinine plasmatique similaire chez la mère et chez le NN - pas de barrière placentaire**
- **Activité MAO A réduite chez la mère mais aussi dans le sang du cordon c-à-d chez le NN**
- **Visage plus crispé chez les NN des mères fumeuses. Association avec l'inhibition de la MAO A?**
- **Conséquences à court et à long-terme?**

Exposition à la fumée du tabac: relation CO dans l'air expiré et les caractéristiques de naissance

Table 1

Newborns' characteristics according to the mothers' expired air carbon monoxide concentration measured during delivery

Expired air carbon monoxide (ppm)	0 to 5, N = 517	6 to 10, N = 113	11 to 20, N = 169	>20, N = 57	P value
Birthweight (g) ^{a,*}	3448 ± 11	2947 ± 39	2739 ± 32	2691 ± 56	<0.0001
Head circumference (cm) ^{b,*}	35.1 ± 0.04	34.7 ± 0.08	34.9 ± 0.07	35.5 ± 0.11	<0.0001
Apgar score ^{c,*}	9.7 ± 0.02	9.5 ± 0.05	9.4 ± 0.04	9.4 ± 0.06	<0.0001
Gestational age (weeks) ^{d,*}	39.1 ± 0.09	38.6 ± 0.15	38.5 ± 0.15	39.8 ± 0.26	<0.0001
Cord blood fetal carboxyhemoglobin (%) ^{e,*}	1.46 ± 0.07	2.38 ± 0.13	3.4 ± 0.13	5.66 ± 0.31	<0.0001
Fetal heart rate during delivery (number with normal heart rate (%)) ^{f,**}	434 (83.9)	65 (57.5)	59 (34.9)	21 (36.8)	<0.0001