Troubles psychiatriques en post-partum

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Troubles psychiatriques périnataux
20 % des femmes

Episodes thymiques périnataux **légers**

30% 1ers épisodes

70% sont des rechutes

Episodes thymiques périnataux **graves**

50% 1ers épisodes

50 % sont des rechutes

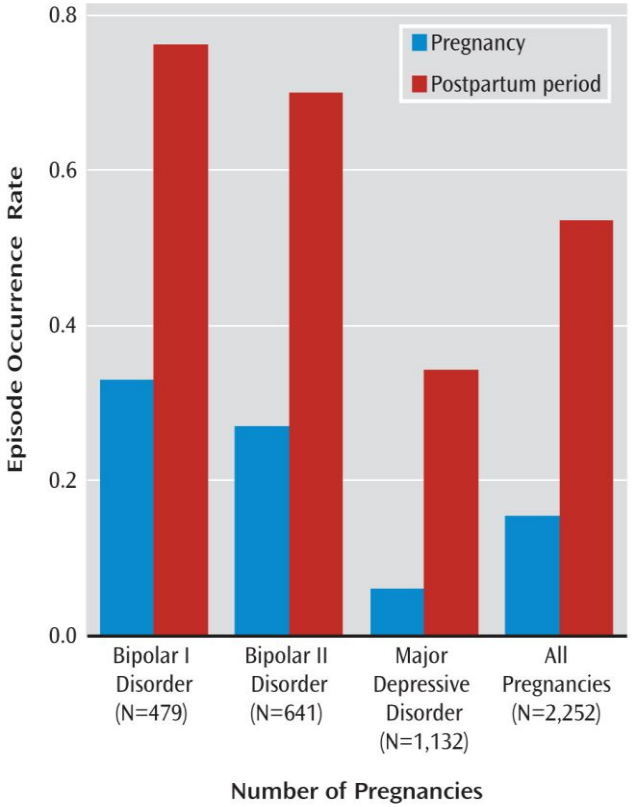
Facteurs de vulnérabilité et de protection connus

Démarche de Santé Publique

Préventions primaires et secondaires

Troubles psychiatriques périnataux

Viguera et al., 2011 ; Rannveig et al., 2019



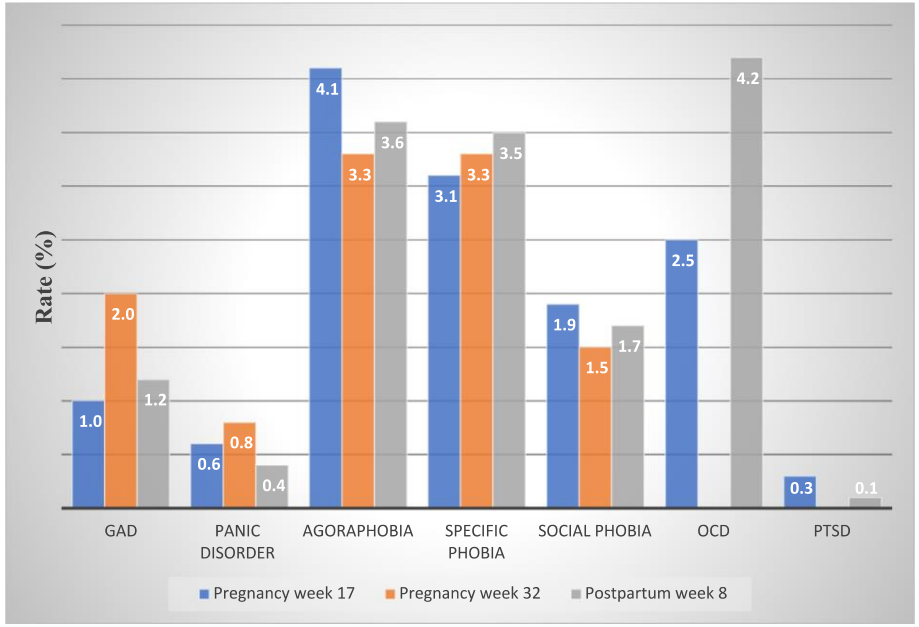
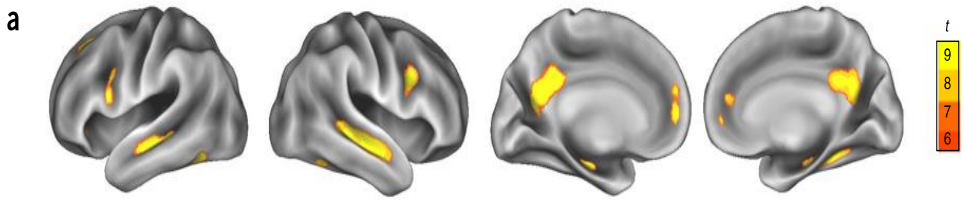


Fig. 3. Prevalence of symptoms in the anxiety categories, as measured by questions based on the Mini-International Neuropsychiatric Interview (MINI). Abbreviations: GAD: Generalized Anxiety Disorder; OCD: Obsessive-Compulsive Disorder; PTSD: Post-Traumatic Stress Disorder. OCD and PTSD were not measured in pregnancy week 32.

Pregnancy leads to long-lasting changes in human brain structure

Elseline Hoekzema[1–3,8], Erika Barba-Müller[1,8], Cristina Pozzobon[4], Marisol Picado[1], Florencio Lucco[4], David García-García[5], Juan Carlos Soliva[1], Adolf Tobeña[1], Manuel Desco[5], Eveline A Crone[2,3], Agustín Ballesteros[4], Susanna Carmona[1,5,6,9] & Oscar Vilarroya[1,7,9]

Pregnancy involves radical hormone surges and biological adaptations. However, the effects of pregnancy on the human brain are virtually unknown. Here we show, using a prospective ('pre'-'post' pregnancy) study involving first-time mothers and fathers and nulliparous control groups, that pregnancy renders substantial changes in brain structure, primarily reductions in gray matter (GM) volume in regions subserving social cognition. The changes were selective for the mothers and highly consistent, correctly classifying all women as having undergone pregnancy or not in-between sessions. Interestingly, the volume reductions showed a substantial overlap with brain regions responding to the women's babies postpartum. Furthermore, the GM volume changes of pregnancy predicted measures of postpartum maternal attachment, suggestive of an adaptive process serving the transition into motherhood. Another follow-up session showed that the GM reductions endured for at least 2 years post-pregnancy. Our data provide the first evidence that pregnancy confers long-lasting changes in a woman's brain.



Hoekzema et al., *Nature Neuroscience*, 2017

Spécificité…?
l'enfant !

14-23 % des enfants ont des parents souffrant d'une maladie mentale - majoritairement troubles thymiques dépressifs

APA, 2019

Child and Adolescent Mental Health

Child and Adolescent Mental Health 24, No. 2, 2019, pp. 142–148 doi:10.1111/camh.12279

Trajectories and predictors of risk for mental health problems throughout childhood

Stewart A. Vella[1,2], Lauren A. Gardner[2], Christian Swann[3] & Mark S. Allen[2]

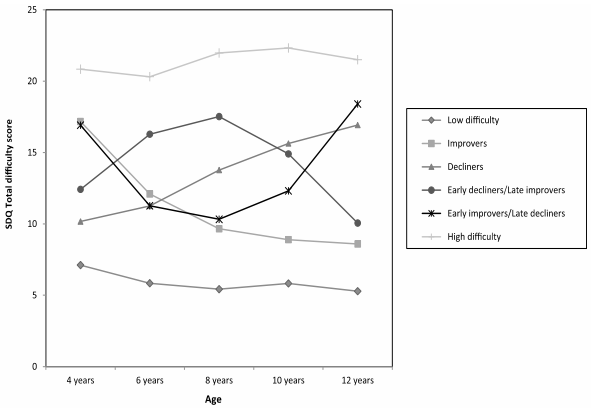


Figure 1. Trajectories of mental health risk. Strengths and Difficulties Questionnaire (SDQ) total difficulty scores for the six latent trajectories at ages 4, 6, 8, 10, and 12 years of age

Table 3. Significant predictors of trajectory

	Odds Ratio (95% Confidence Interval)				
	Improvers	Early decliners/ Late improvers	Decliners	Early improvers/ Late ecliners	High difficulty
Sociability	0.760 (0.689–0.840)*	1.203 (1.049–1.380)*	1.186 (1.067–1.319)*	0.863 (0.731–1.019)	0.838 (0.687–1.023)
Parental Warmth	0.215 (0.167–0.277)*	0.614 (0.428–0.880)*	0.951 (0.707–1.278)	0.484 (0.313–0.749)*	0.244 (0.154–0.386)*
Sports participation					
Yes	Ref	Ref	Ref	Ref	Ref
No	1.923 (1.505–2.458)*	1.373 (0.992–1.899)	1.617 (1.254–2.086)*	2.036 (1.340–3.094)*	2.063 (1.260–3.376)*
Sex					
Boys	2.196 (1.717–2.810)*	2.410 (1.719–3.377)*	2.369 (1.822–2.082)*	1.812 (1.202–2.732)*	6.337 (3.490–11.504)*
Girls	Ref	Ref	Ref	Ref	Ref
Weekly income					
$0–$999 per week	Ref	Ref	Ref	Ref	Ref
$1000–$1999 per week	0.419 (0.325–0.538)*	0.478 (0.340–0.672)*	0.617 (0.470–0.809)*	0.380 (0.244–0.592)*	0.177 (0.101–0.310)*
>$2000 per week	0.110 (0.064–0.191)*	0.230 (0.128–0.414)*	0.446 (0.301–0.660)*	0.247 (0.120–0.509)*	<0.001*

Results are presented as Odds Ratio's using the 'Low Difficulty' trajectory as the reference category.
*$p < .05$.

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Review Article

Effect of parental depressive symptoms on offspring's brain structure and function: A systematic review of neuroimaging studies

Giulia Cattarinussi [a,*,1], Mohammad Hadi Aarabi [a,1], Hossein Sanjari Moghaddam [b], Maryam Homayoun [c], Mahnaz Ashrafi [d,e], Hamid Soltanian-Zadeh [d,f,g], Fabio Sambataro [a]

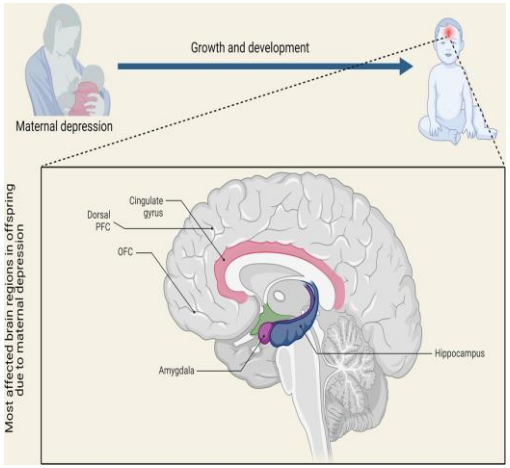


Fig. 2. The most commonly affected brain regions in offspring exposed to maternal depression.

Perinatal Depression (PND) is a severe mental disorder that appears during pregnancy or in the post-partum. Although PND has been associated with behavioral problems in the offspring, its effects on brain development are unclear. With this review we aimed at summarizing the existing literature on the effects of perinatal depressive symptoms on children's brains. A search on PubMed and Embase of structural, functional Magnetic Resonance Imaging (MRI) and Diffusion Tensor Imaging (DTI) studies exploring the effect of PND on offspring's brain was conducted. We selected twenty-six studies, ten structural MRI, five DTI, six fMRI and five with combined techniques. Overall, the studies showed: a) gray matter alterations in amygdala and fronto-temporal lobes; b) microstructural alterations in amygdala, frontal lobe, cingulum, longitudinal fasciculus and fornix; and c) functional alterations between limbic and mesocortical networks. The small sample size and the heterogeneity in populations and methodologies limit this review. In conclusion, PND seems to influence structure and function of offspring, that may contribute to the risk of behavioral disturbances later in life.

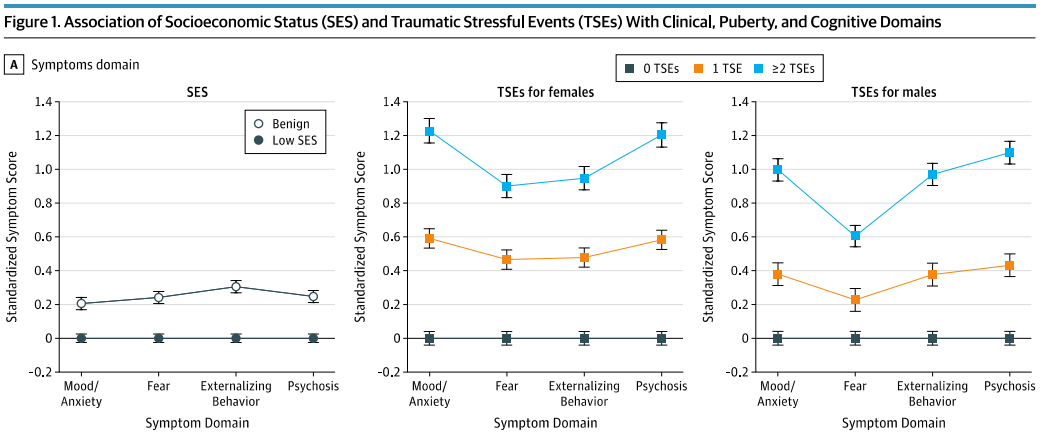
Transmission

- **Héritabilité**
  - Part d'expression clinique liée au gènes
    - Troubles bipolaires: 80%
    - Schizophrénie: 80%
    - Autisme: 80%
    - Hyperactivité: 80%
    - Dépendance à l'OH: 60%
    - Dépression: 40%
    - Troubles anxieux: 30-40%
    - Troubles de la personnalité
      - Inconnue
      - « Genetic overlap » avec BIP, SCZ et MDD (Witt et al., 2017)

Transmission
Facteurs d'environnement

- Evènements de vie traumatiques de l'enfance
  - Interagissent avec de nombreux gènes codant pour différents systèmes biologiques (HPA, transmission sérotoninergique, neuroplasticité, immunité, signaux calciques, rythmes circadiens…)

Aas et al., 2016 ; Herzog & Schmahl, 2018



JAMA Psychiatry | Original Investigation

Burden of Environmental Adversity Associated With Psychopathology, Maturation, and Brain Behavior Parameters in Youths

Raquel E. Gur, MD, PhD; Tyler M. Moore, PhD; Adon F. G. Rosen, BS; Ran Barzilay, MD, PhD; David R. Roalf, PhD; Monica E. Calkins, PhD; Kosha Ruparel, MSE; J. Cobb Scott, PhD; Laura Almasy, PhD; Theodore D. Satterthwaite, MD, MA; Russell T. Shinohara, PhD; Ruben C. Gur, PhD

Dépressions périnatales

- Tout trouble dépressif
  - Sans caractéristiques psychotiques
  - Année suivant la naissance
- Prévalence: 10-20 %
- Incidence: 14,5% à 3 mois PP
- 30%: 1er épisode: 70% = rechutes
- 2 x plus de risque de rechute EDC dans les 5 ans

Cooper & Murray, 1995
Gaynes et al., 2005
Liu et al., 2017
Sharma et al., 2018

Dépressions périnatales
Facteurs de risque

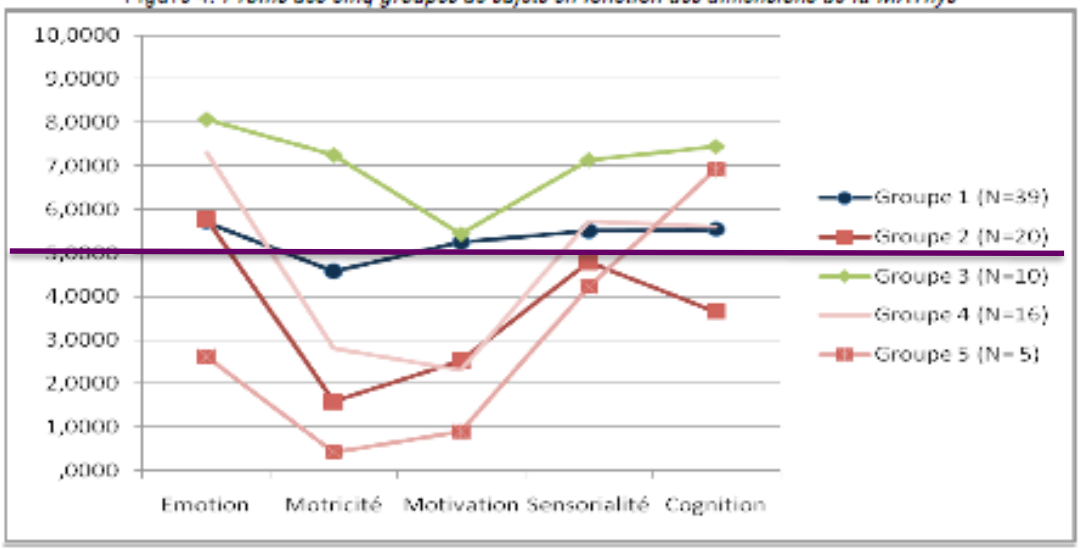
- Facteurs psychosociaux
  - Forts à modérés
    - **ATCD trouble de la régulation émotionnelle**
    - **Episode dépressif de la grossesse**
    - **Anxiété durant la grossesse**
    - Qualité du soutien social
    - Evènements de vie stressant
  - Modérés à faibles
    - SSE faible
    - Qualité du soutien conjugal
    - Variables obstétricales
    - **Tempérament de l'enfant**

« Dépression périnatale » …

Manie

Dépression

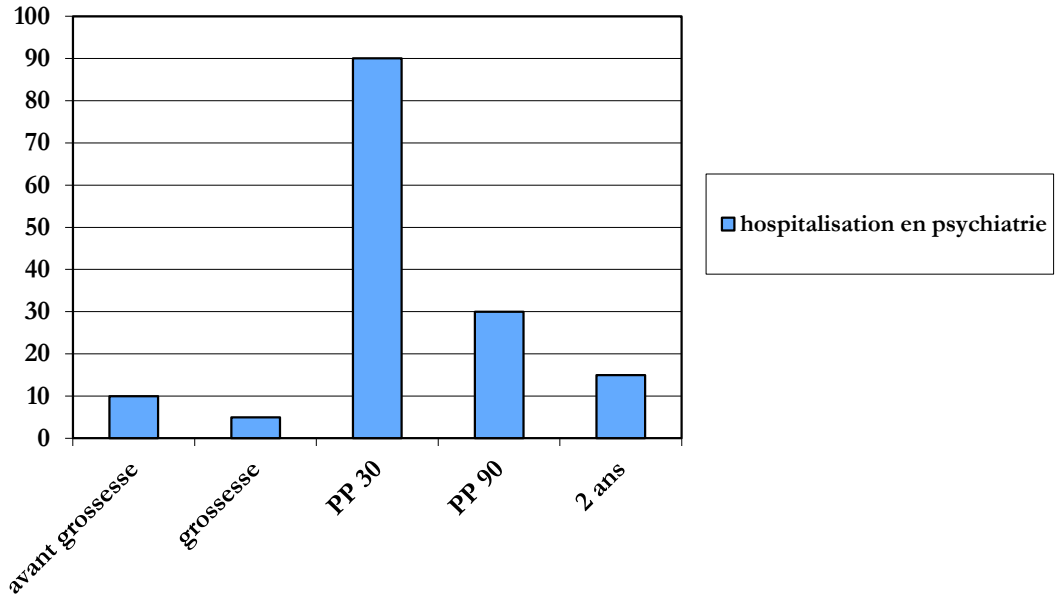
Figure 4. *Profils des cinq groupes de sujets en fonction des dimensions de la MAThys*



Balès M., M2R, 2011

Psychoses puerpérales
Kendell et al, 1987

- 12 ans
- 54 087 naissances
- **2 pour mille**
- RR 22 dans les 30 jours PP



Psychoses puerpérales

- Urgence psychiatrique absolue: risque suicidaire
- 90 % épisodes mixtes + caract. psychotiques

  Kendell et al, 1987 ; Klompenhouwer, 1991, 1995
- Symptômes d'hypomanie caractéristiques du PP précoce

  Heron et al, 2008
- 50% patientes sans ATCD personnels

  Valdimirovitch, 2009
- Sommeil
  - Prévention

  Sharma & Mazmanian, 2003

SUICIDALITÉ
EN PÉRIODE PÉRINATALE

Idées suicidaires

3-34 % idées suicidaires périnatales

Gentile, 2011, Orsolini *et al.,* 2016, Gelaye *et al.,* 2016

4,1% au cours de la grossesse

3,4% dans le postpartum

1,1% à haut risque

Kim *et al.,* 2015

Idées suicidaires périnatales
Trouble bipolaire

Au cours de la grossesse

- **25%** idées suicidaires
- **8%** TS

Taylor *et al.,* 2016

Dans le post-partum

- **11.6%** de TS dans le post-partum

	Polarity of postpartum episodes		*p*
	Depressive (*N*=165)	(Hypo)manic or mixed (*N*=42)	
Suicide attempts during postpartum episodes, *N* (%)	19 (11.5)	5 (11.9)	0.940

Maina *et al.,* 2014

Tentatives de suicide périnatales

44 pour 100 000 naissances

Schiff *et al.,* 2006

Post-partum précoce >> T1 >> T2 et T3

Czeizel, 2011 – Schiff *et al.,* 2006

Risk factors for suicide attempt in pregnancy and the post-partum period in women with serious mental illnesses

Florence Gressier [a, b, *], Virginie Guillard [a], Odile Cazas [a], Bruno Falissard [c], Nine M-C. Glangeaud-Freudenthal [d], Anne-Laure Sutter-Dallay [e]

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[b] Université Paris-Saclay, Univ. Paris-Sud, UVSQ, CESP, INSERM U1178, Bicêtre University Hospital, 78 rue du Général Leclerc, 94275 Le Kremlin Bicêtre, France
[c] Université Paris-Saclay, Univ. Paris-Sud, UVSQ, CESP, INSERM U1178, Department of Biostatistics, Maison de Solenn, 97 Bld de Port-Royal, 75679 Paris Cedex 14, France
[d] INSERM, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Center for Epidemiology and Biostatistics (U1153), Paris-Descartes University, Paris, France
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ABSTRACT

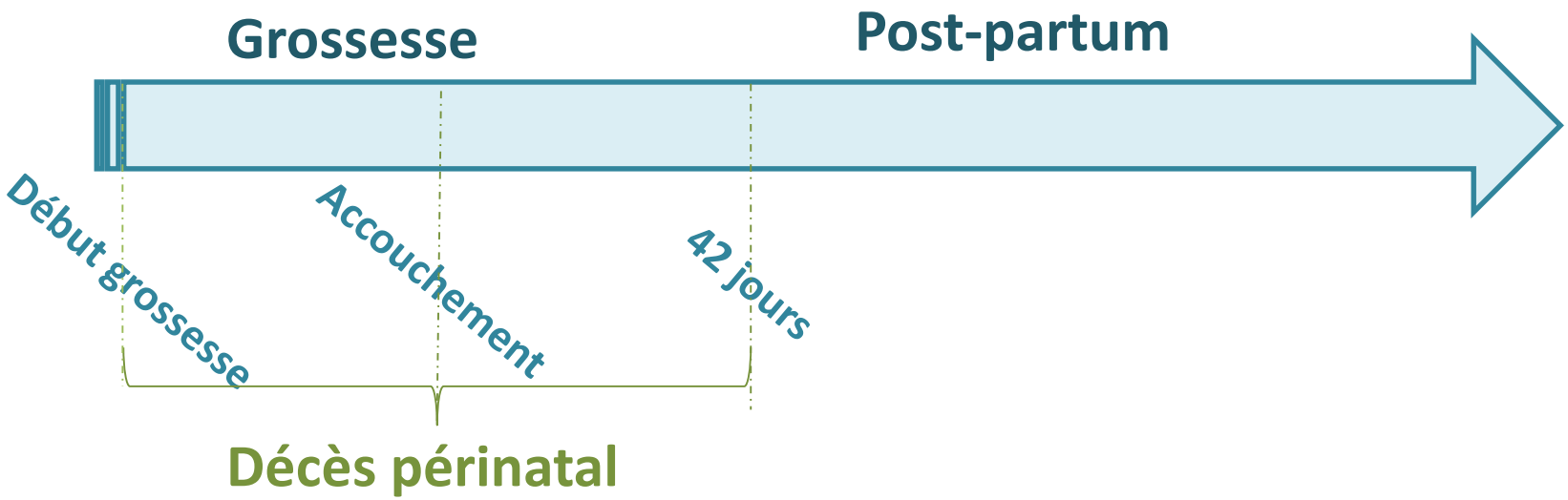
Suicide is a major public health concern worldwide, and mental disorders have been identified as a main risk factor. Suicide is also one of the leading causes of perinatal maternal mortality, but very few studies have focused on suicide attempts (SA) in the perinatal period. This work aims to assess risk factors associated with SA in pregnancy and in the post-partum period in women with mental health disorders.

Women (n = 1439) with psychiatric disorders jointly admitted with their infant to 16 psychiatric Mother-Baby Units over 10 years (2001–2010) were assessed retrospectively for the occurrence of SA in pregnancy or the postpartum period. Multinomial logistic regression was used to explore the independent impact of maternal sociodemographic characteristics, history of childhood maltreatment and abuse, current mental illness and pregnancy data on SA in pregnancy and/or postpartum.

One hundred and fifty-four women (11.68%) attempted suicide: 49 in pregnancy (3.71%) and 105 (7.97%) in the post-partum period. SA in pregnancy was related to alcohol use (OR = 2.37[1.02–5.53]; p = 0.04) and smoking during pregnancy (OR = 1.87[1.01–3.49]; p = 0.04) and also to a history of miscarriage (OR = 2.29[1.18–4.41]; p = 0.01). SA in the post-partum period was associated with major depressive episode (OR = 2.72[1.40–5.26]; p = 0.003) or recurrent depression (OR = 4.12[2.25–7.51], p < 0.001) and younger age (OR = 0.96[0.93–0.99], p = 0.03).

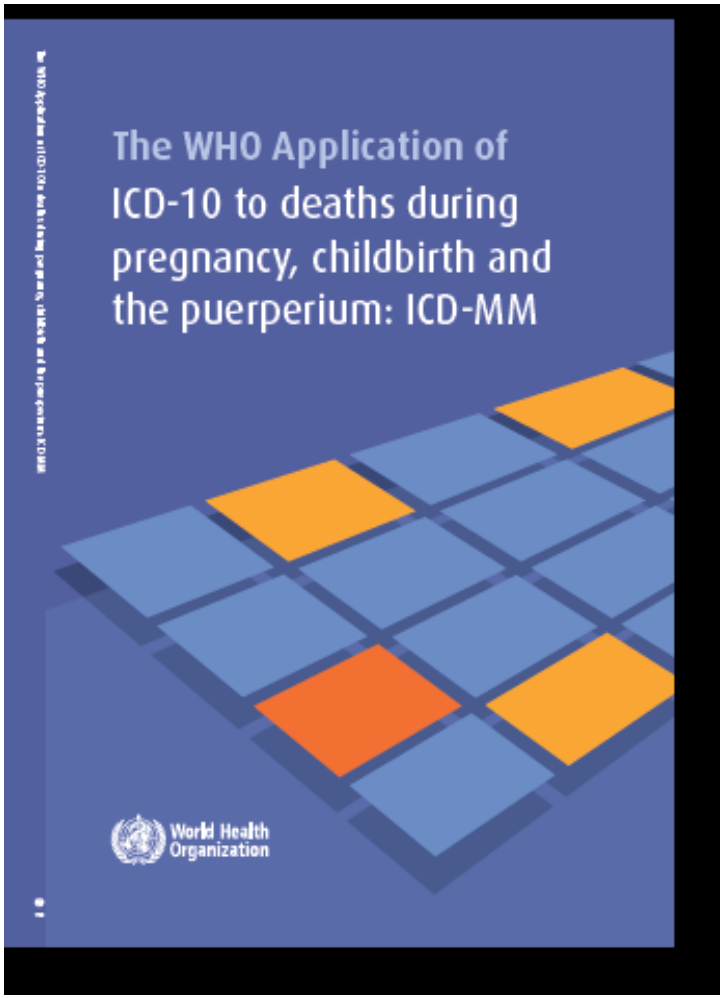
SAs in the course of pregnancy and the postpartum period have different risk factors. Special attention to risk of suicide is needed during pregnancy for women with severe mental illness and a history of miscarriage, alcohol or cigarette use, young age and depression in the perinatal period.

Décès maternel



OMS

Recommandations internationales

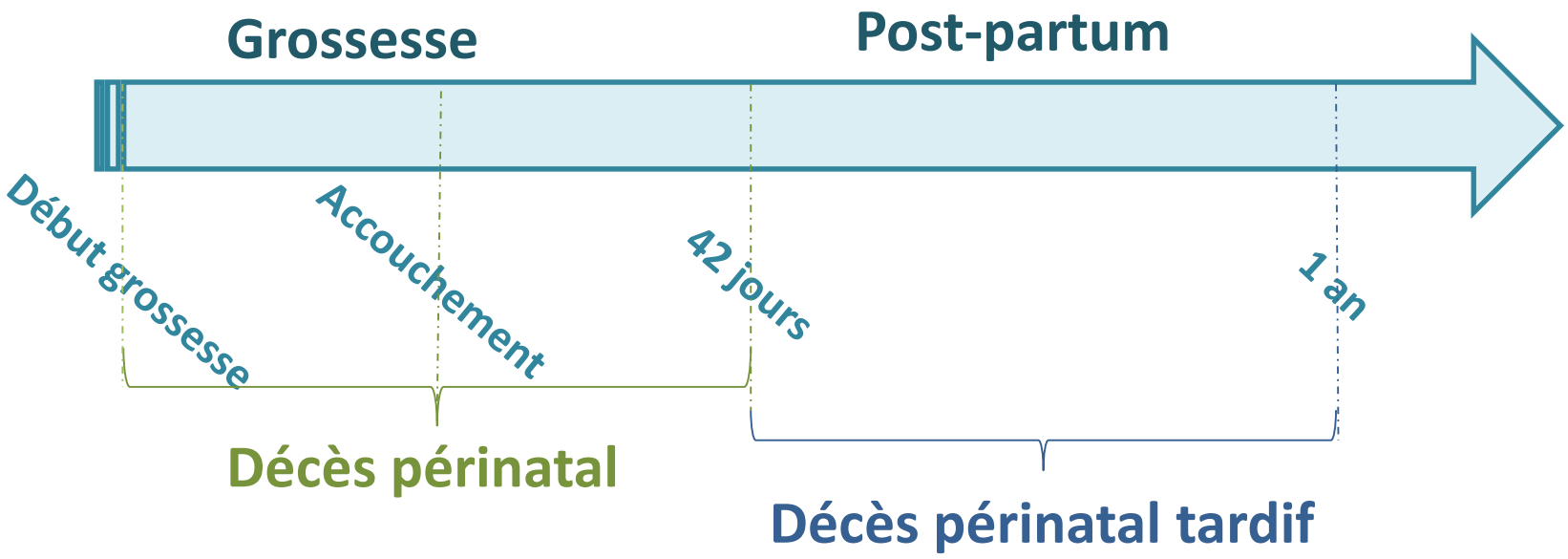


(2012)

- Considérer **tous les suicides jusqu'à 1 an** après la grossesse comme des **morts maternelles** directes

- **Justification**
  - Evaluation du rôle causal de la grossesse très difficile
  - Incitation à prise de conscience du risque suicidaire maternel, risque encore largement méconnu

Décès maternel



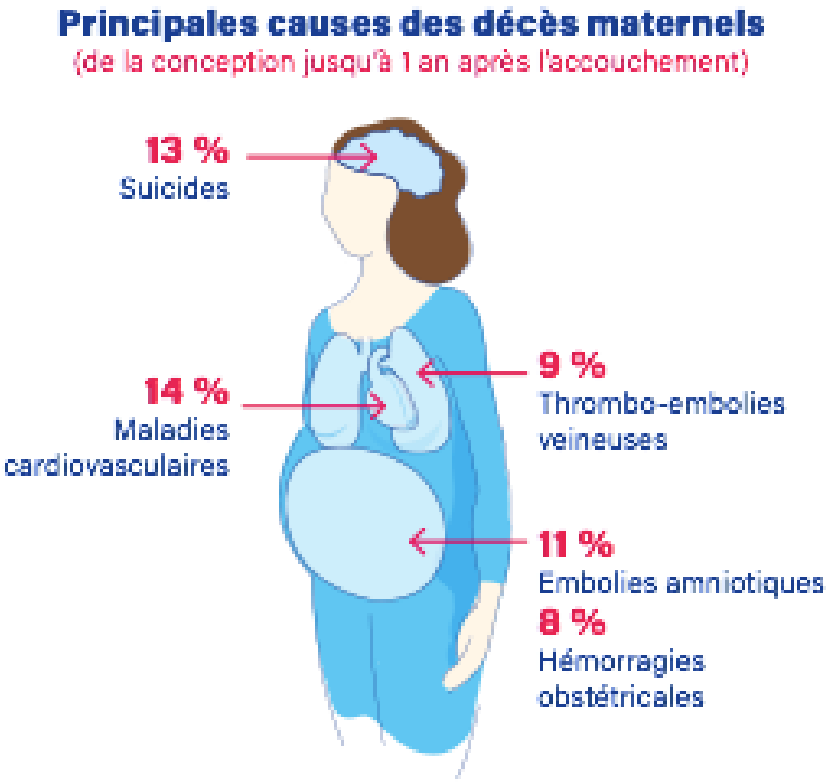
OMS – Esscher *et al.*, 2016

	Inclusion de tous les suicides Jusqu'à 42 jours PP			Inclusion de tous les suicides Jusqu'à 1 an PP		
	RMM de base*	Facteur d'↑ du RMM	% des suicides dans la MM	RMM de base*	Facteur d'↑ du RMM	% des suicides dans la MM
Pays-Bas 1996-2005	11,4	1,08	5,3%	14,1	**1,31**	**18%**
Royaume-Uni 2003-2005	13,9	1,08	3,7%	17,8	**1,34**	**13%**
France 2007-2009	9,5	1,08	4,5%	10,3	**1,31**	**20%**

(*/100 000 naiss)

CNEMM, Deneux-Tharaux

Les **maladies cardiovasculaires et les suicides** sont les causes les plus fréquentes, mais aussi parmi les plus évitables

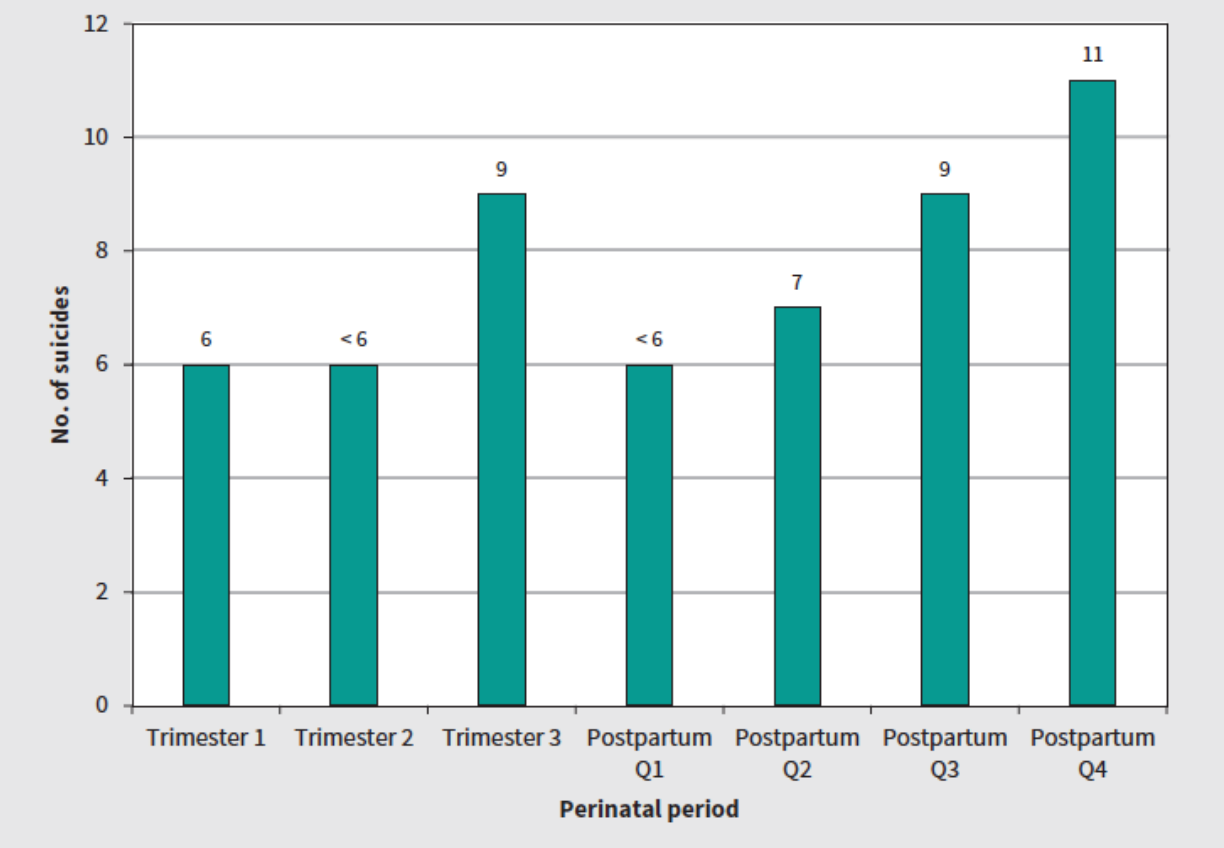


Suicide: 1,4/100 000 naissances vivantes

2/3 trouble psychiatrique

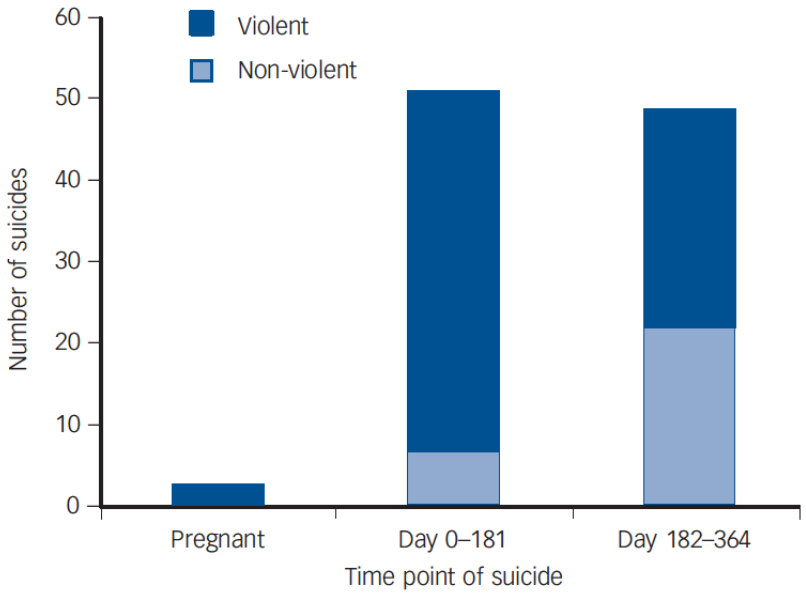
Gelaye *et al.,* 2015 - Oates *et al.,* 2003

Suicide maternel: période à risque



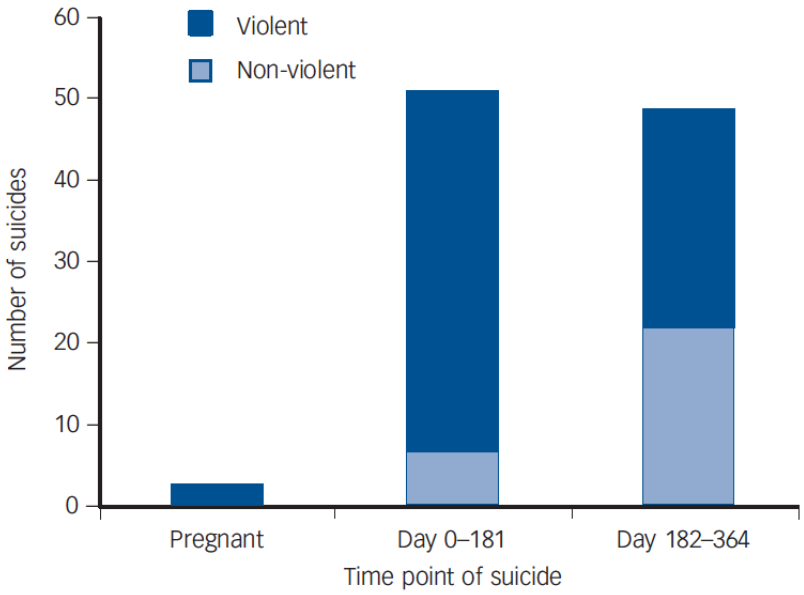
Grigoriadis *et al.*, 2017

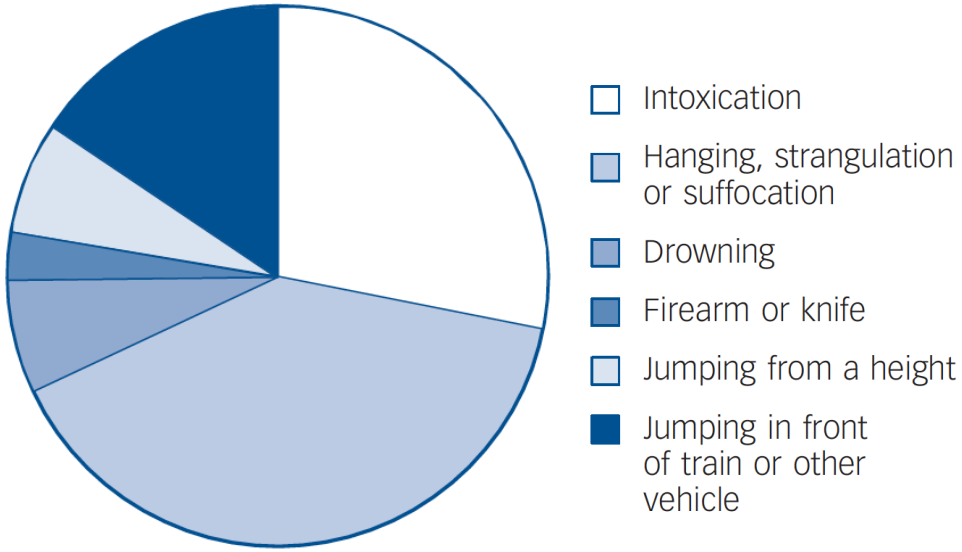
Suicide maternel



Esscher *et al.*, 2016

Suicide maternel





Esscher *et al.*, 2016

Facteurs associés à la suicidalité périnatale

Socio-démographiques

- Jeune âge
- Célibat

Khalifeh *et al.*, 2016 – Celik *et al.*, 2015 – Gavin, 2011 – Kim *et al.*, 2015 – Sit *et al.*, 2015

- Trauma infantile

Gelaye *et al.*, 2016

- Conflits familiaux
- Violences conjugales
- Faible de support social

Alhusen *et al.*, 2015 – Stewart, 2015 – Fisher *et al.*, 2013

- Discrimination raciale
- Minorité ethnique / religieuse

Kim *et al.*, 2015

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  Kim *et al.*, 2015

Obstétricaux

- Grossesse non désirée

  Newport *et al.*, 2007
- Idées d'IVG

  Coelho *et al.*, 2014 - da Silva *et al.*, 2012
- Traumatismes périnéaux

  Kim *et al.*, 2015

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Obstétricaux

- Grossesse non désirée

  Newport *et al.*, 2007
- projet IVG

  Coelho *et al.*, 2014 - da Silva *et al.*, 2012
- Traumatismes périnéaux

  Kim *et al.*, 2015

Cliniques

- Antécédents familiaux
- Antécédents personnels

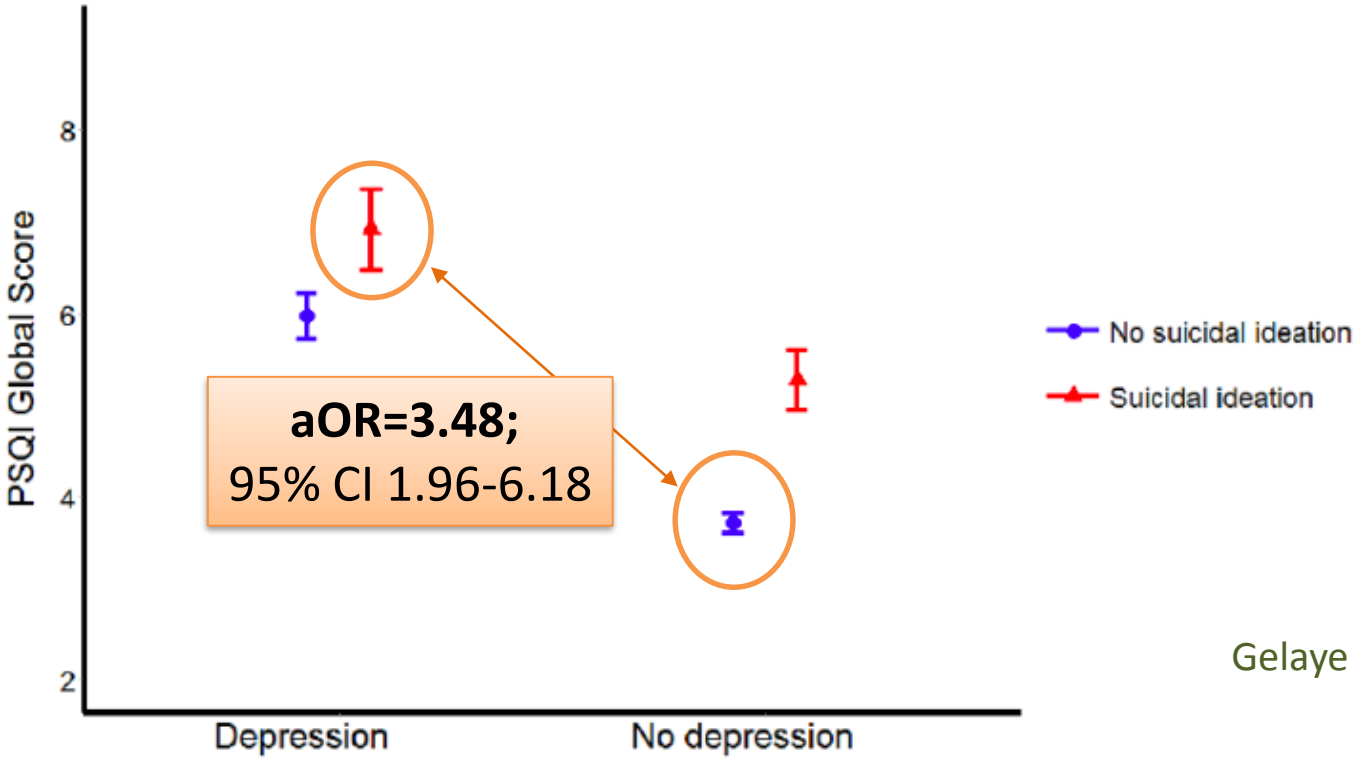
  Khalifeh *et al.*, 2016 – Celik *et al.*, 2015 – Gavin, 2011 – Kim *et al.*, 2015 – Sit *et al.*, 2015
- Anxiété

  Newport *et al.*, 2007 – Celik *et al.*, 2015

Idées suicidaires périnatales & sommeil

Au cours de la grossesse

Qualité du sommeil & dépression



Gelaye *et al.*, 2015

Conclusions

- ✓ Moins fréquent qu'en dehors la période périnatale
  - ✓6,5 pour 100 000 en population générale
  - ✓1,4 pour 100 000 naissances vivantes
- ✓ 2ème cause de décès maternel
- ✓Spécificités sémiologiques
  - ✓ Moyens violents
  - ✓Trouble psychiatrique sévère
  - ✓ Dépression, antécédent de TS, trouble du sommeil

Take home messages

- ✓ Prévention
- ✓ Travail pluridisciplinaire: sage-femme, obstétricien, anesthésiste, MG, PMI, pédiatre, psychologue, psychiatre, infirmière…
- ✓ Consultation pré-conceptionnelle si antécédents psychiatriques +++
- ✓ Poursuite des traitements psychotropes +++
- ✓ Evaluation psycho-sociale: facteurs de protection

Perspectives

Hypothèses immunitaires…

- Association primiparité
  - Eclampsie
    - Sous-expression de gènes impliqués dans l'inflammation et la régulation immunitaire
  - Psychoses puerpérales

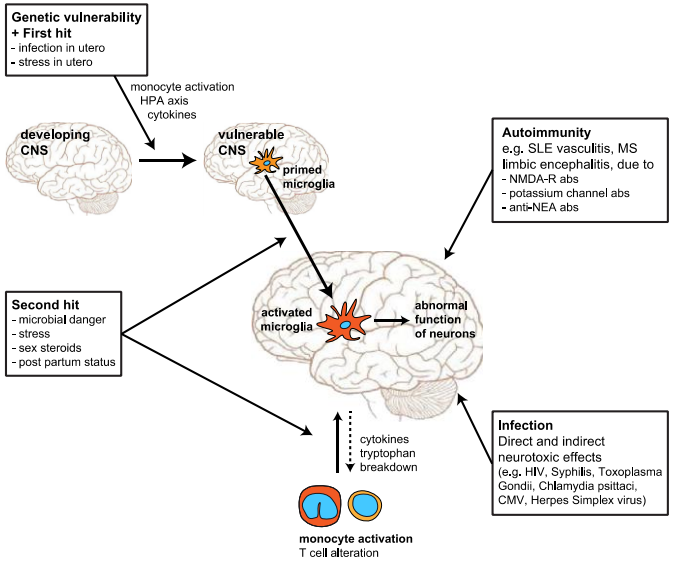


Figure 1. An immune-mediated two-hit model for psychosis. This figure shows three immune pathways, discussed in the literature and reviewed in this chapter, to arrive to psychosis. The first pathway is via direct autoimmune mechanisms, e.g., in which autoantibodies induce vasculitis or receptor autoantibodies interfere with important neuroreceptors. The second pathway is via infections of the brain, e.g. human immunodeficiency virus (HIV) infections or infections with *Toxoplasma gondii*. The third pathway represents a more complex immune-mediated developmental two-hit model for psychosis: in genetically susceptible individuals, environmental influences (infection or stress in utero or early life, representing first hits) induce excessive inflammatory activation of monocytes/microglia and hypothalamic-pituitary-adrenal (HPA) axis changes leading to developmental brain abnormalities (a vulnerable brain) with primed microglia, e.g., defective in supporting sufficient neuronal growth and axon guidance for important brain areas. The second hit occurs later in the form of various environmental or endogenous alterations (microbes, stress, puberty, postpartum period), leading to a further and excessive activated microglia resulting in abnormalities of the neuronal circuitry in the brain and psychosis. abs, antibodies; anti-NEA, amino terminal (propto)-enolase; CMV, cytomegalovirus; CNS, central nervous system; MS, multiple sclerosis; NMDAR, *N*-methyl-D-aspartate receptor; SLE, systemic lupus erythematosus.

Hypothèse GABAergique

- Alloprégnanolone
  - Neuro-stéroide modulateur allostérique positif des R. GABA-A
- Etudes précliniques convaincantes
- Mise sur le marché aux USA en 2019
  - Brexanolone

Merci pour votre attention !