ALCOOL & EPIGENETIQUE DU REMODELAGE DE LA CHROMATINE A LA THERAPEUTIQUE

15e Congrès de la Société Francophone de Tabacologie

25 & 26 novembre 2021

Sortir du tabac : une priorité pour tous !

Pr Mickael Naassila

grap
GROUPE DE RECHERCHE SUR L'ALCOOL & LES PHARMACODÉPENDANCES

Alcool Conso Science

Améliorer les **connaissances** sur l'usage d'**alcool**

Pour une **communication** basée sur la **science**

www.sfalcoologie.asso.fr • @SFAlcoologie

Société Française d'Alcoologie

Inserm
La science pour la santé
From science to health

UNIVERSITÉ de Picardie Jules Verne

Mes liens d'intérêts…

attention, un lien d'intérêt n'est pas un conflit d'intérêt

- **Bioprojet Biotech**
- **Indivior**
- **Lundbeck**

Président

European Society for Biomedical Research on Alcoholism

Membre bureau exécutif

ISBRA

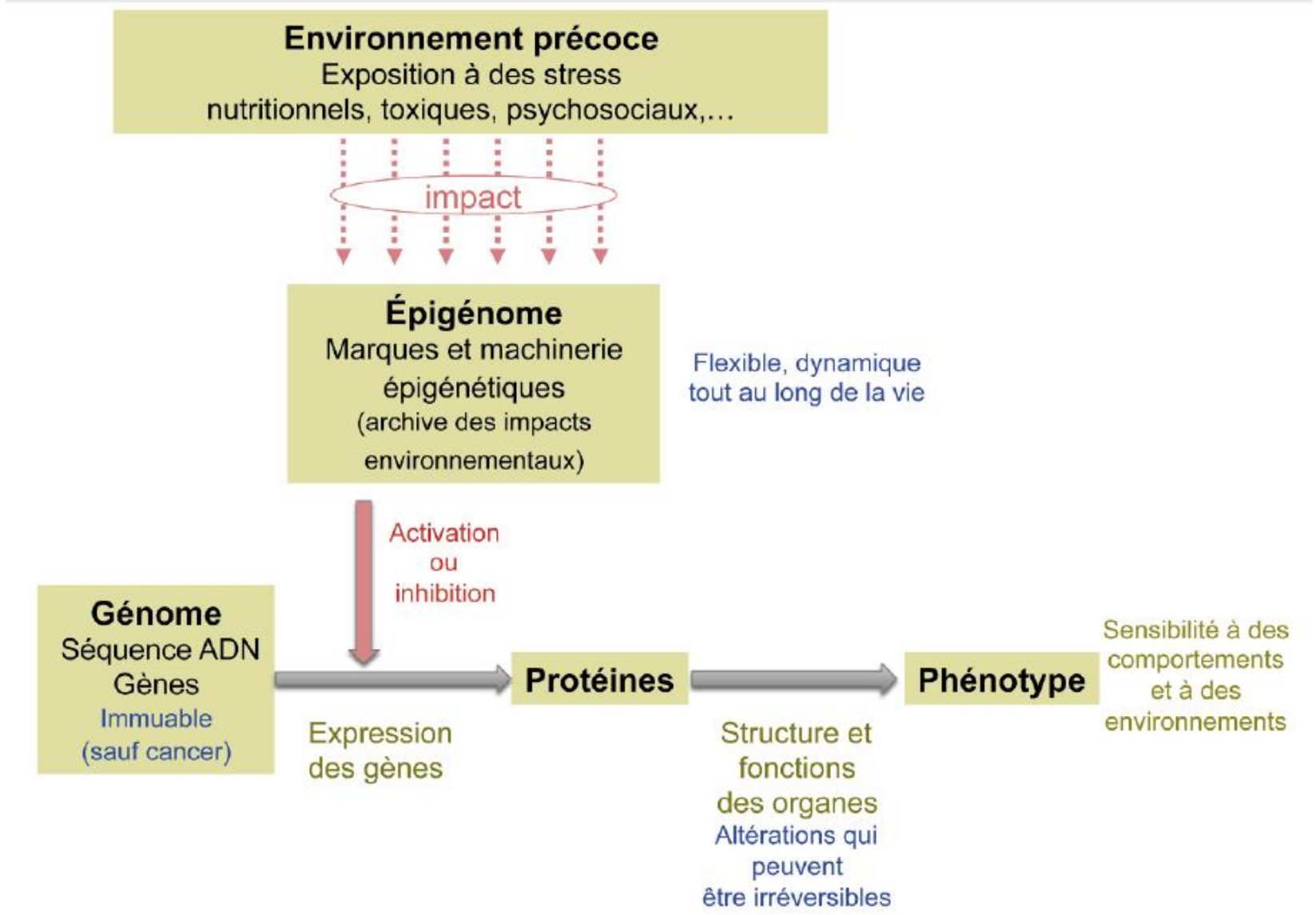
Président

Société Française d'Alcoologie

Vice-Président

FFA
Fédération Française d'Addictologie

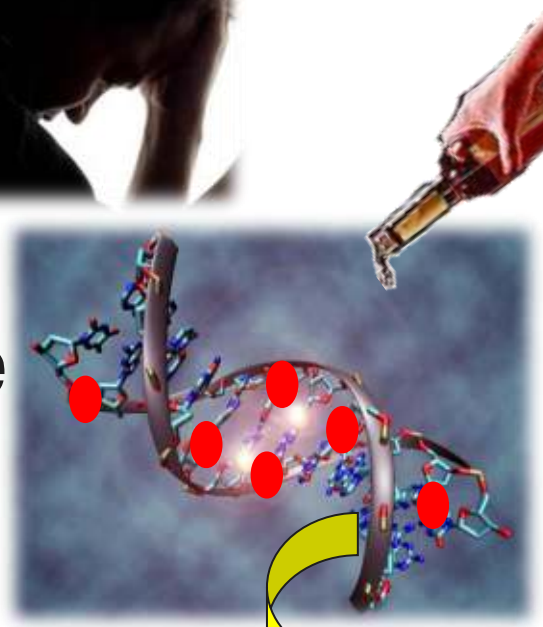
Epigénétique, ou l'adaptation sur une génération



Epigénétique, Inné/acquis: fin du dogme

Environnement

Epigénome

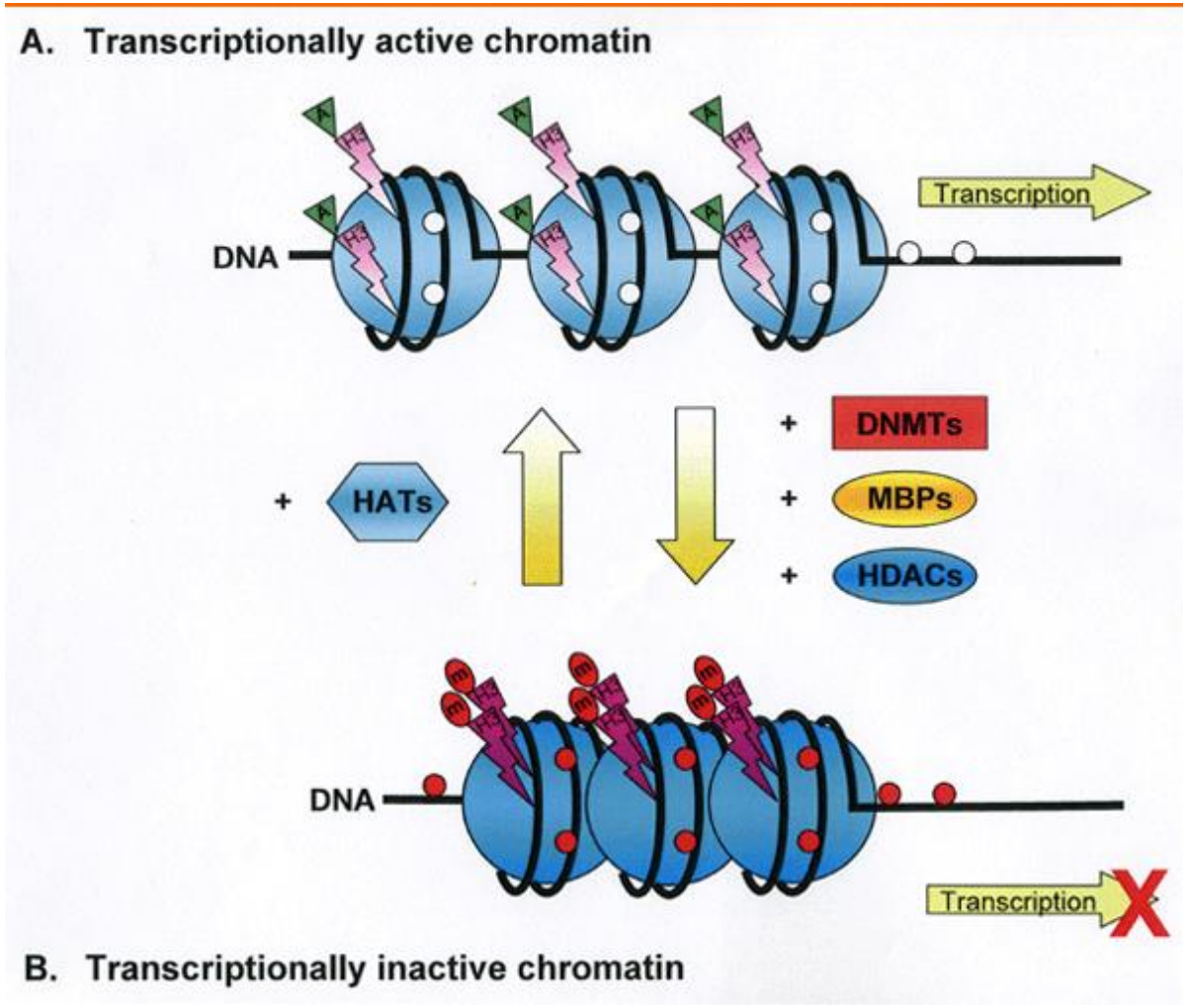


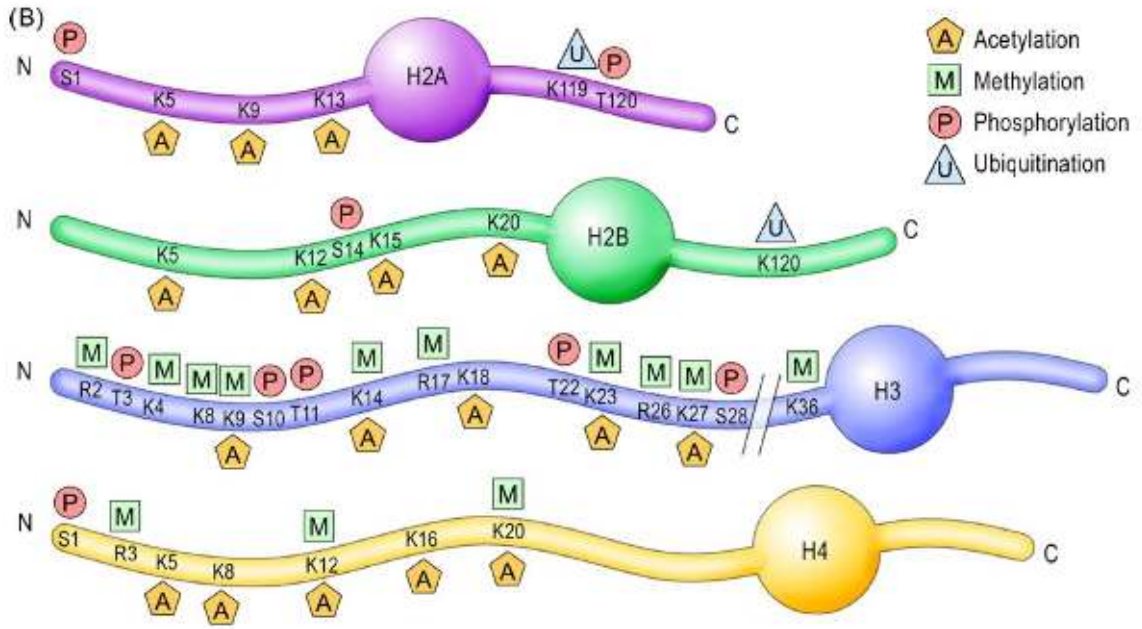
Anatomie
Physiologie
Comportement

Maladies:
Dépression
Addiction…

Transmission entre les générations

Epigénome, les modifications chimiques ADN et histones

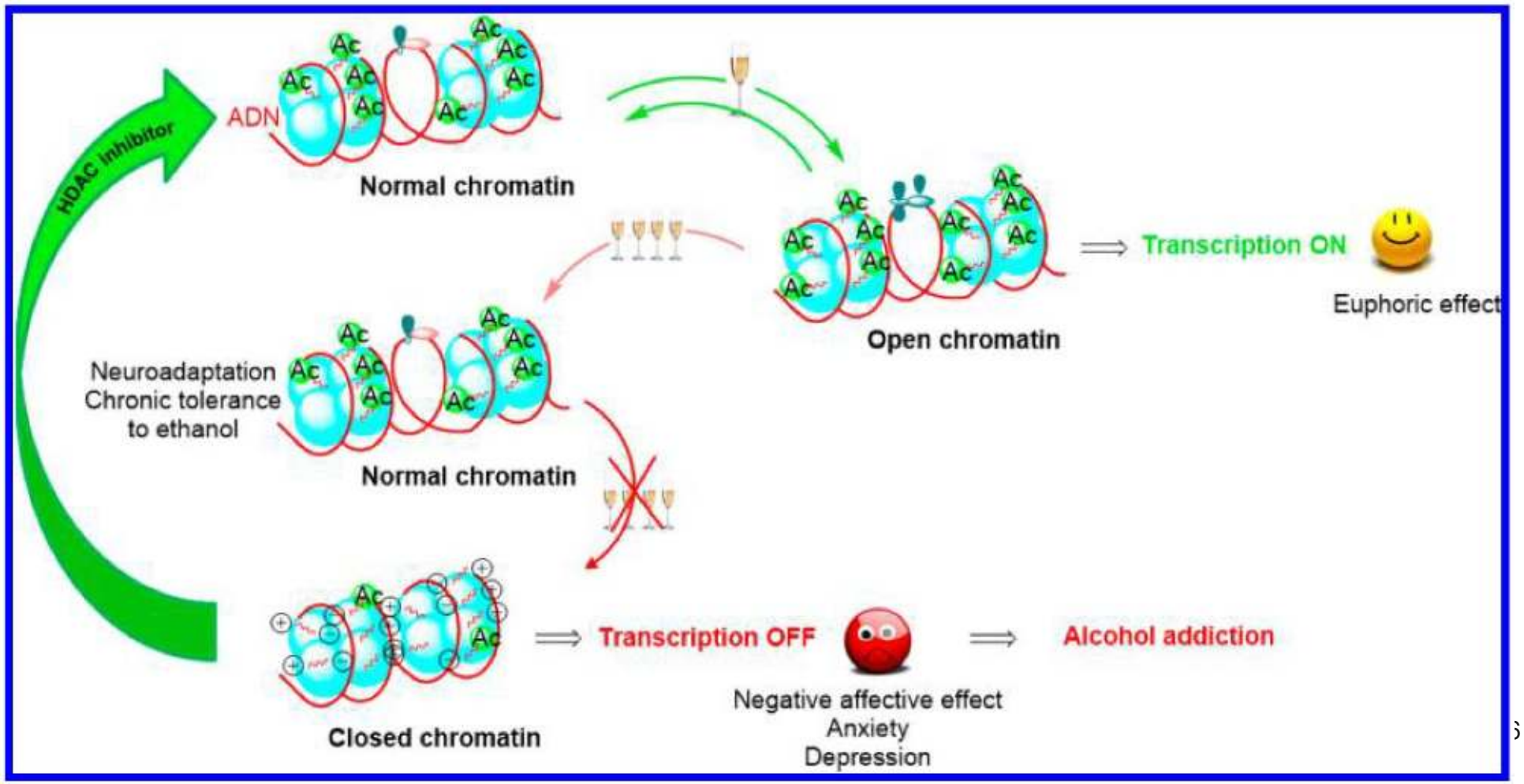




Journal of Medicinal Chemistry
Perspective
pubs.acs.org/jmc

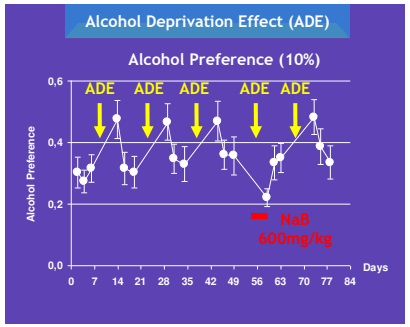
Class I HDAC Inhibitors: Potential New Epigenetic Therapeutics for Alcohol Use Disorder (AUD)

Erika Bourguet,[*,†,⊥] Katarzyna Ozdarska,[†,‡] Gautier Moroy,[§] Jérôme Jeanblanc,[∥,⊥] and Mickaël Naassila[*,∥,⊥]

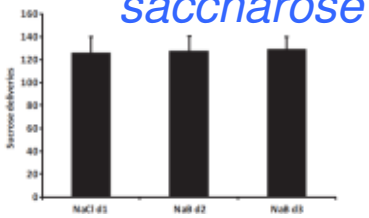


Efficacité du butyrate de sodium et du MS-275

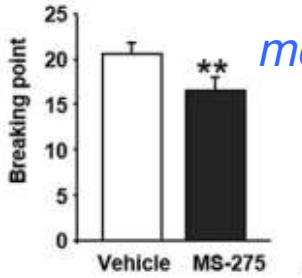
Rebond après privation



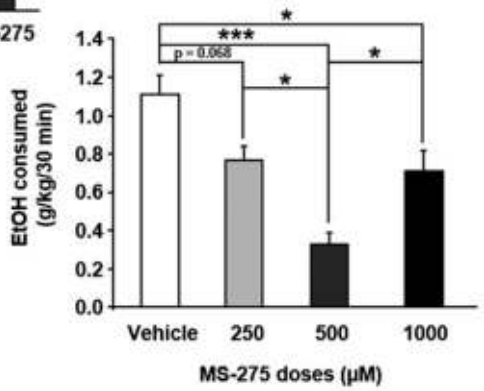
saccharose



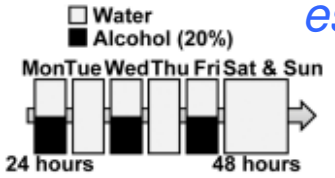
motivation

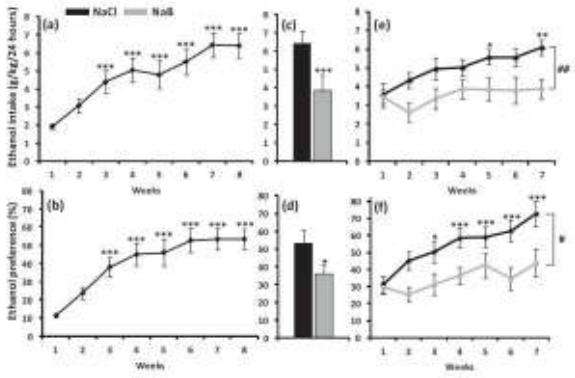


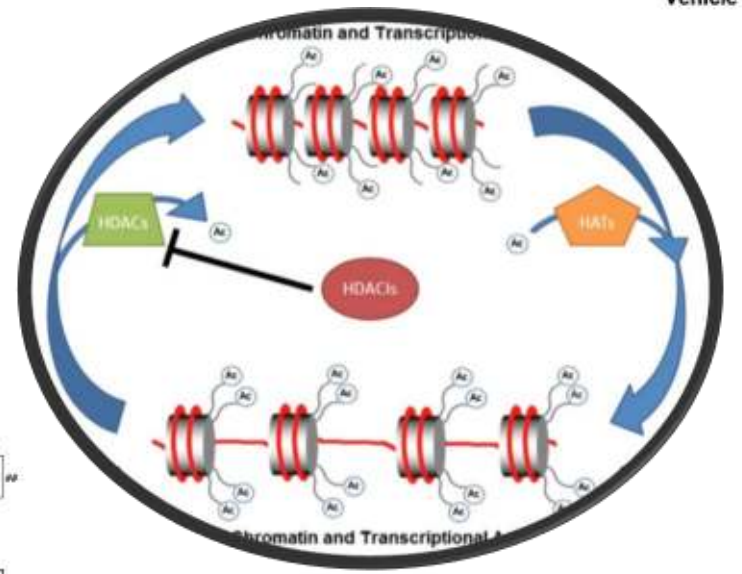
consommation



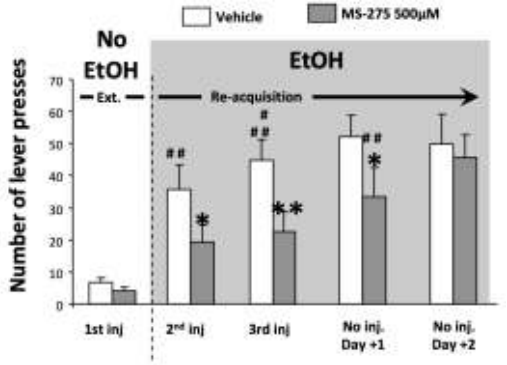
escalade







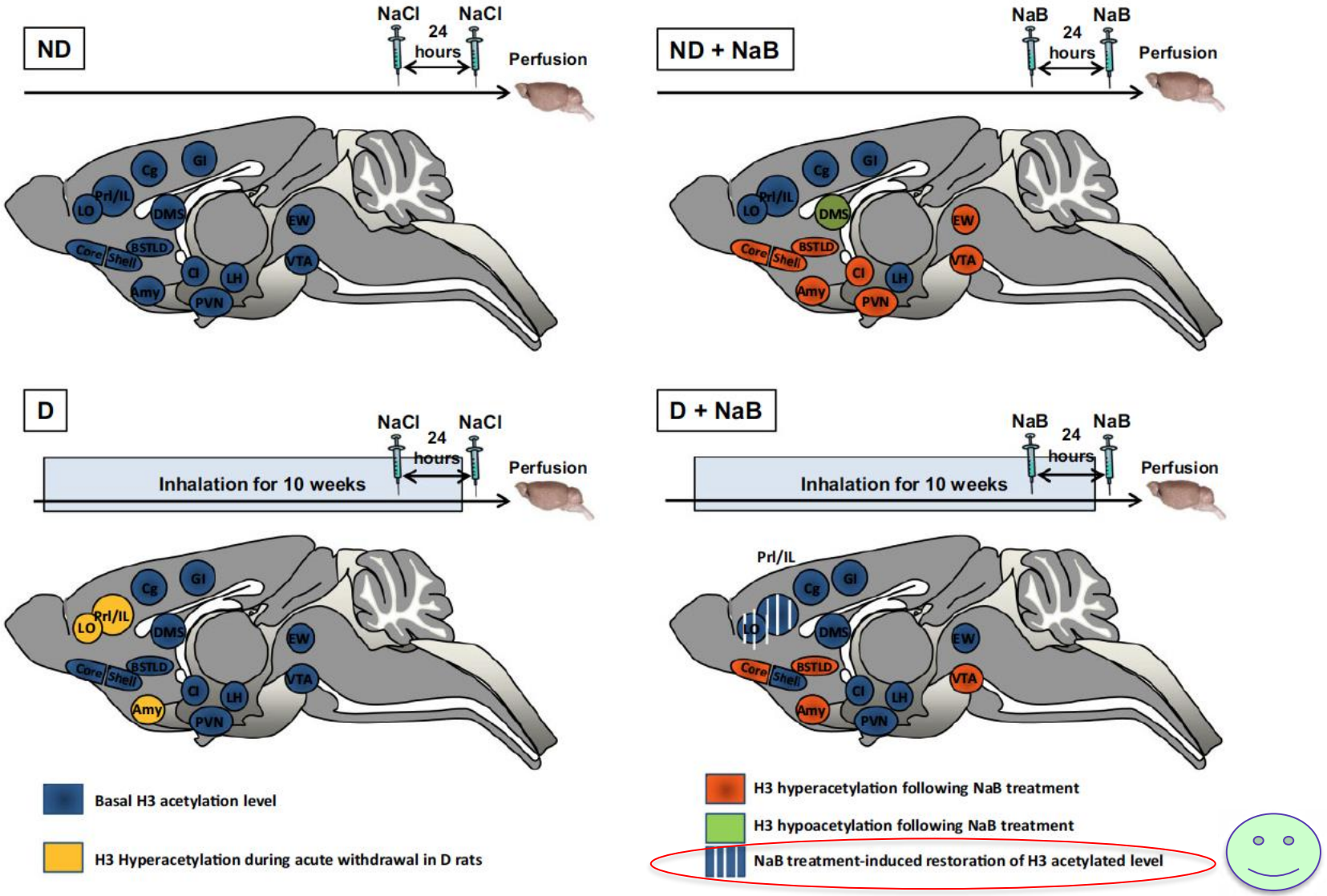
Rechute



Simon O'Brien et al 2015 Addiction Biol

J Jeanblanc et al Int J Neuropsychopharmacol 2015

Effet spécifique du butyrate de sodium sur Ac-H3



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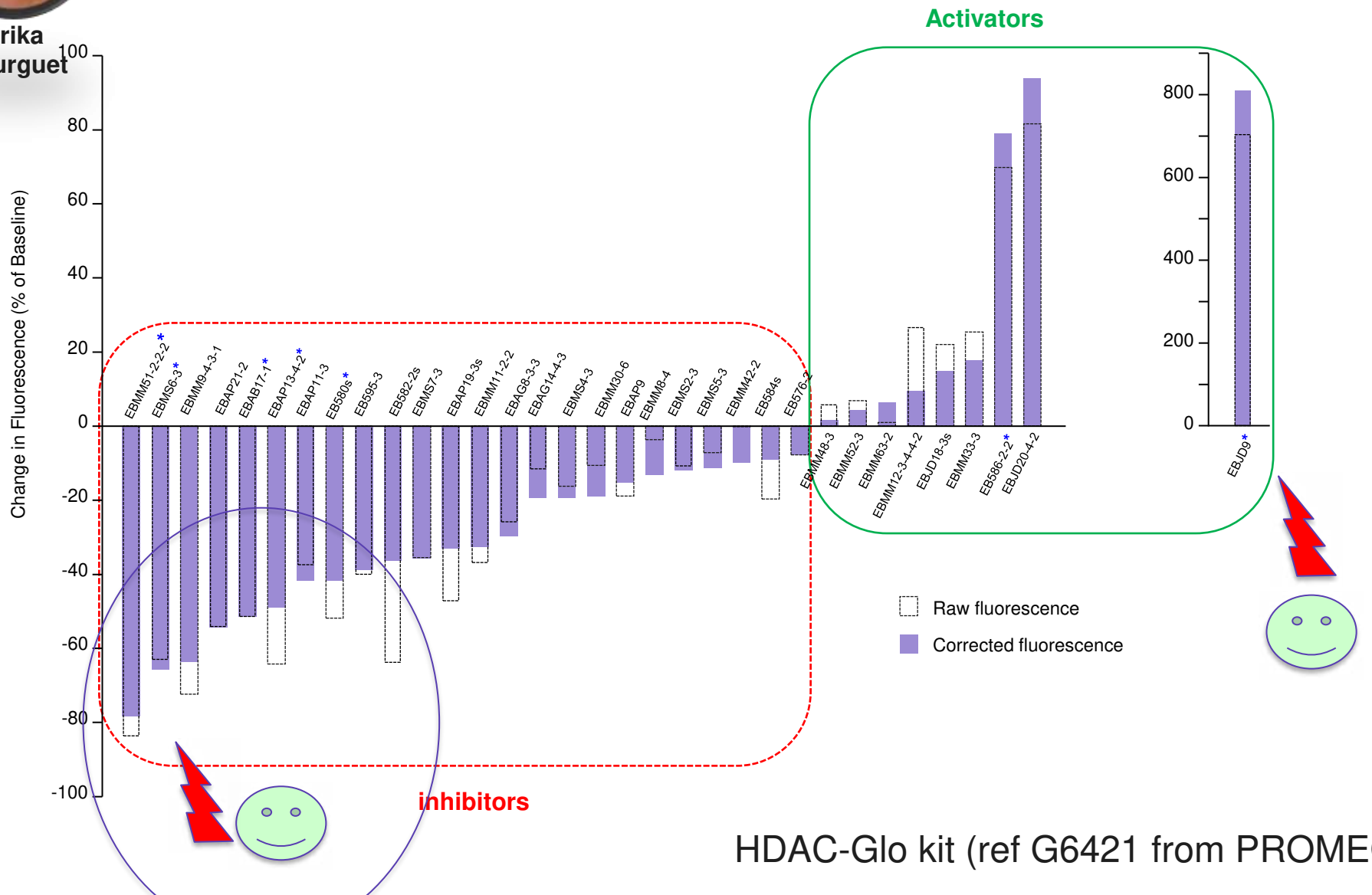
Simon O'Brien et al 2015 Addiction Biol

Erika Bourguet

Criblage de molécules inhibitrices et activatrices

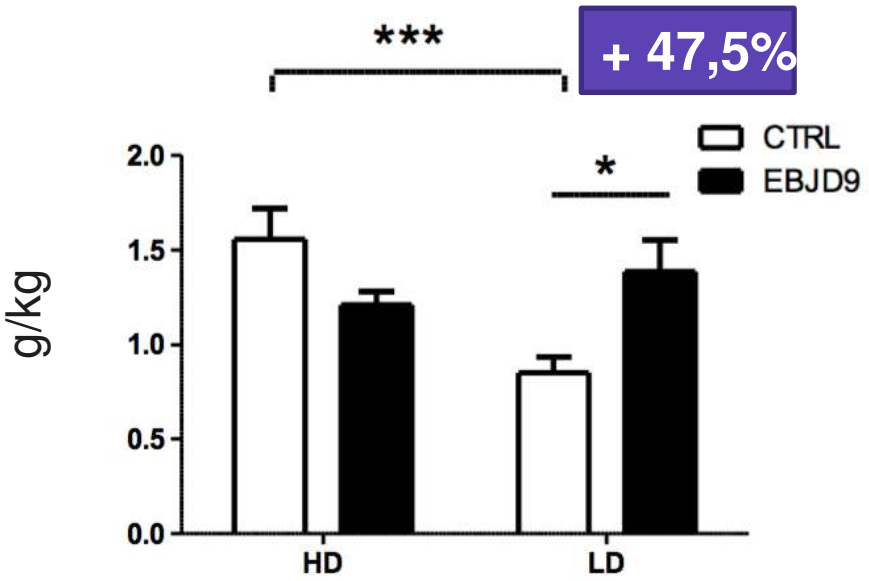


HDAC-Glo kit (ref G6421 from PROMEGA)

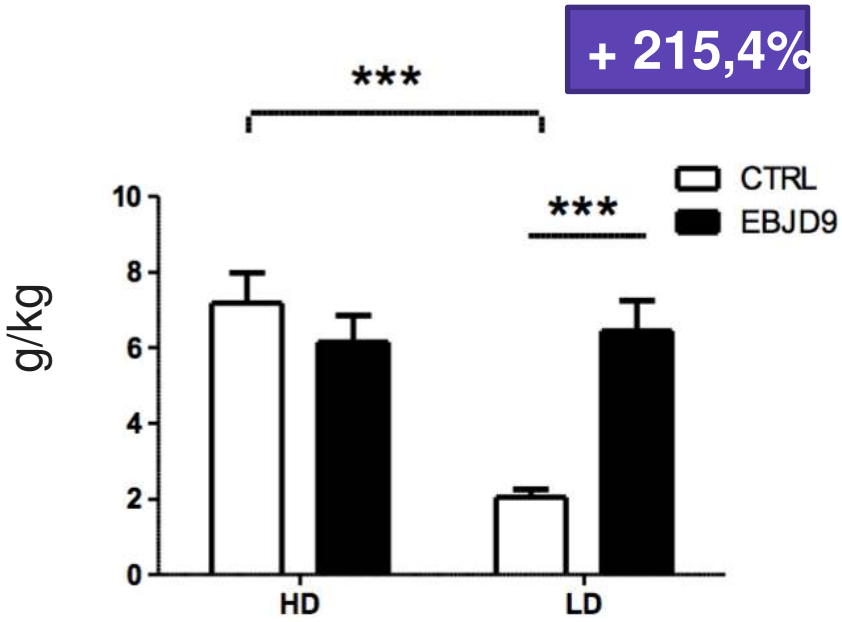
L’activateur augmente la conso des « faibles » buveurs

Effet d’une seule injection

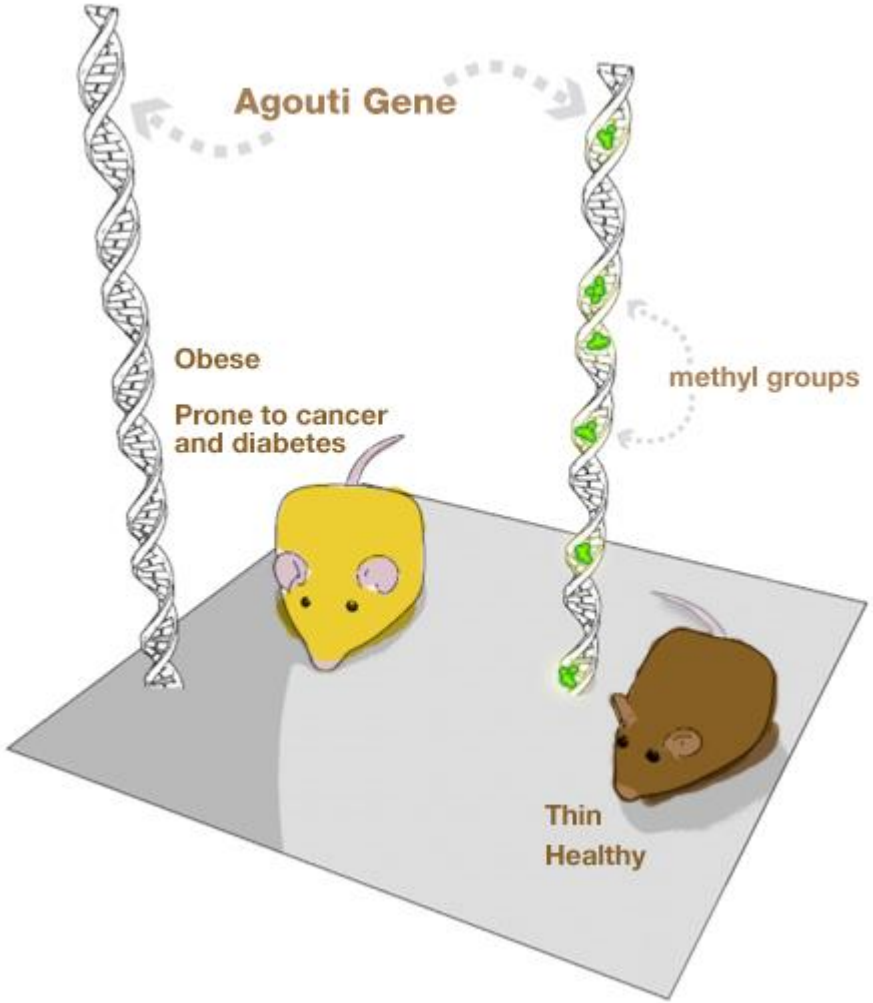
Conso 2h



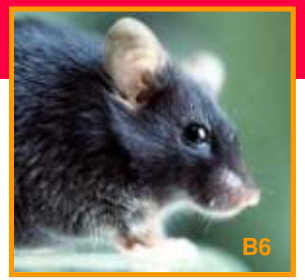
Conso 24h



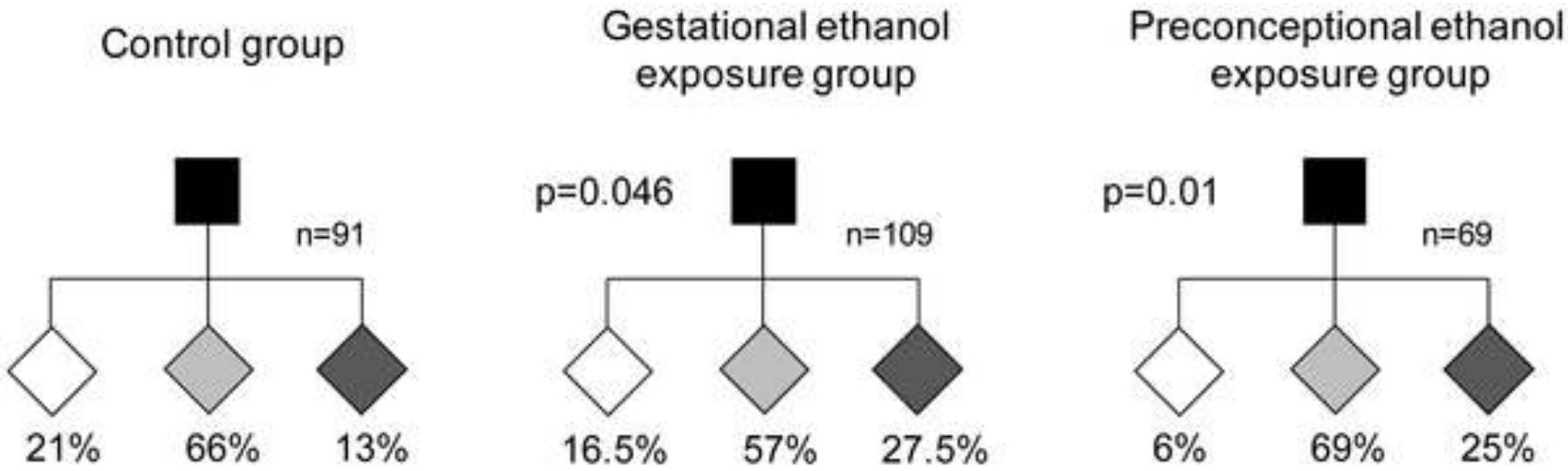
Gène Agouti, couleur du pelage et vulnérabilité à certaines pathologies…



Gène Agouti, couleur du pelage et vulnérabilité à certaines pathologies…

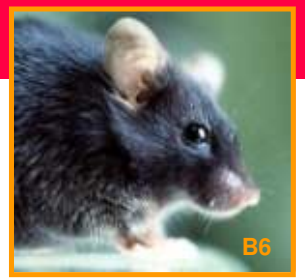


- Consommation volontaire d'alcool 10% (pic alcoolémie estimé 1g/l)
- Exposition gestationnelle et pré-conceptionnelle entraîne une plus grande proportion se souris pseudoagouti Avy.

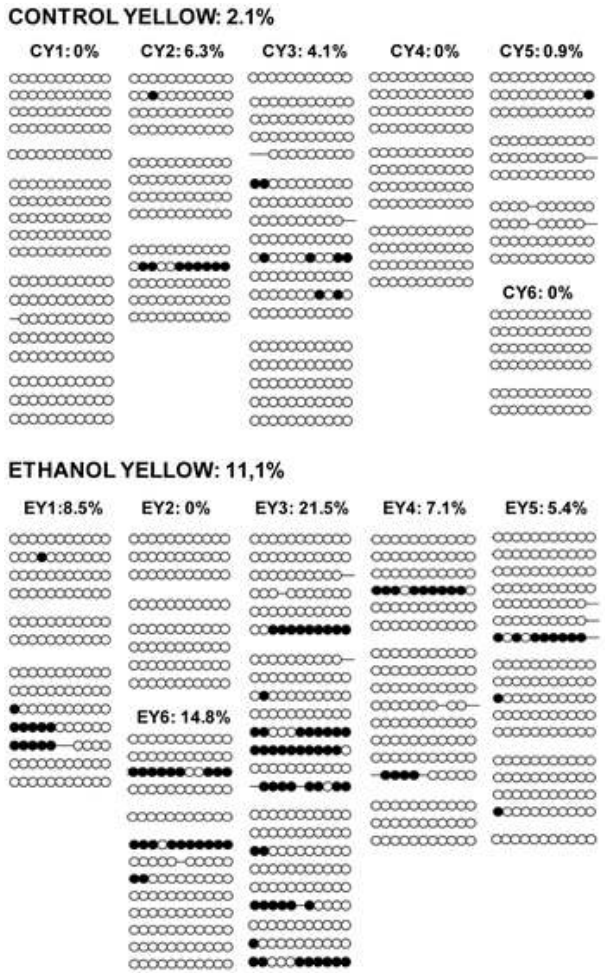


Maternal ethanol consumption alters the epigenotype and the phenotype of offspring in a mouse model. Kaminen-Ahola N, PLoS Genet. 2010 Jan 15;6(1):e1000811.

Gène Agouti, couleur du pelage et vulnérabilité à certaines pathologies…



- Méthylation Avy dans la descendance témoin et exposée à l'alcool *in utero*.
- Il y a plus de clones hyperméthylés chez les souris qui ont été exposées à l'alcool



Maternal ethanol consumption alters the epigenotype and the phenotype of offspring in a mouse model. Kaminen-Ahola N, PLoS Genet. 2010 Jan 15;6(1):e1000811.

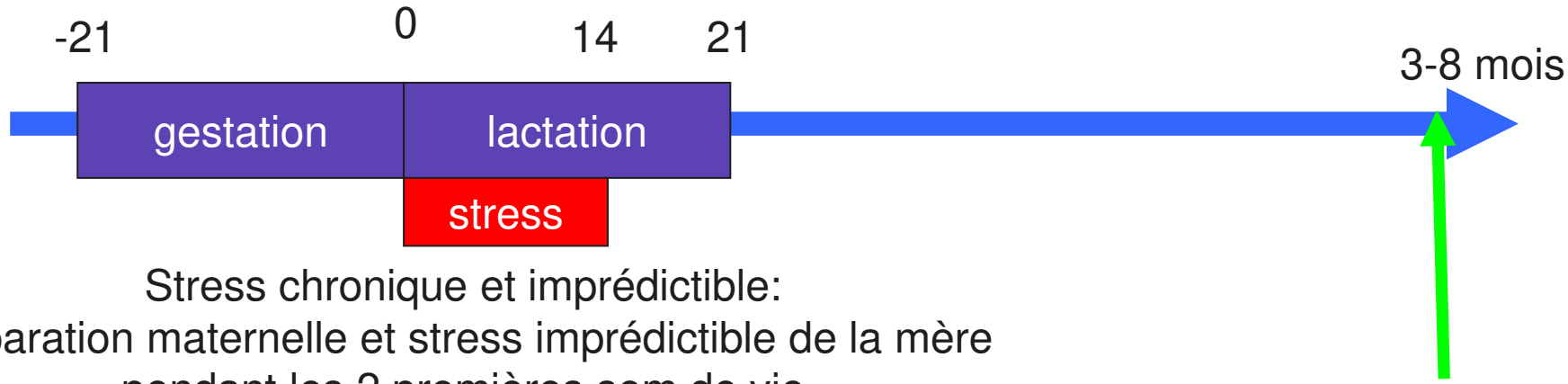
Epigenetic Transmission of the Impact of Early Stress Across Generations

Tamara B. Franklin, Holger Russig, Isabelle C. Weiss, Johannes Gräff, Natacha Linder, Aubin Michalon, Sandor Vizi, and Isabelle M. Mansuy

0006-3223/$36.00
doi:10.1016/j.biopsych.2010.05.036

BIOL PSYCHIATRY 2010;68:408–415

- **Traumatismes à un âge précoce => dévlpt troubles émotionnels / comportementaux à l'âge adulte ET transmission entre les générations**



Stress chronique et imprédictible:
séparation maternelle et stress imprédictible de la mère pendant les 2 premières sem de vie

Comportement de type dépressif (nage forcée; saccharose)
Réactivité nouveauté/environnement aversif (open field, exploration)

ENVIRONMENTAL EPIGENETICS

Environmental Epigenetics, 2018, 1–8

doi: 10.1093/eep/dvy023
Research Article

RESEARCH ARTICLE

Transgenerational inheritance of behavioral and metabolic effects of paternal exposure to traumatic stress in early postnatal life: evidence in the 4th generation

Gretchen van Steenwyk , Martin Roszkowski , Francesca Manuella, Tamara B. Franklin [1] and Isabelle M. Mansuy *

Laboratory of Neuroepigenetics, Brain Research Institute, Faculty of Medicine, University of Zurich & Institute for Neuroscience, Department of Health Science and Technology, ETH Zurich, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland

Stress de la mère
ET séparation des petits

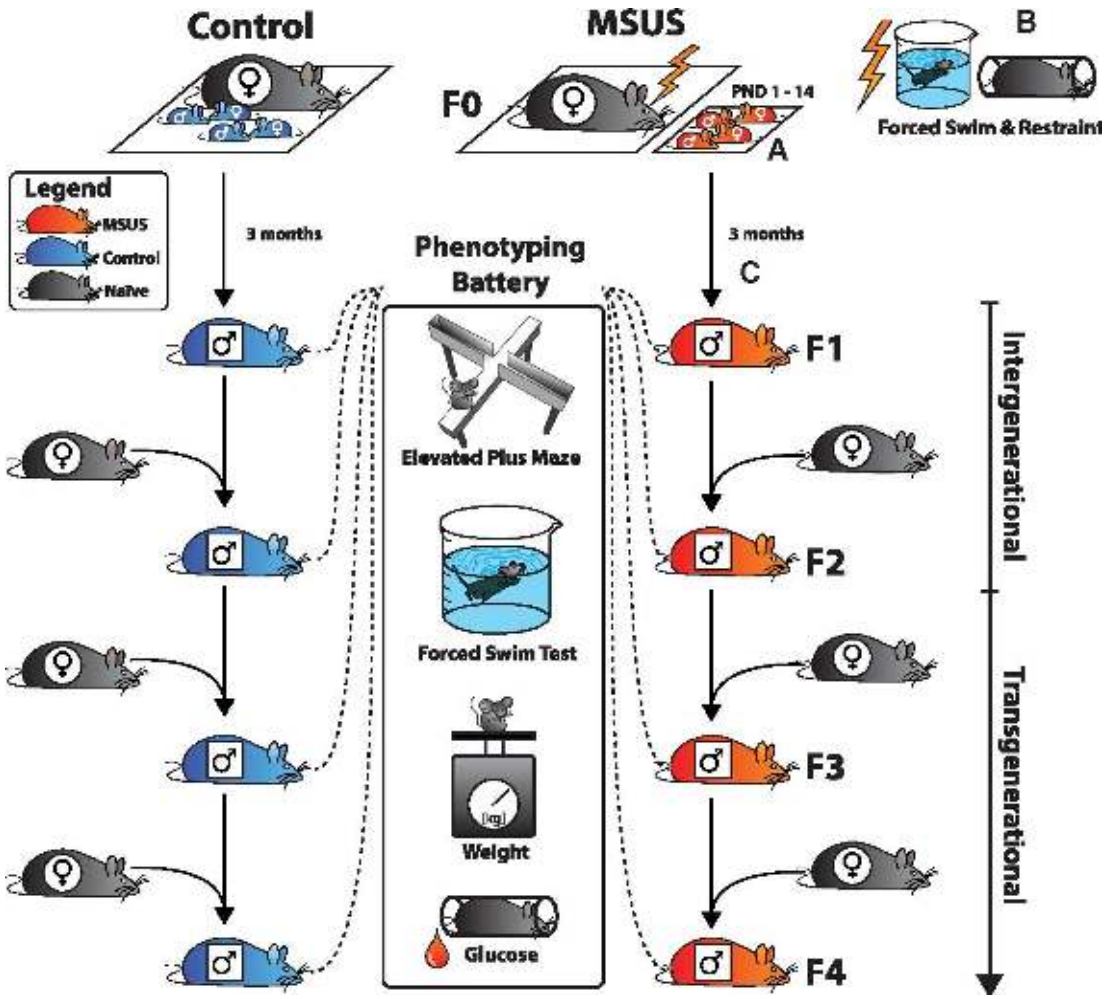
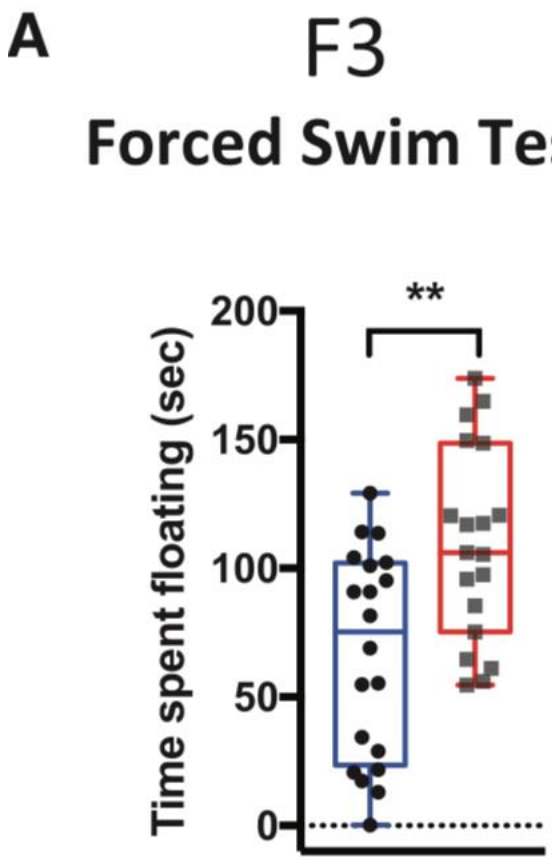


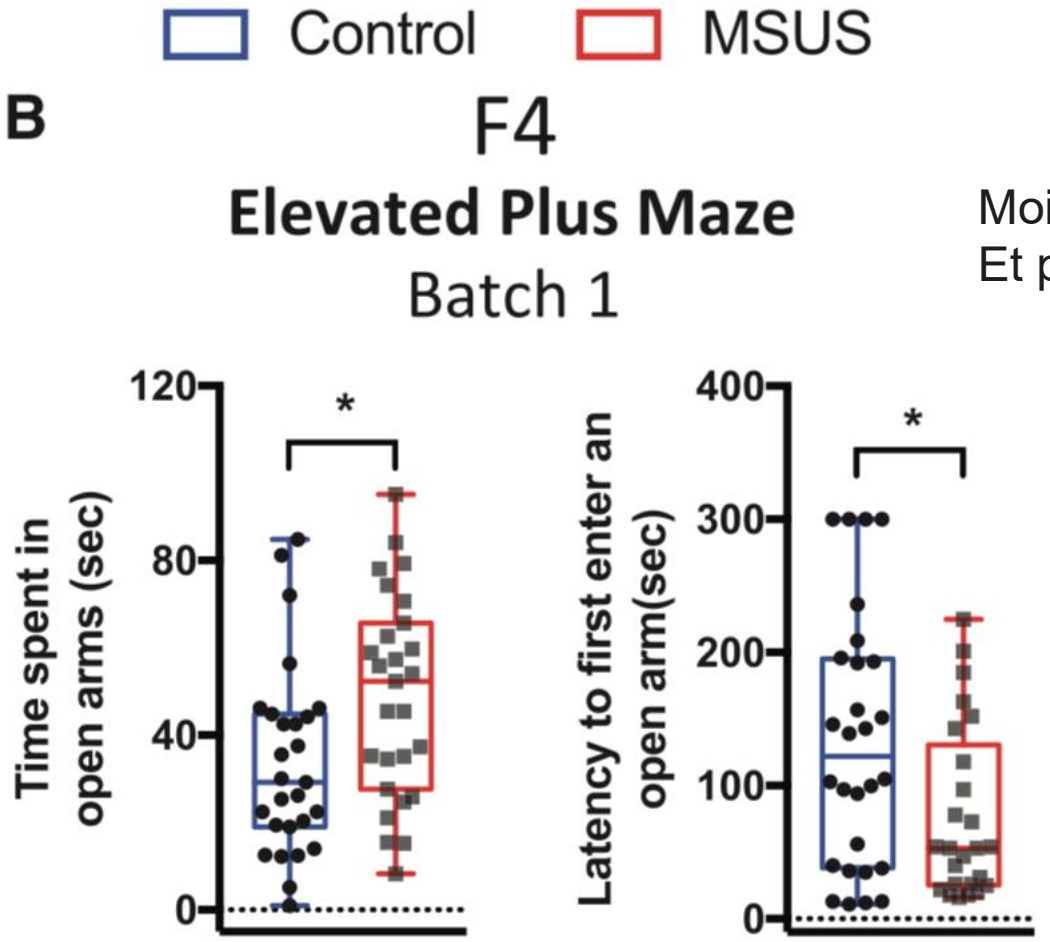
Figure 1: MSUS paradigm. MSUS consists of (A) separating mouse pups (F1) from their mother (F0, naïve primiparous ...

Résultats chez les mâles

Symptômes de type dépressif

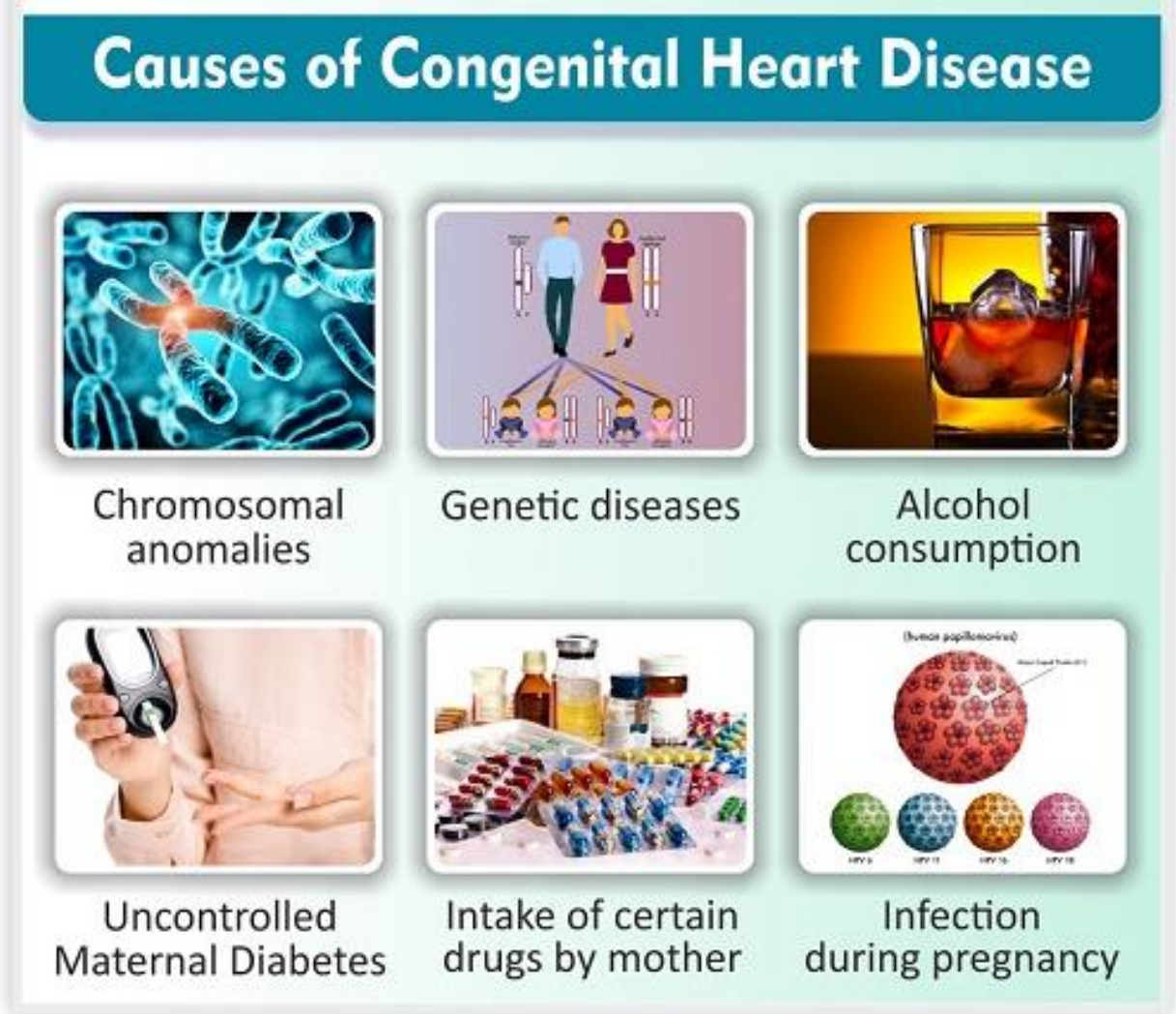


Symptômes de type anxieux



Moins d'aversion
Et plus d'impulsivité

Exemple d'étude chez l'Homme: Maladie cardiaque congénitale



- Chez 28.5% des enfants touchés par le SAF (Burd et al Congenit Heart Dis 2007)

European Journal of Preventive Cardiology

ESC European Society of Cardiology

Review

European Journal of Preventive Cardiology
0(00) 1–12

DOI: 10.1177/2047487319874530
journals.sagepub.com/home/cpr

SAGE

Parental alcohol consumption and the risk of congenital heart diseases in offspring: An updated systematic review and meta-analysis

Senmao Zhang, Lesan Wang, Tubao Yang, Lizhang Chen, Lijuan Zhao, Tingting Wang, Letao Chen, Ziwei Ye, Zan Zheng and Jiabi Qin

Abstract

Objective: The aim of this study was to provide updated evidence to assess the association between parental alcohol consumption and the risk of total congenital heart diseases (CHDs) and specific CHD phenotypes in offspring, and explore the possible dose–response pattern.

Methods: PubMed, Embase and Chinese databases were searched with an end-date parameter of July 24, 2019 to identify studies meeting pre-stated inclusion criteria. A random-effects model was used to calculate the overall combined risk estimates. A meta-analysis of the dose–response relationship was performed. Subgroup analysis, sensitivity analysis, and Galbraith plot were conducted to explore potential heterogeneity moderators.

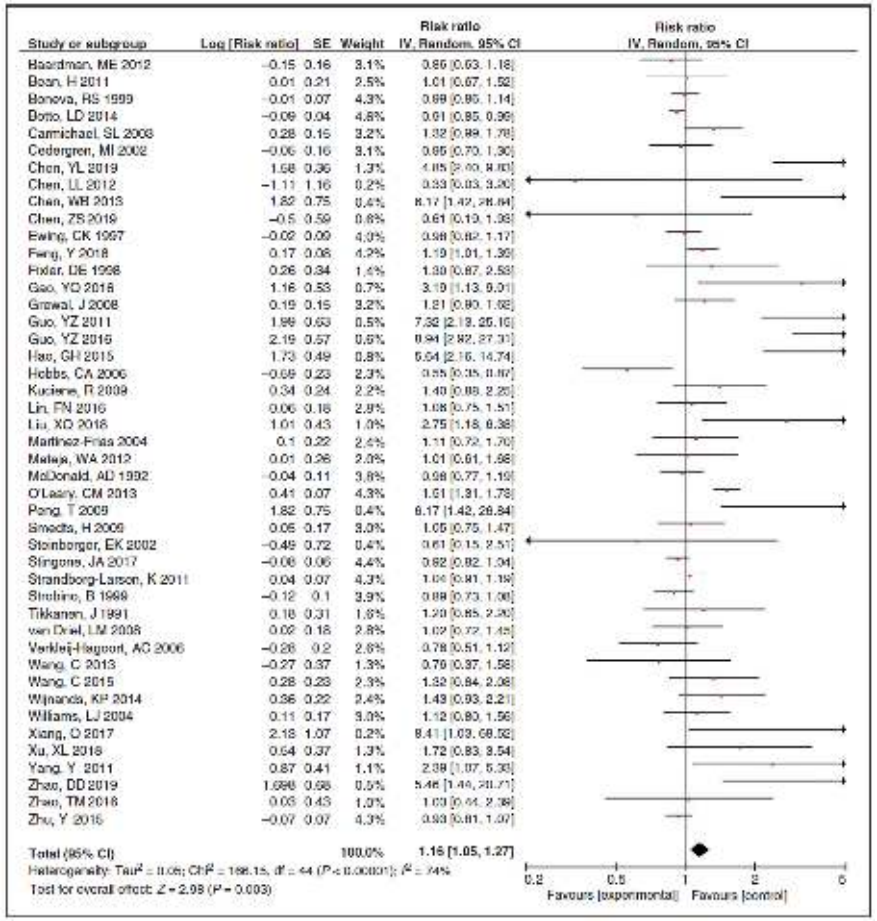
Results: A total of 55 studies involving 41,747 CHD cases and 297,587 controls were identified. Overall, both maternal (odds ratio (OR) = 1.16; 95% confidence interval (CI): 1.05–1.27) and paternal (OR = 1.44; 95% CI: 1.19–1.74) alcohol exposures were significantly associated with risk of total CHDs in offspring. Additionally, a nonlinear dose–response relationship between parental alcohol exposure and risk of total CHDs was observed. With an increase in parental alcohol consumption, the risk of total CHDs in offspring also gradually increases. For specific CHD phenotypes, a statistically significant association was found between maternal alcohol consumption and risk of tetralogy of fallot (OR = 1.20; 95% CI: 1.08–1.33). Relevant heterogeneity moderators have been identified by subgroup analysis, and sensitivity analysis yielded consistent results.

Conclusions: Although the role of potential bias and evidence of heterogeneity should be carefully evaluated, our review indicates that parental alcohol exposures are significantly associated with the risk of CHDs in offspring, which highlights the necessity of improving health awareness to prevent alcohol exposure during preconception and conception periods.

Exposures and outcomes of interest

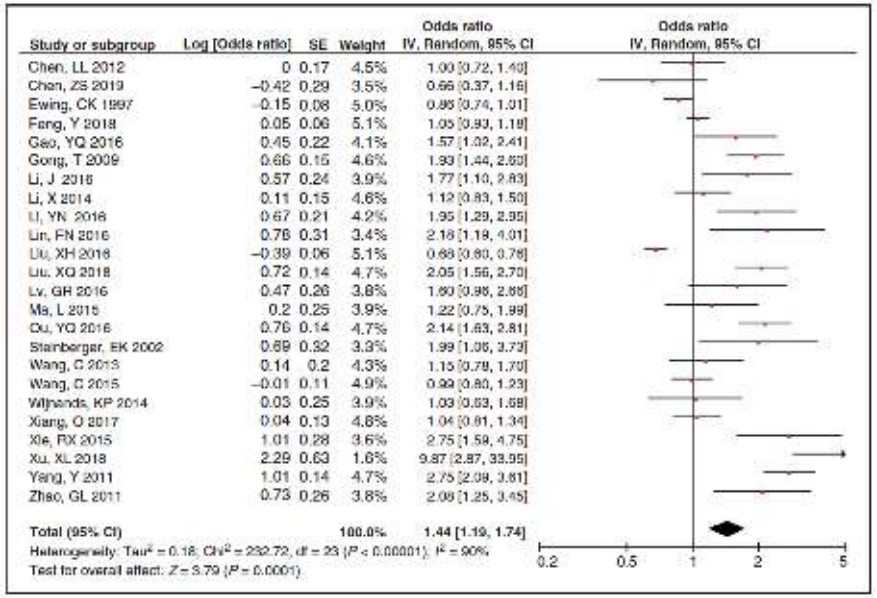
In the present study, the exposures of interest were parental alcohol consumption. Alcohol exposure was defined as any alcohol taken during the peri-conception period (three months before the pregnancy and the first trimester of pregnancy).[24] Additionally, we also examined the association between parental binge drinking (defined as five or more drinks per sitting[25]) and risk of CHDs. The outcomes of interest were CHDs. In this review, we focused not only on the risk of total CHDs, but also on the risk-specific CHD phenotypes, including ventricular septal defect (VSD), atrial septal defect (ASD), atrioventricular septal defect (AVSD), d-transposition of the great arteried (TGA), tetralogy of fallot (TOF), pulmonary valve stenosis (PVS), and so on. Because variations in the definition of exposures and outcomes exist across countries and cultures, it is extremely difficult to define uniform standards. Some of the included studies did not always define exposures and outcomes, and in such cases, we relied on the corresponding terminology in the original articles.

Conso maternelle



+16%

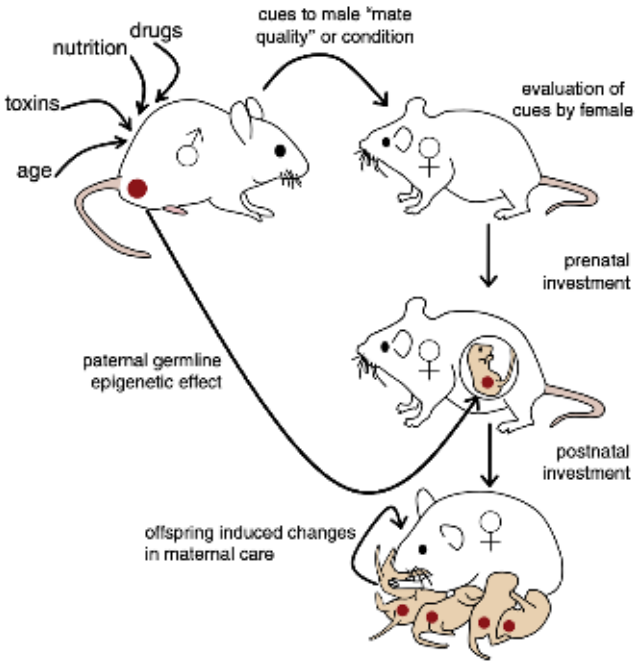
Conso paternelle

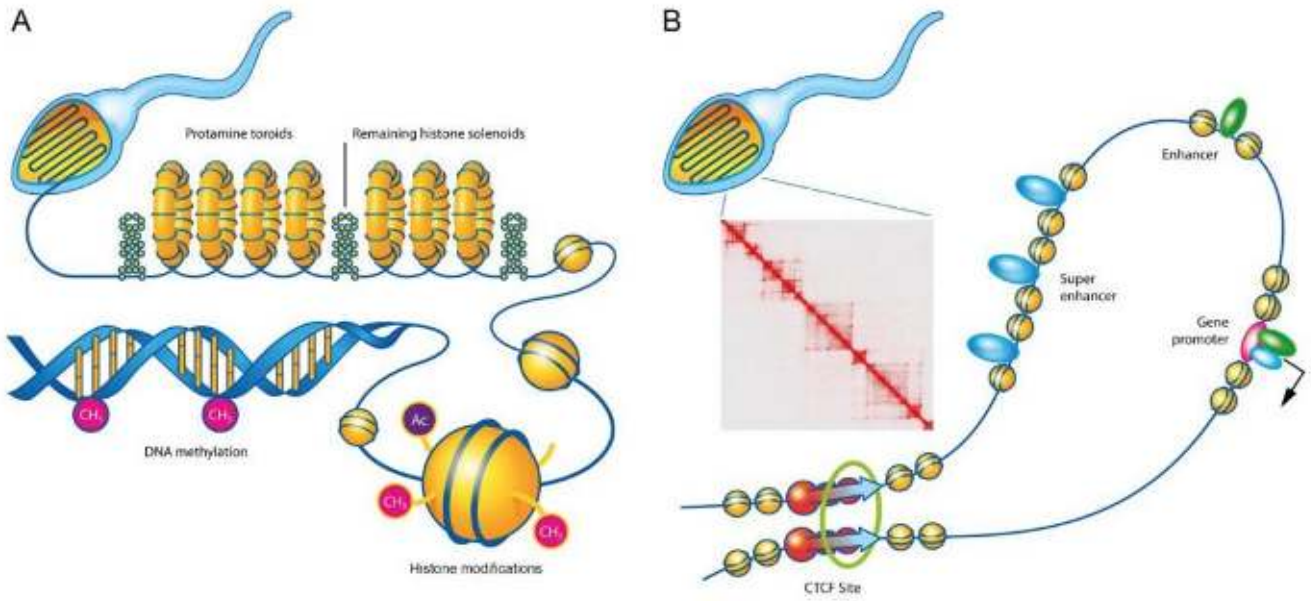


+44%

Consommation paternelle

- **Modifications épigénétiques dans les spermatozoïdes: méthylation ADN, modifications des histones, de l'expression des microARN**






Désir de grossesse
Grossesse
Allaitement
Zero alcool
Ne consommez pas d'alcool avant et pendant votre grossesse ou lors d'un allaitement.
Ne proposez pas d'alcool à une femme enceinte ou qui allaite.


Merci de votre attention