Congrès Fondation Jonas, Casablanca – 3 & 4.03.23

Dynamiques des TND : *du normal au pathologique*

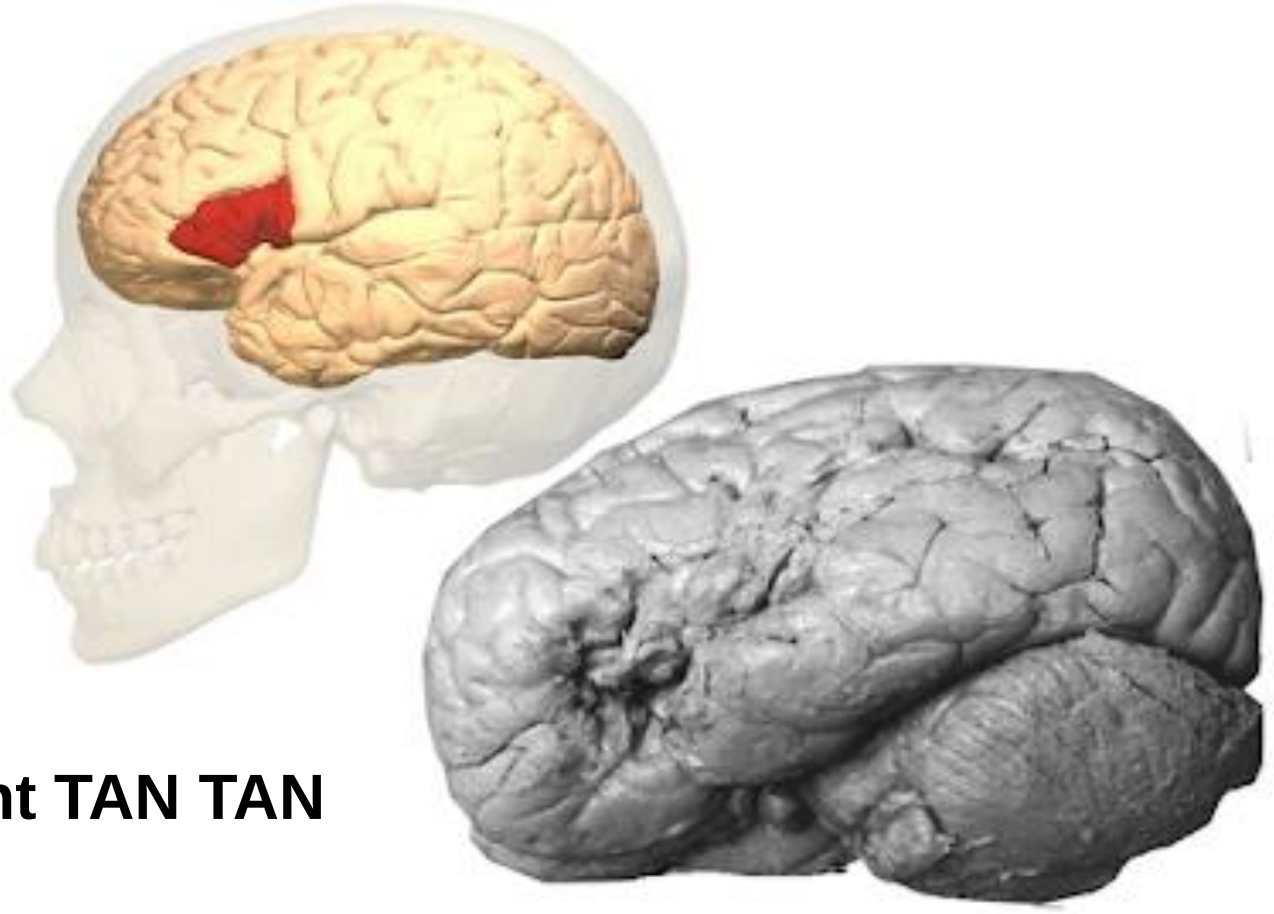
Pr Pierre Fourneret, *pédopsychiatre*
Psychopathologie du Développement – HFME
&
UCB Lyon 1 – UMR 5229 CNRS

Préambule

- Il semblerait que les Troubles du neurodéveloppement (TND) soient partout et dorénavant le nouvel horizon de toute la clinique infanto juvénile.

- Entre illusion réductionniste, pseudo mythes et préjugés tenaces, nous tenterons de dépasser la vision souvent simpliste du débat contemporain, en soulignant la complexité des dynamiques à l'œuvre dans les nouveaux modèles de compréhension des troubles du développement qui n'excluent en rien les effets de rencontres et le poids des facteurs environnementaux et de vie.

Deux mots d'histoire…



Le patient TAN TAN

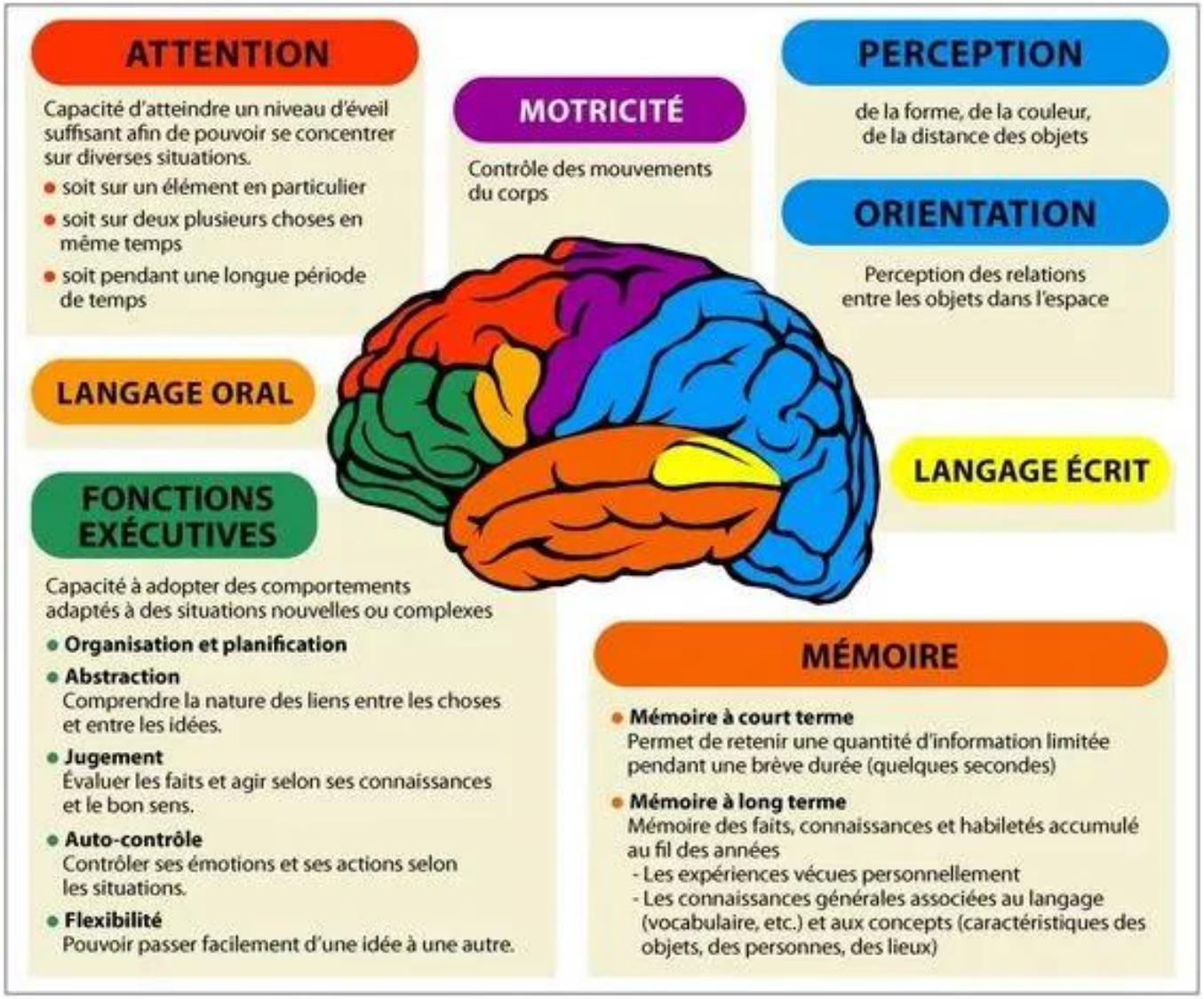
Luc Perino, in Patients Zéro, 2021

Deux mots d'histoire…

- **Approche structurelle (XIX° S)**
  - Corrélations anatomocliniques
  - Naissance de l'aphasiologie
    - Ex : le patient TAN et l'aire de Broca (1861)
  - Lecture catégorielle

- **Approche fonctionnelle (> 1940)**
  - Non lésionnelle
  - Lecture dimensionnelle & développementale

Le cerveau comme interface d'intégration



De l'importance du langage…

- Le meilleur prédicteur de TSA avant 3 ans…

  → ***retard de langage***

- **81 %** des enfants de 5 à 12 ans consultant pour des problèmes affectifs et comportementaux ont… (Hollo, Wehby, & Oliver, 2014)

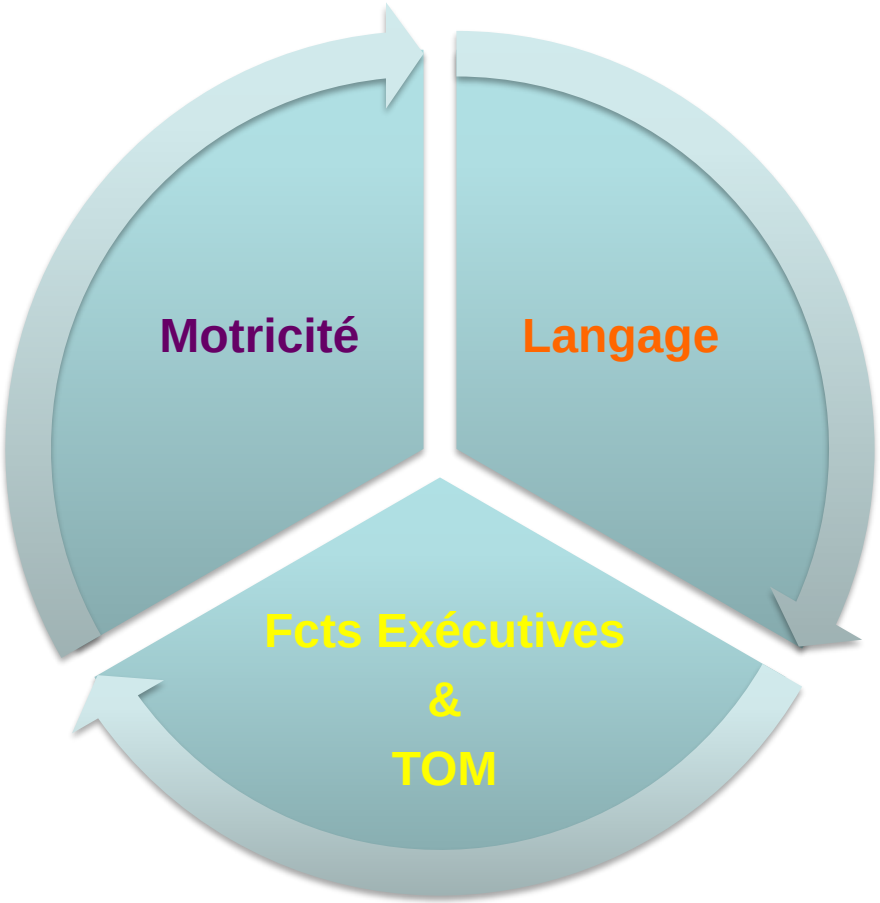
  → Un ***déficit langagier*** ***significatif non identifié***

- Co morbidités : c'est la règle et non l'exception…

  → **> 50% : TSA, TDAH**, **TDC**, Tb Dys Rég Emotionnelle

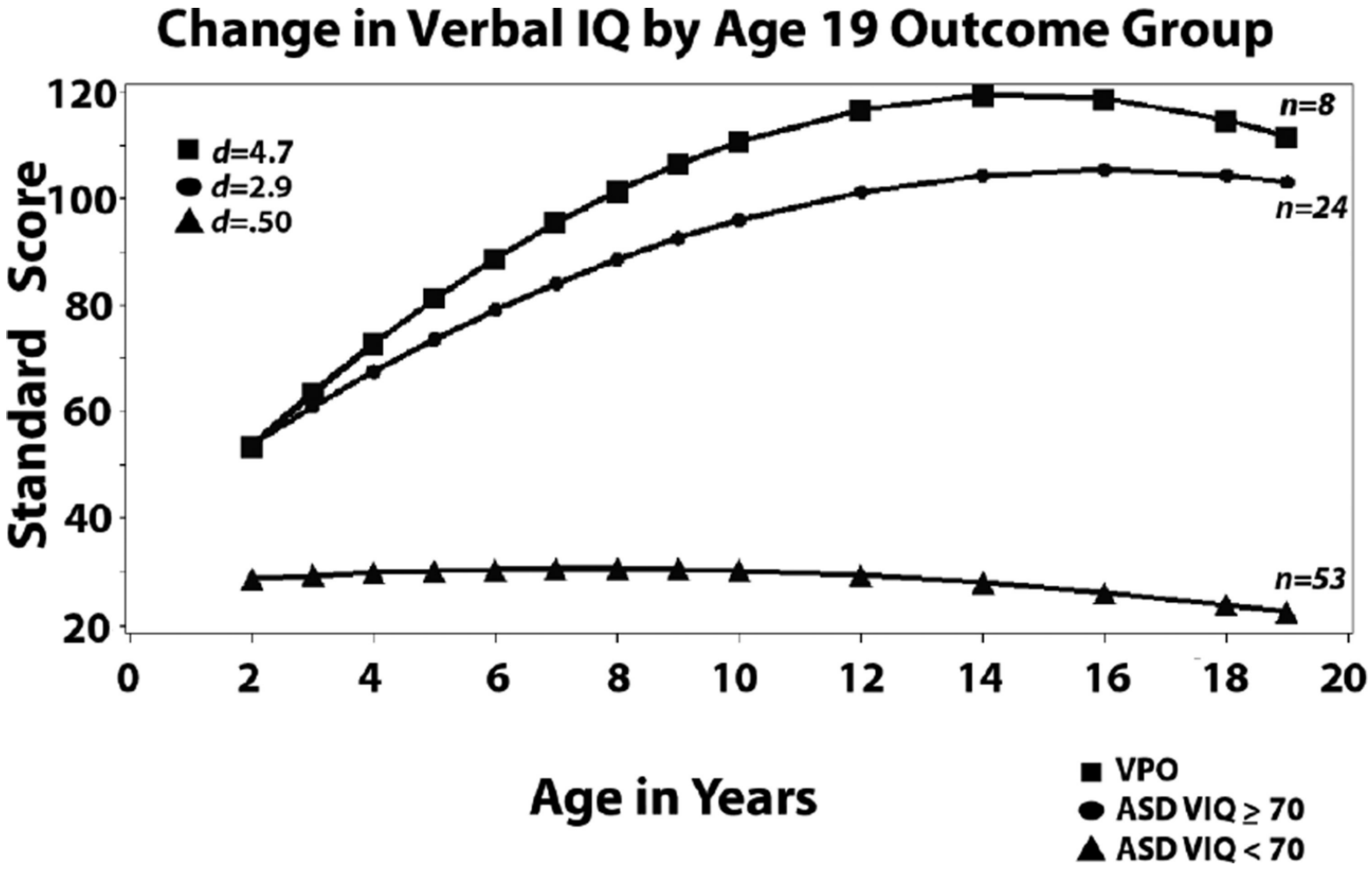
Gauld C et al. EMC 2022

Le langage : lego ® de la pensée



Reboul, 2015 ; Durrleman & Delage, 2015

Trajectoires développementales



Lord et al. Am J Med Genet C Semin Med Genet, 2015

Les nosographies évoluent…

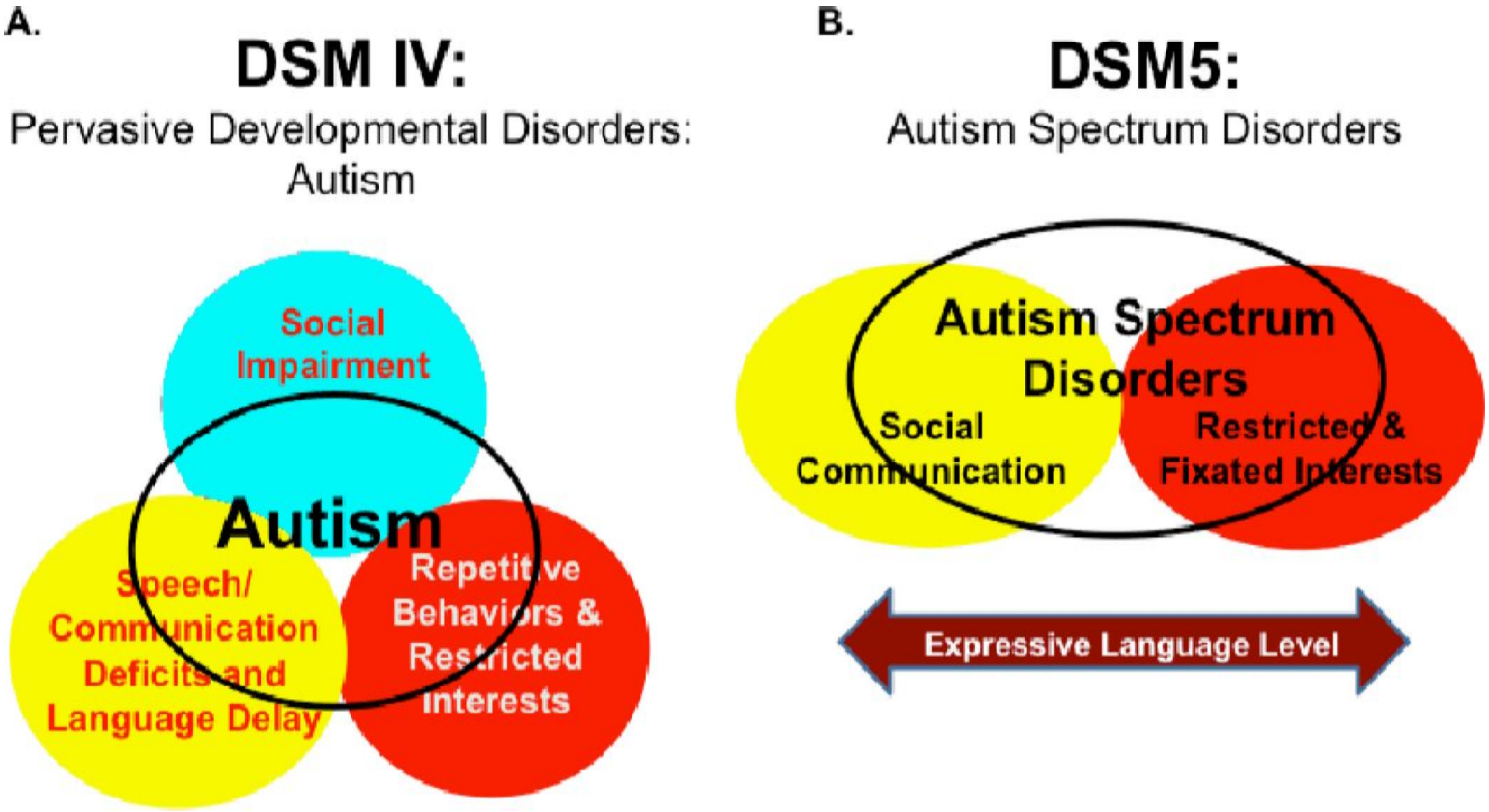
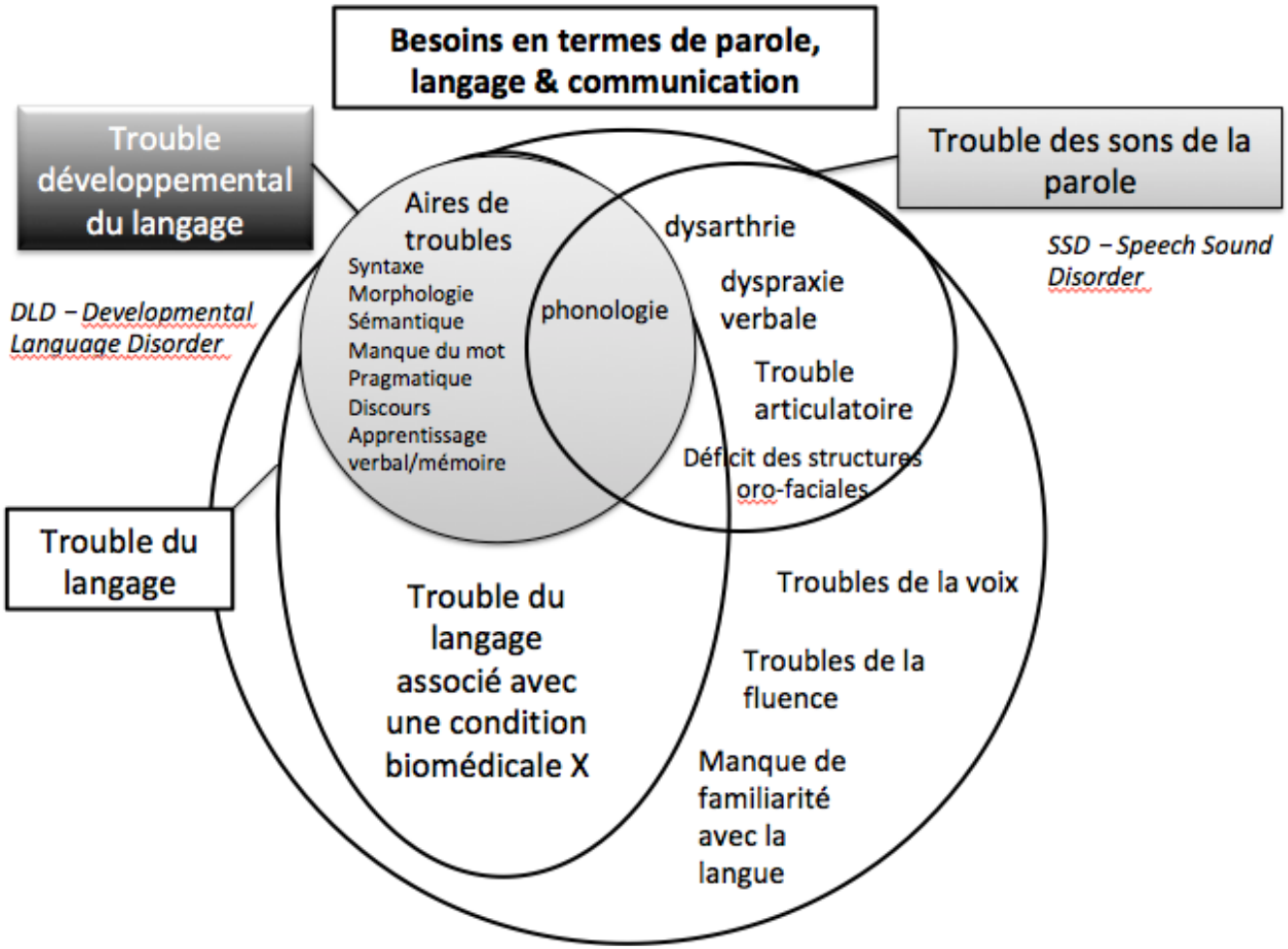


Figure 2.
(a). Existing diagnostic classification according to the DSM-IV for Pervasive Developmental Disorders. (b). Proposed DSM-5 classification dimensions for Autism Spectrum Disorders.

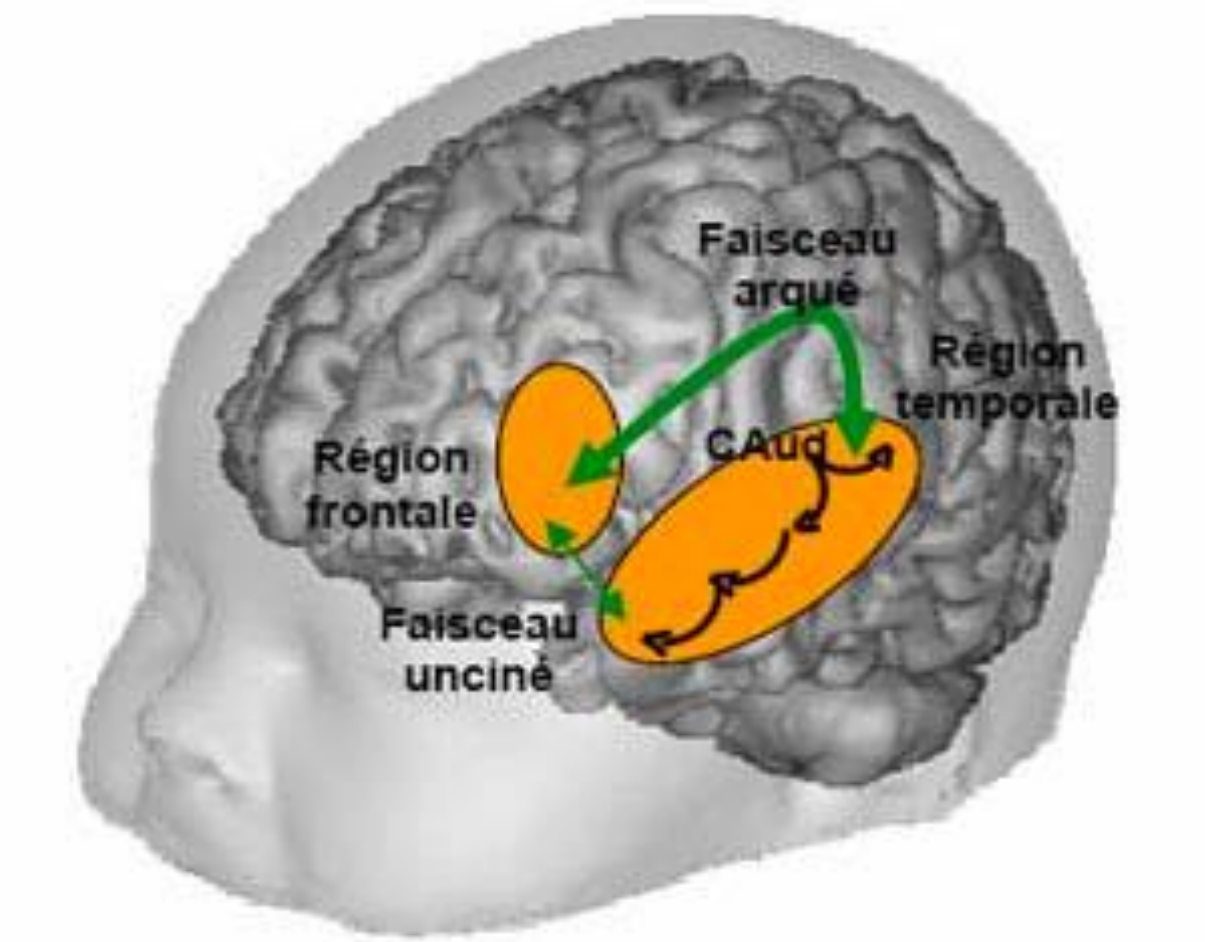
Lord & Jones. J Child Pyschol Psychiatry, 2012

Les TDL : nouvelle terminologie



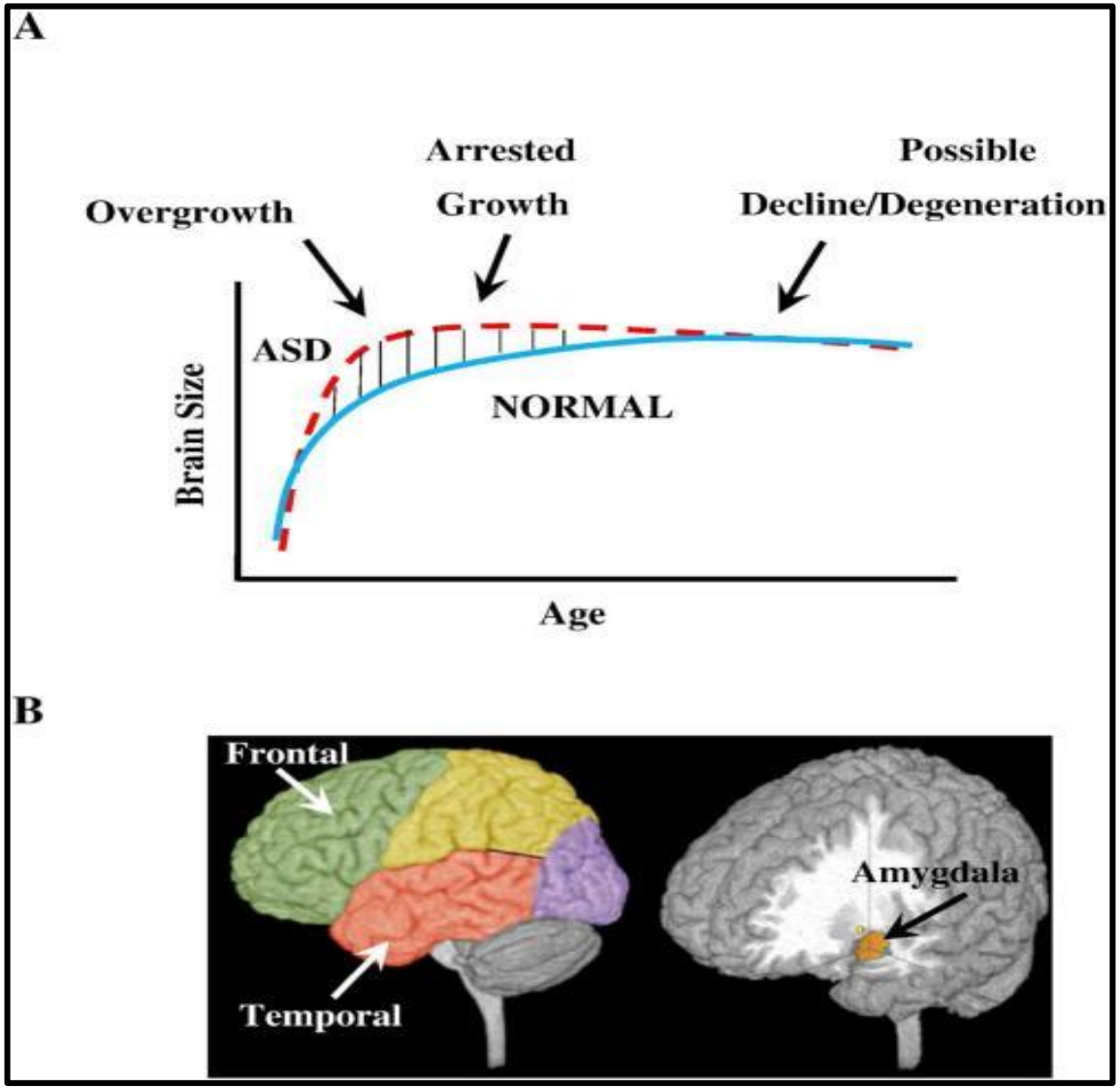
Bishop et al, 2017 . Gauld et al, 2022

La dynamique du Neurodéveloppement



G Lambertz Dehaene, 2006

Les TND : la dynamique du neuro développement



Majahan et al, 2015

TSA & TDAH : une association fréquente en pratique clinique

✓ Forte comorbidité croisée

- 33 - 37% de TDAH dans les TSA
- 15 – 25% de TSA dans le TDAH

✓ Le **TDAH** aggrave l'impact négatif des troubles cognitifs et psycho relationnels associés aux TSA

✓ Le **TDAH** accélère le risque de troubles comorbides secondaires :

- troubles internalisés (anxio dépression)
- troubles externalisés (tb du cpt et des conduites)

Antschel et al. Expert Rev Neuroteh, 2016
Berenquer-Former et al. Rev Neurol 2015
Mansour et al. Res Dev Disabilit, 2017

CORTEX 48 (2012) 194–215

Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

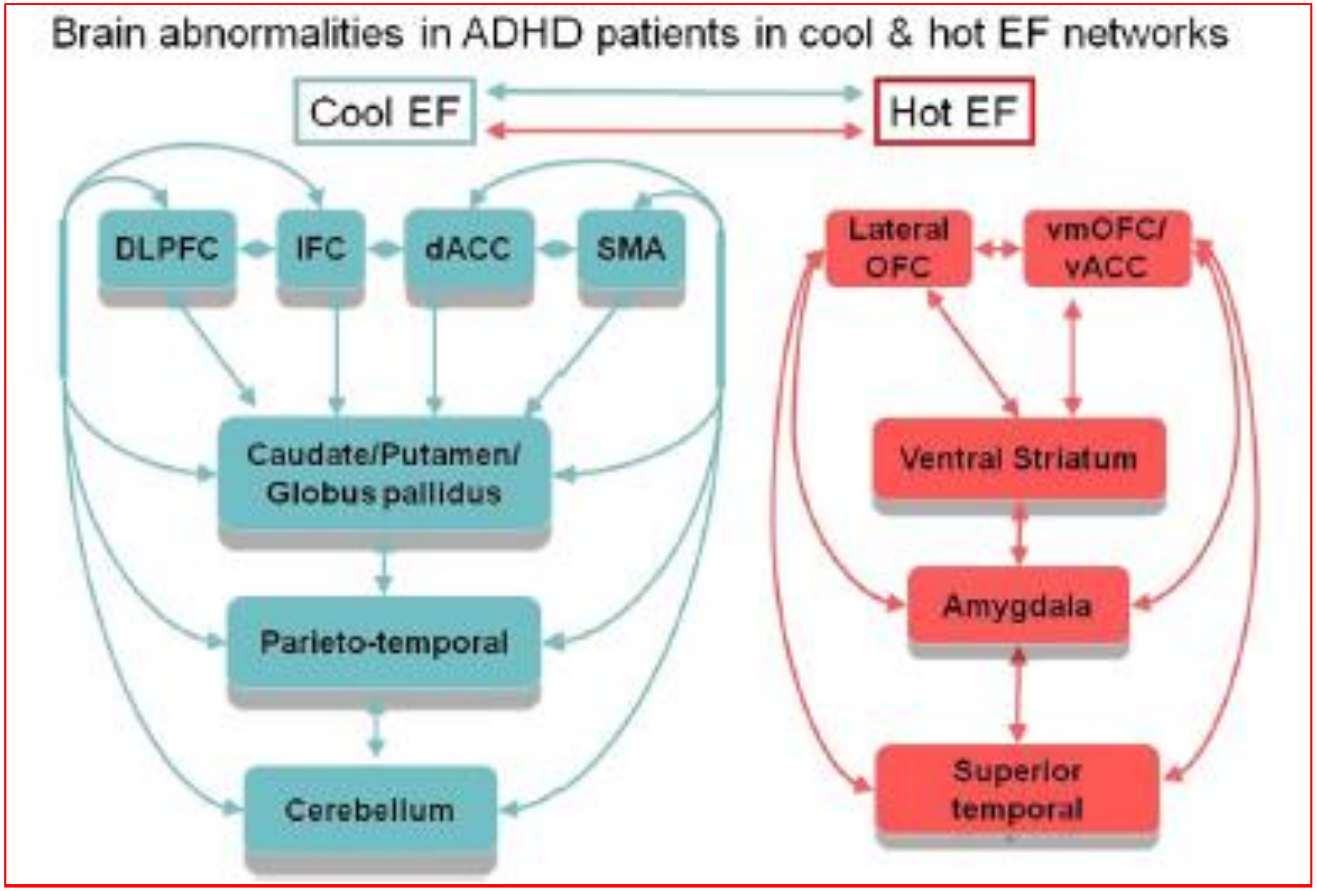
Special issue: Research report

A review of fronto-striatal and fronto-cortical brain abnormalities in children and adults with Attention Deficit Hyperactivity Disorder (ADHD) and new evidence for dysfunction in adults with ADHD during motivation and attention

*Ana Cubillo, Rozmin Halari, Anna Smith, Eric Taylor and Katya Rubia**

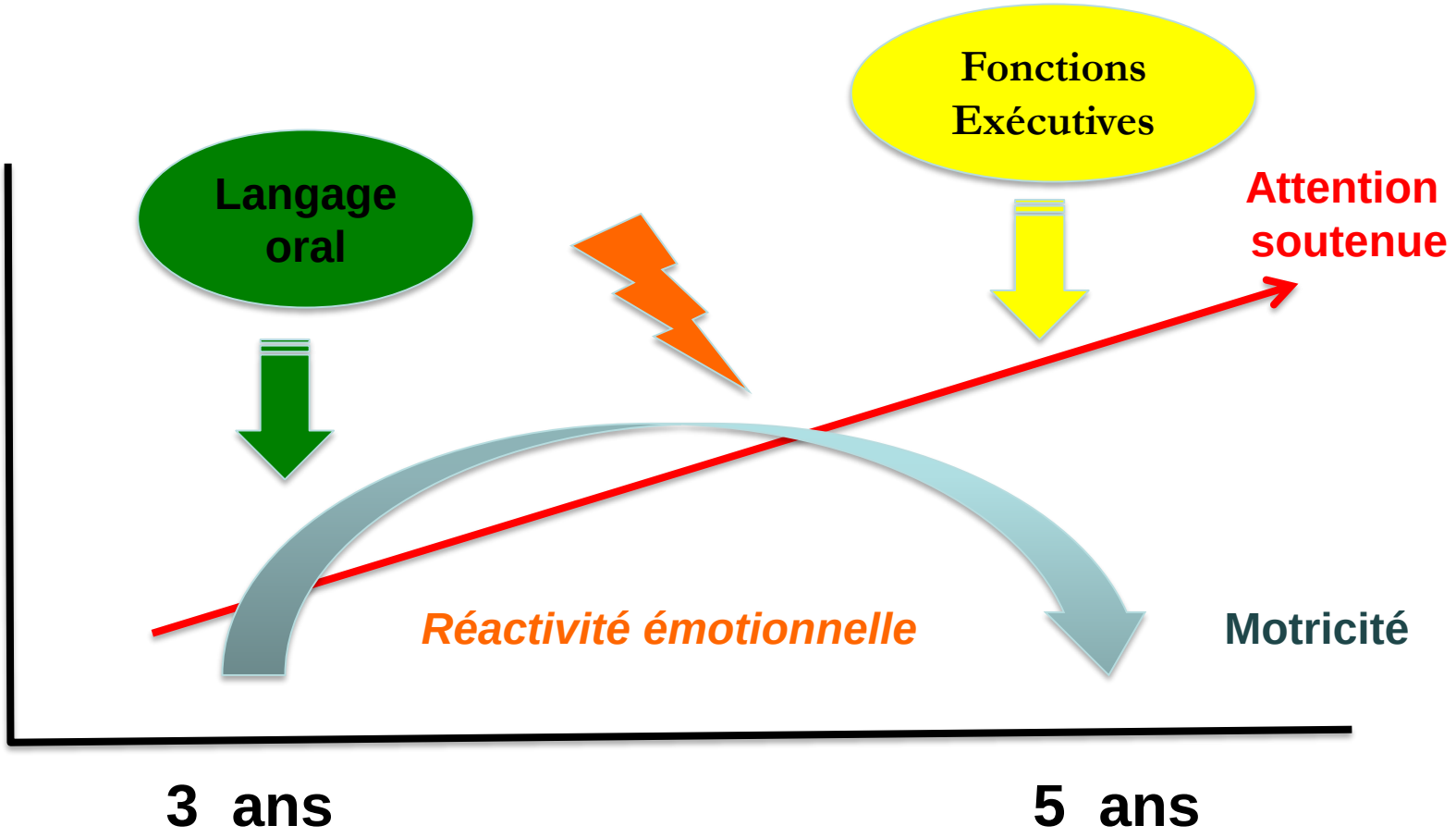
Department of Child Psychiatry, Institute of Psychiatry, King's College London, UK

Fig. 6 – Schematic representation of the MRI evidence for structural and functional brain abnormalities in children and adults with ADHD in overlapping neural networks that mediate "cool" cognitive-abstract and "hot" reward-associated executive and cognitive functions. "Cool" cognitive networks of dysfunction in ADHD include inferior, dorsolateral and medial fronto-striatal, fronto-parieto-temporal and fronto-cerebellar regions and networks that mediate functions such as motor response and interference inhibition, cognitive flexibility, temporal foresight, selective and sustained attention, working memory, motor and timing processes. "Hot" EF network dysfunctions in ADHD patients have been observed in the context of temporal discounting, reward processing and reward anticipation. IFG = inferior frontal gyrus; OFC = orbitofrontal cortex; DLPFC = dorsolateral prefrontal cortex; vmOFC = ventromedial orbitofrontal cortex; d/vACC = dorsal/ventral ACC cortex; SMA = Supplementary Motor Area.



Cortex, 2012

Approche développementale



Michel, 2005 ; Rothbart, 2005 ; Calkins & Bell, 2010

Opinion

Cell PRESS

Executive function and developmental disorders: the flip side of the coin

Mark H. Johnson

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Several common developmental disorders emerge during early to middle childhood (e.g. autism, attention deficit and hyperactivity disorder) and are associated with impairments in executive function (EF). Contrary to the prevailing view, I suggest that, within populations at-risk, the association with EF is found because individuals with strong EF skills are better able to compensate for atypicalities in other brain systems early in life, and are therefore less likely to receive a diagnosis later in life. I discuss evidence consistent with this view from considerations of individual variability, neuroimaging, and genetics. To the extent that this view is correct, it offers hope for remediation of some later emerging symptoms, as evidence from typical groups indicates that training programs for EF in preschoolers may be effective in improving skills.

Trends in Cognitive Sciences, 2012

Box 2. Training EF skills in early life

A number of programmes for training of EF skills in children are currently being developed and assessed, including 'Tools of the mind' and 'CogMed' (for reviews see [35,36]). These programmes involve procedures such as working memory 'games' or gaze-contingent eye tracking. A recent review of evidence from different cognitive training studies suggests that certain EF training programmes in younger children provide the best evidence for transfer of training to other tasks [37]. Although some of these procedures have been applied to children with developmental disorders [38], the application of such programmes to infants and children at-risk, ideally during infancy before the onset of overt symptoms, seems worthy of further investigation.

In a recent study, Wass *et al.* [39] showed that gaze-contingent eye tracking can be used to train some attentional control skills in typical developing low-risk infants. In this study, a group of 11-month-olds showed improvements in measures of cognitive control, sustained attention, saccadic reaction times, and reduced latency to disengage attention. For some measures, the amount of training received correlated with the degree of improvement. Future work with infants at-risk is currently planned.

Environnement & TND : *l'exemple de la prématurité*

- En France, 1 bébé naît prématuré toutes les 8 minutes soit **60 000** bébés prématurés par an. Parmi ces bébés nés avant terme, 85 % sont des prématurés moyens (< 37 SA) & 15 % sont des grands à très grands prématurés (< 6 à 7 mois de grossesse).

- Le taux de prématurité augmente depuis plusieurs années passant de 4,5 % en 1995 à **7%** aujourd'hui.

- Selon l'OMS, le taux des prématurés chaque année au **Maroc** est estimé à **13,41%** des naissances, soit environ **91 400**.

Environnement & TND : *l'exemple de la prématurité*

- Le taux de prématurité augmente régulièrement. Plusieurs raisons à cela :
  - l'âge de la maternité ne cesse de reculer, or une grossesse tardive présente plus de risques de manière générale pour le bébé ;
  - les fécondations in vitro, susceptibles de provoquer davantage de complications ;
  - Le mode de vie des futures mères entre également en compte : consommation de tabac, d'alcool, précarité sociale, mais aussi stress et fatigue liés au travail favorisent les naissances avant terme.

- On estime que ***15 millions*** de nourrissons naissent chaque année prématurément, soit plus d'un nourrisson sur dix (OMS, 2022).

- Or la prématurité reste la ***principale cause de décès*** chez les enfants de moins de 5 ans, dans le monde.

→ Enjeu de santé publique majeur (OMS, 2022)

L'enfant prématuré : études de suivi longitudinales

- **Cohorte nationale néerlandaise**

N= 1338 GPM < 32 SA /PPN < 1500 grs suivi sur **19 ans**

53% des sujets adultes presentent des difficultés

→ ***du développement cognitif***

→ ***du fonctionnement psychosocial***

→ ***d'intégration socio professionnelle***

Main outcomes of the POPS study at 19 years of age (significant differences, compared to norm data).

	POPS-19	Norm data in population, 19 year olds
IQ	97.8 (95% CI: 96.5–99.1)	100 (IQ test standardized around 100)
Significant hearing loss (%)	1.8	0.1
Neuromotor examination, total score	57.6 (95% CI: 56.8–58.4)	60–66
Moderate to severe problems in education (%)	24.0	12.8
No paid job, while not following any education (%)	7.6	2.6
Self-reported; total problem behavior score on YASR, women	34.57	29.22 ($p < .05$)
Self-reported; internalizing problem behavior score on YASR, women	10.83	8.43 ($p < .05$)
Parent-reported; total problem behavior score on YABCL, men	22.10	15.73 ($p < .05$; also on both internalizing & externalizing problem behavior)
Parent-reported; total problem behavior score on YABCL, women	25.80	16.59 ($p < .05$; also on both internalizing & externalizing problem behavior)
Having a relationship (%), men	32.1	54.8
Having a relationship (%), women	48.3	59.6

Van der Pal de Bruin et al. Early Human Development, 2015

Etudes de suivi longitudinal

- **Cohorte bavaroise**

N= 260 (vs 229 contrôles) suivis de l'âge de 5 mois à 26 ans

→ 25% des GPM présentent un déficit cognitif sévère

TABLE 2 Raw Means With Their 95% CI and Tests of Group Differences in Mean IQ Scores

	VP/VLBW Whole Sample, *n* = 260			Term-Born Whole Sample, *n* = 229			ES[a]	VP/VLBW With Impairment, *n* = 69			VP/VLBW Without Impairment, *n* = 191			ES[b]	ES[c]
	n	Mean	95% CI	*n*	Mean	95% CI		*n*	Mean	95% CI	*n*	Mean	95% CI		
DQ 5 mo	248	96.3	93.7–98.8	229	107.1	105.7–108.5	0.59	62	78.9	73.9–84.0	186	102.0	99.6–104.5	1.07	0.35
DQ 20 mo	244	93.7	91.4–96.0	229	106.9	106.0–107.7	0.86	59	73.6	67.5–79.7	185	100.1	98.7–101.5	1.45	0.81
IQ 4 y	230	87.2	84.8–89.6	228	101.8	100.5–103.2	0.85	53	66.0	61.4–70.7	177	93.5	91.6–95.5	1.39	0.68
IQ 6 y	218	87.2	85.1–89.3	229	102.0	100.5–103.4	0.92	52	68.4	64.2–72.6	166	93.1	91.4–94.8	1.52	0.81
IQ 8 y	233	90.3	88.2–92.5	227	102.0	100.7–103.3	0.76	55	69.1	64.6–73.6	178	96.9	95.4–98.4	1.60	0.56
IQ 26 y	216	86.2	83.6–88.9	197	102.6	100.9–104.4	0.77	58	59.4	55.9–62.9	158	96.1	94.4–97.8	1.79	0.55

Tests and ESs are corrected for socioeconomic status; all tests are significant with $P < .001$. CI, 95% confidence interval; ES, effect size.

[a] Comparison between whole VP/VLBW and term-born sample.

[b] Comparison between VP/VLBW individuals with and without cognitive impairment.

[c] Comparison between VP/VLBW and term-born individuals without cognitive impairment.

Breeman et al. Pédiatrics, 2015

Développement cognitif

→ ***Déficit stable au cours du développement***
→ ***Score global prédictif dès l'âge de 20 mois pour les GPM***

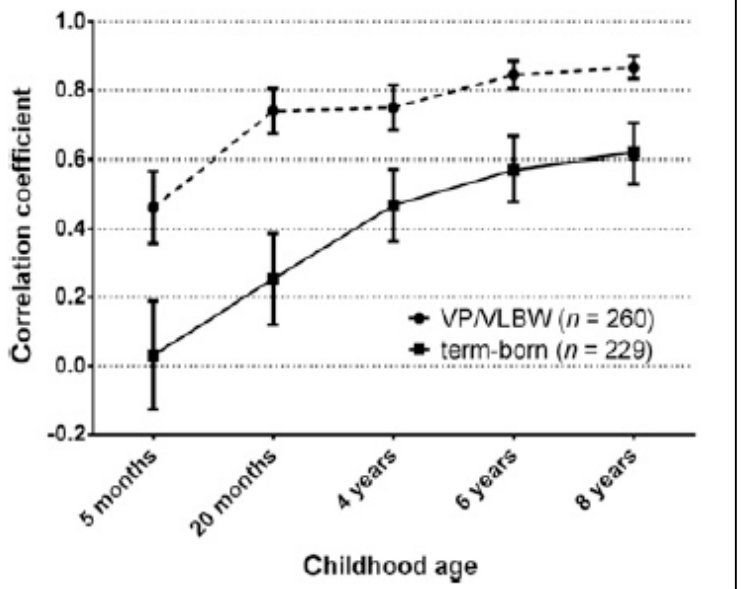


FIGURE 2
Stability of IQ scores. Correlations between IQ scores in childhood and IQ score as measured in adulthood (26 years of age) with 95% confidence intervals. Differences are all significant ($P < .001$).

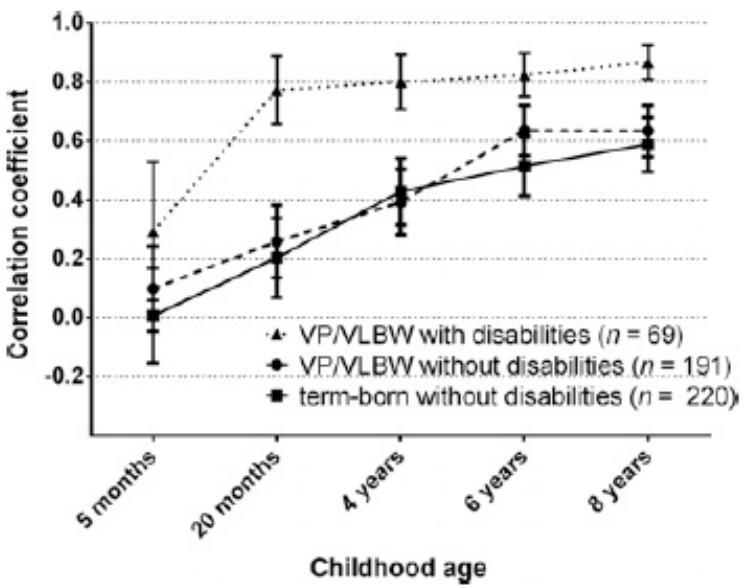
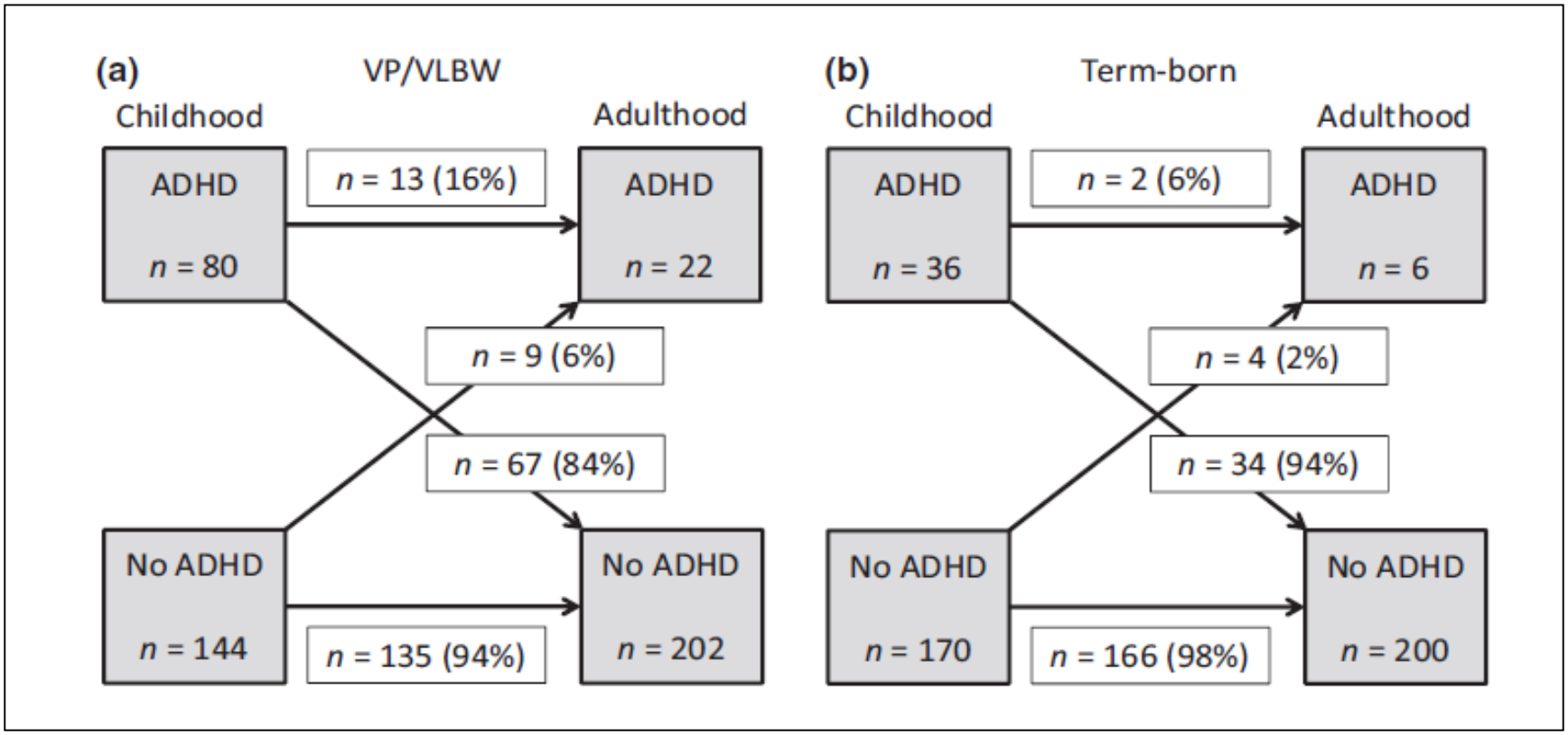


FIGURE 3
Stability of IQ scores for individuals with and without cognitive impairment. Correlations between IQ scores in childhood and IQ score as measured in adulthood (26 years of age) with 95% confidence intervals.

Breeman et al. Pédiatrics, 2015

Développement cognitif des GPM

→ ***Plus de difficultés attentionnelles et de TDA/H chez les GPM quelque soit l'âge de développement***



Breeman et al. J Child Psycho & Psychia, 2015

Troubles psycho émotionnels

- → Risque accru de troubles internalisés à l'âge adulte (Anxiété, Dépression)
- → Risque accru de Troubles de la Personnalité
- → Profil atypique (évitant)
- → Le statut des GPM est fortement corrélé à ce profil à risque (beta=0,33; p< 0.001)

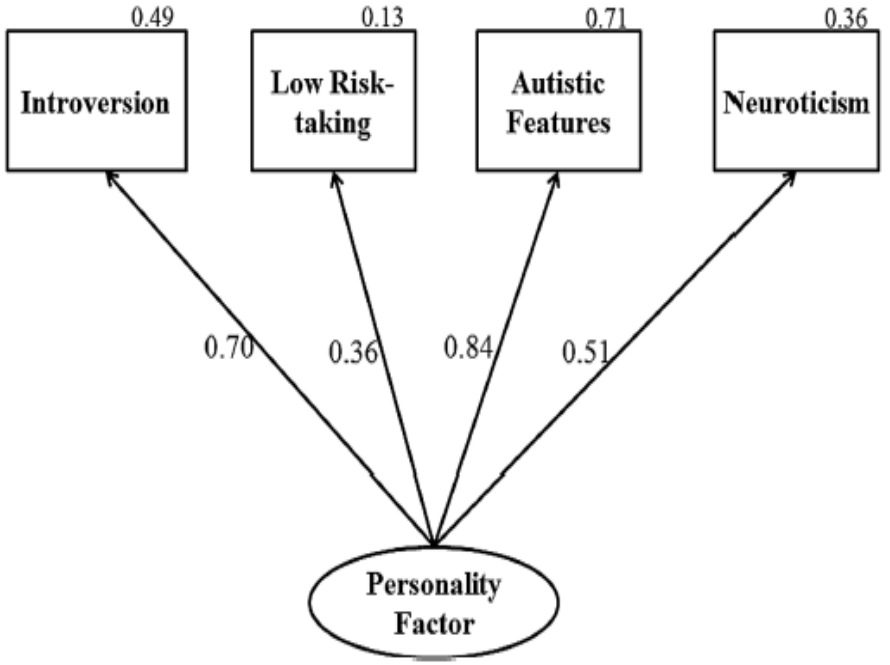


Figure 1 Confirmatory factor analysis for the whole sample. Scores next to arrows indicate regression weights; scores above the individual measures indicate the amount of variance explained in each measure by the overall personality factor (χ^2=7.71, df=2, ns; comparative fit index=0.981; root mean square of approximation=0.08, ns).

Eryigit Madzwamuse et al. BMJ, 2015

Impact du milieu psychosocial sur le devenir des GPM

→ ***Fonctionnement psychosocial est clairement impacté à long terme***

→ ***Forte corrélation des performances, en fonction du niveau socio économique des familles***

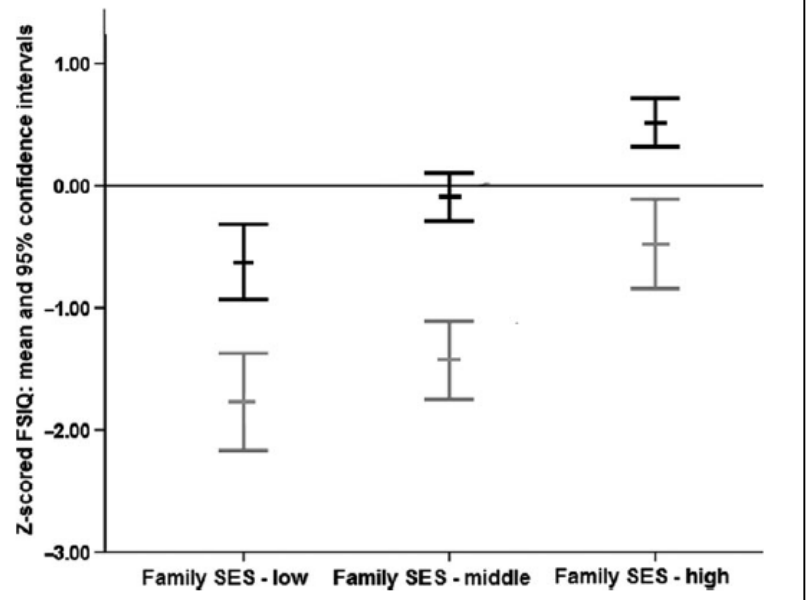


Figure 3 Full-Scale IQ (FSIQ) mean scores with 95% CI for the VP/VLBW and term controls born into low, medium, and high family SES. Full-Scale IQ (FSIQ) means with their 95% confidence intervals in SD units are presented for VP/VLBW sample – total and term controls by family SES categories (low, medium, and high) computed in a weighted, population representative sample. Control sample (n = 197). VP/VLBW sample (n = 217)

Eryigit Madzwamuse et al. J Child Psycho & Psychia, 2015

Qualité des interactions mère-bébé chez le GPM

- **L'immaturité cérébrale des GPM rend plus difficile les interactions précoces mère – bébé**
- **Niveau de stress plus élevé chez les parents (1 an de vie)**
- **Résultats plus contrastés**

  → Les mères de GPM ne sont pas moins sensibles ou attentives dans leurs interactions avec leur bébé

Gray et al. Early Hum Dev, 2013
Bilgin & Wolke. Pediatrics, 2015
Edwards et al. Early Hum Dev, 2016

Qualité des interactions mère-bébé chez le GPM

- ***Le dispositif expérimental du Face to Face*** (Tronick, 1970)

  – Comparaison des performances socio émotionnelles entre 25 dyades MBN et 25 dyades MBP

  → Pas de différence significative

  → GPM moins bonne autorégulation cpt (+ distanciation / - de coordination dyadiques)

  → GPM ont un plus haut niveau de stress et de moins bonnes capacités de régulation socio émotionnelle même dans les interactions normales

Montirosso et al. Br J Dev Psychol, 2010

Prématurité & Dépression maternelle

Prématurité

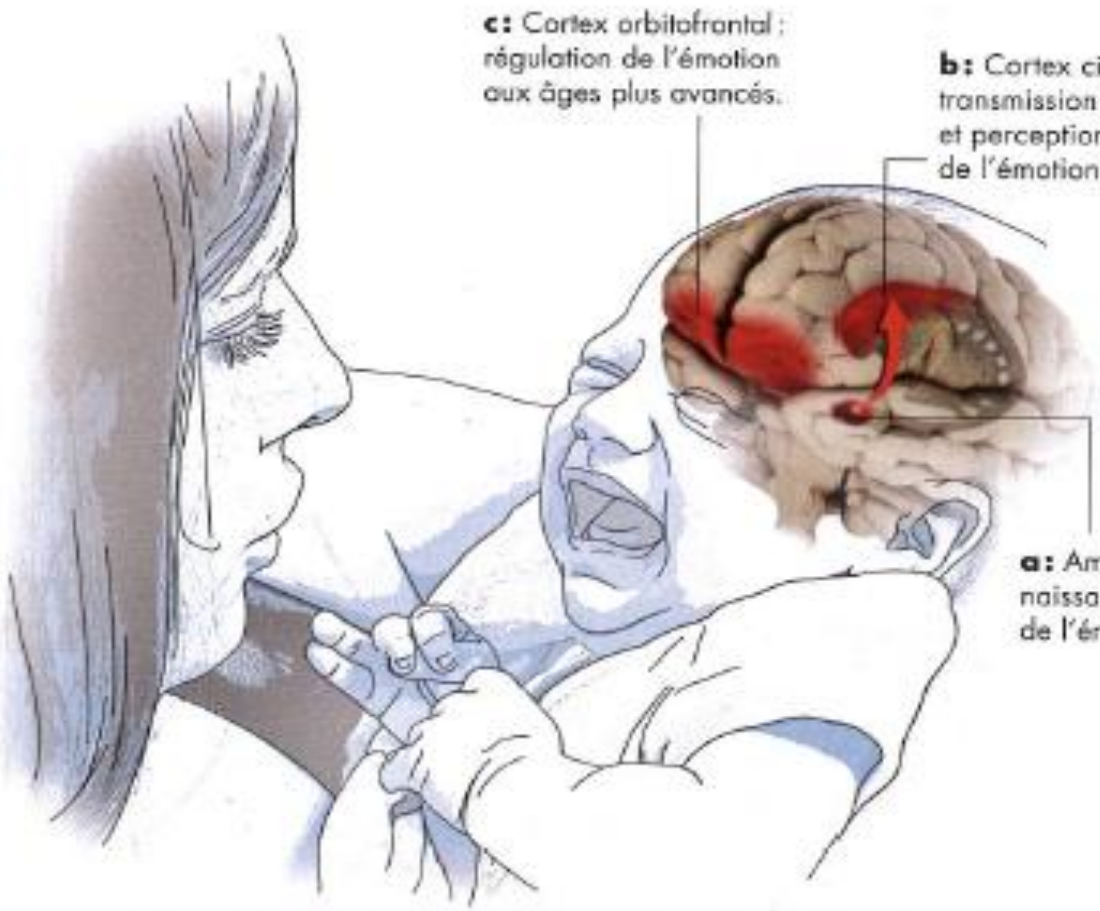
Dépression maternelle

Gelaye et al. Lancet Psychiatry 2016

Synchronie & Attachement

L'attachement sécure: une expression libre des émotions

Un attachement sécure s'établit lorsqu'un enfant peut exprimer ses émotions et les voir prises en compte. Chez un enfant qui a peur, par exemple, l'émotion part de l'amygdale (a) et gagne le cortex cingulaire (b) qui lui permettra par la suite d'être perçue et exprimée. Si le parent ne répond pas à ces attentes, le cortex cingulaire interdira à l'avenir à l'émotion de quitter l'amygdale. L'émotion sera séquestrée, inconsciente, difficilement exprimable et régulable. Plus tard, chez l'enfant ou l'adolescent, elle ne pourra pas gagner le cortex orbitofrontal nécessaire à sa régulation (c).



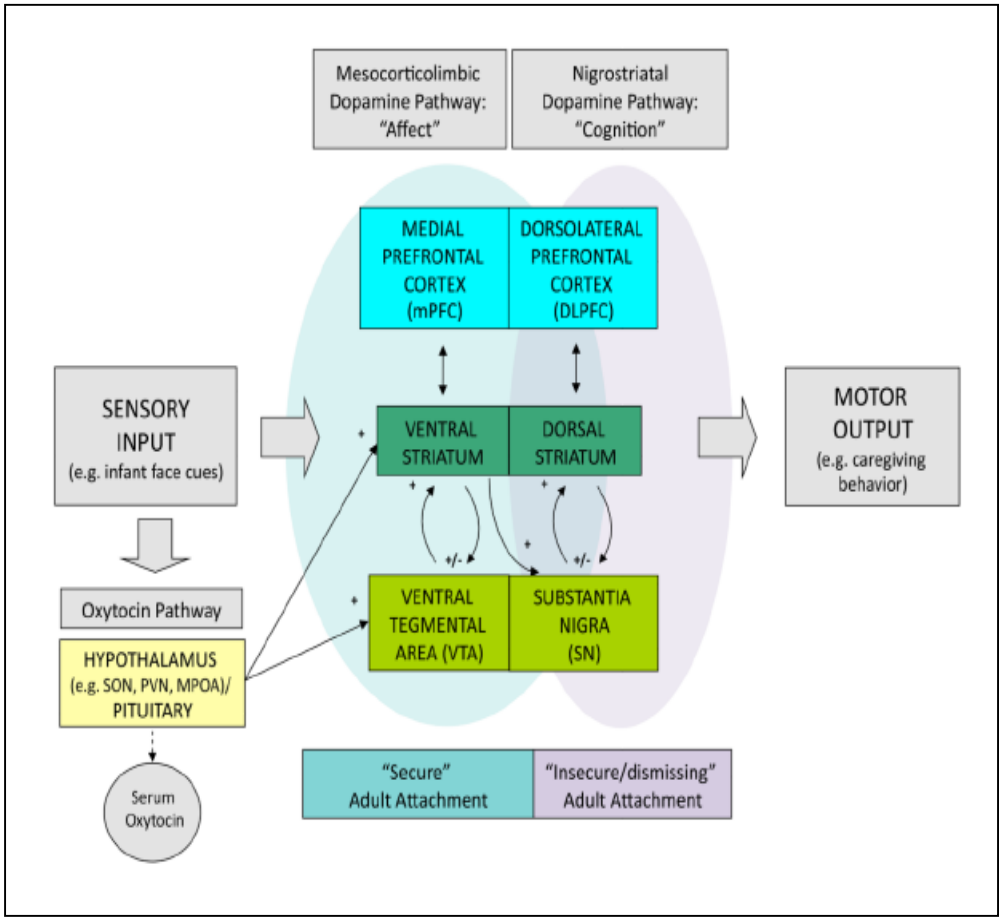
Wiart 2015

Modèles de Compréhension

→***Dysmaturité cérébrale***
- Hippocampe
- Boucles d'Alexander

→***Dysrégulation neuroendocrine***
- Axe du cortisol

→***Dysrégulation émotionnelle***
- Dopamine
- Ocytocine



Thompsson et al, Hum Brain Mapp, 2014
Kalpakidou et al, PlosOne, 2014
Strathearn.J Neuroendocrinology 2011

DEPRESSION AND ANXIETY 32:82–90 (2015)

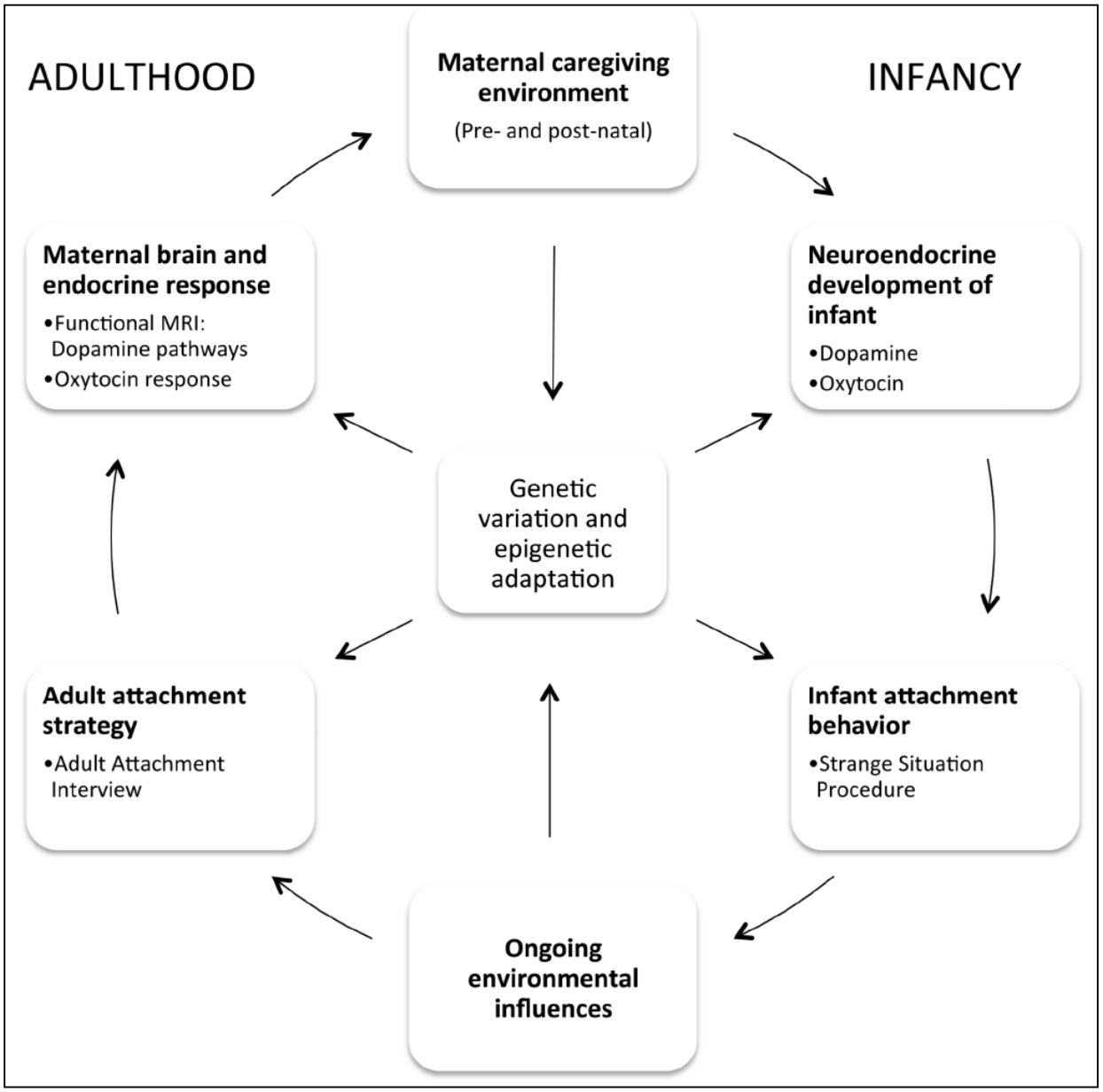
Research Article

THE RELATIONSHIP BETWEEN MATERNAL DEPRESSIVE, ANXIOUS, AND STRESS SYMPTOMS DURING PREGNANCY AND ADULT OFFSPRING BEHAVIORAL AND EMOTIONAL PROBLEMS

Kim S. Betts, M.P.H., B.Ed.,[1]* Gail M. Williams, Ph.D.,[1] Jakob M. Najman, Ph.D.,[2] and Rosa Alati, Ph.D., M.Appl.Sc., Grad.Dip.[3]

Background: *Prenatal maternal depressive, anxious, and stress symptoms have been found to be associated with child and adolescent behavior problems. In this paper, we investigate their impact on behavior problems and depressive symptoms in adulthood.* **Methods:** *Participants included 3,099 mother–offspring pairs from the Mater University Study of Pregnancy (MUSP), an Australian based, prebirth cohort study. We used latent class growth analysis (LCGA) with parallel processes to identify trajectories of maternal depressive, anxious, and stress symptoms over four time periods between the mothers' first clinic visit and 5 years postpregnancy. We fitted the estimates from the maternal trajectories in multivariate logistic regression models to predict internalizing and externalizing behavior at age 21. We adjusted for a wide range of prenatal and postnatal factors, including maternal life events, relationship quality, contact with the new born, as well as concurrent maternal depressive and anxious symptoms and father's history of mental health problem.* **Results:** *LCGA found seven groups of mothers; one group of mothers exhibited high levels of depressive, anxious, and stress symptoms during pregnancy but not at later time points. Their offspring experienced increased levels of behavior problems and depressive symptoms.* **Conclusions:** *This paper provides the first evidence that high levels of maternal subjective depressive, anxious, and stress symptoms experienced in early pregnancy may predict internalizing and externalizing behavior problems and depressive symptoms in young adults. Depression and Anxiety 32:82–90. 2015.*

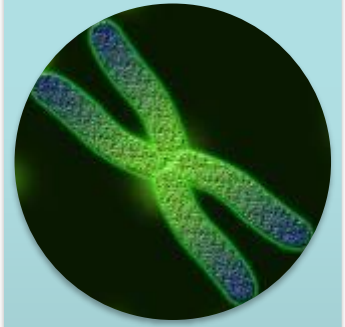
Le cycle du caregiving maternelle



Strathearn, 2011.

Les troubles du NeuroDéveloppement

ce n'est qu'un long continuum…



Gènes

Réseaux neuronaux

Processus cognitifs

Régulation émotionnelle

Capacités d'adaptation

Interdépendances dynamiques & évolutives

Les TND en pratique : *quelles perspectives thérapeutiques…*

- **L'enjeu du dépistage précoce**
  < 5 ans

- **L'intérêt de la lecture multi-dimensionnelle…**

Spittel et al. Cochrane Data Base Rev, 2012

Tout est une question de représentation…

Tout est une question de représentation…

Tout est une question de représentation…

En pratique…

- **Importance des regards multiples**

  → ***Evaluation multimodale***

  (Regard global : bio psycho social)

- **Importance du dialogue partagé**

  → ***Réunion de concertation***

  (Description des faits et des ressentis en évitant la surinterprétation)

- **Importance des prises en charge intégrées**

  →***Approche multidimensionnelle***

  . Personnalisée (attente & besoin)

  . Planifiée (objectifs clairs, établis dans le temps)

  . Evaluation régulière (ajustement et/ou réorientation)

Quelle place pour les thérapies innovantes ?

- ***Le programme H-HOPE***

Hospital to home : Optimizing the Infant's Environnement

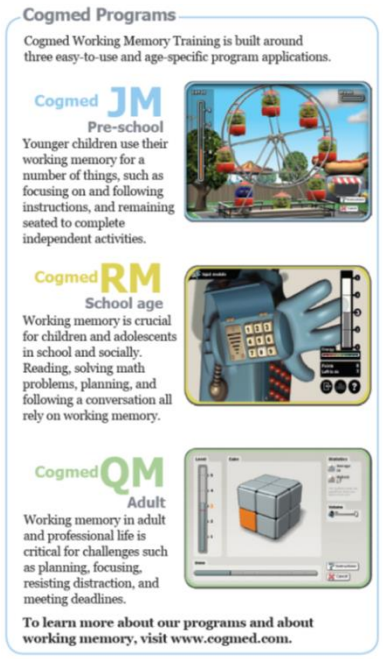
– Suivi à domicile intégrant :
  - Stimulation polysensorielle bi quotidienne
  - 4 séances de guidance maternelle
  - 2 appels téléphoniques
– Evaluation de la qualité des échanges dyadiques à 6 semaines d'âge corrigé

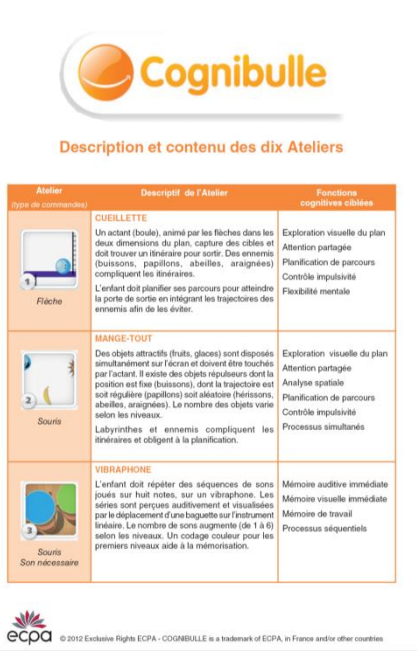
→ ***Amélioration significative***

White-Traut et al. Infant Behav Dev, 2013

La troisième vague…

- **La remédiation cognitive**

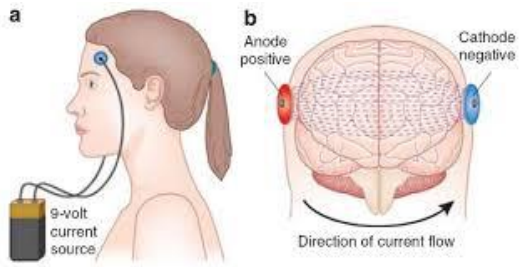




La neuro modulation

→ ***Le neuro feedback***

→ ***La tDCS***



Fourneret, 2012, 2016
Demirtas-Talidede et al. Neuropharmacology, 2014

L'hypothèse de la « programmation fœtale »

Génotype

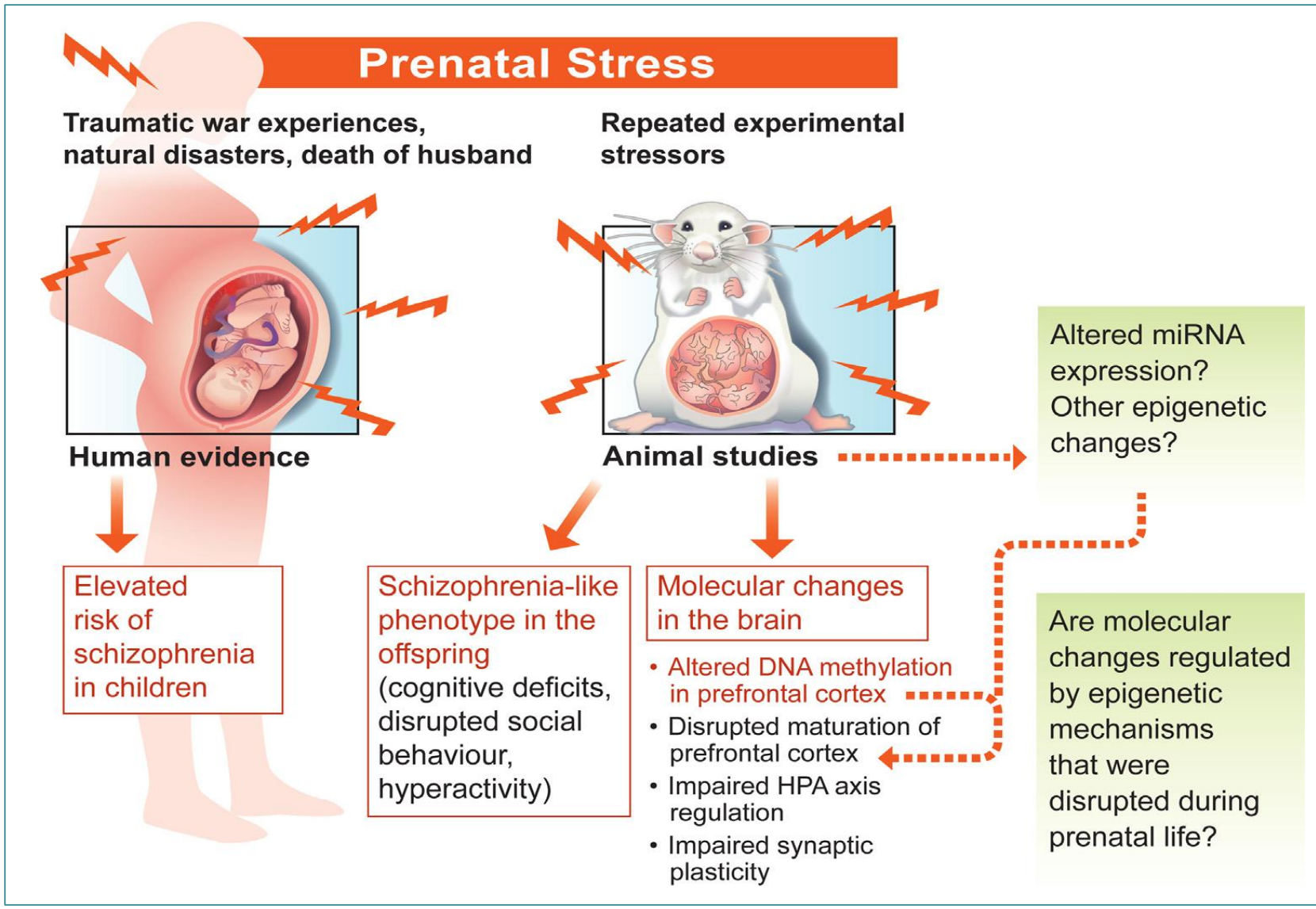
Phénotype

Modification de l'expression des gènes sans modification de l'ADN

Traits de développement atypiques

Van den Bergh et al, Neuroscience & Behav Reviews, 2005 ; Marcus S et al, Infant Behav Dev 2011

Stress prénatal & épigenèse cérébrale



Babenko et al, Neurosciences & Beh Rew 2015

La SF s’invite dans les TND

Le futur est déjà là ...

European Journal of Obstetrics & Gynecology and Reproductive Biology 208 (2017) 61–70

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Review article

Artificial placenta: Analysis of recent progress

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ARTICLE INFO

Article history:
Received 19 July 2016
Received in revised form 18 October 2016
Accepted 10 November 2016

Keywords:
Coagulation
Extracorporeal life supports (ECLS)
Extracorporeal membrane oxygenation (ECMO)
Extremely preterm birth
Fetus
Greyzone
Haemocompatible
Haemodialysis
Haemodynamic
Homeostasis
Inflammation
Kidney

ABSTRACT

The artificial placenta (AP) has for many decades captured the imagination of scientists and authors with popular fiction including The Matrix and Aldous Huxley's "Brave New World", depicting a human surviving ex-utero in an artificial uterine environment (AUE). For scientists this has fascinated as a way forward for extremely preterm infants (EPIs) born less than 28 weeks of gestation. Early successes with mechanical ventilation (MV) for infants born above 28 weeks of gestation meant that AP research lost momentum.

More recently, the gestational age limit for survival now borders on 23 weeks and corresponds to the biological milestone of lung development marked by the early canalicular stage of lung morphogenesis. The so called greyzone of 23–25 weeks represents a steep increase in mortality with decreasing gestational age and current options in neonatal care are on the fringes of efficacy for this population. A shift in thinking recognizes the vitality of EPIs as a fetus rather than a 37–40 week neonate and this has reinvigorated the concept of the AP. This review will discuss the scale of extreme preterm birth with special reference to previable infants born in the greyzone. Recent AP studies using sheep models are compared, technical obstacles discussed and future research themes identified.

nature COMMUNICATIONS

ARTICLE

Received 25 Apr 2016 | Accepted 2 Mar 2017 | Published 25 Apr 2017

DOI: 10.1038/ncomms15112 OPEN

An extra-uterine system to physiologically support the extreme premature lamb

Emily A. Partridge[1,*], Marcus G. Davey[1,*], Matthew A. Hornick[1], Patrick E. McGovern[1], Ali Y. Mejaddam[1], Jesse D. Vrecenak[1], Carmen Mesas-Burgos[1], Aliza Olive[1], Robert C. Caskey[1], Theodore R. Weiland[1], Jiancheng Han[1], Alexander J. Schupper[1], James T. Connelly[1], Kevin C. Dysart[2], Jack Rychik[3], Holly L. Hedrick[1], William H. Peranteau[1] & Alan W. Flake[1]

In the developed world, extreme prematurity is the leading cause of neonatal mortality and morbidity due to a combination of organ immaturity and iatrogenic injury. Until now, efforts to extend gestation using extracorporeal systems have achieved limited success. Here we report the development of a system that incorporates a pumpless oxygenator circuit connected to the fetus of a lamb via an umbilical cord interface that is maintained within a closed 'amniotic fluid' circuit that closely reproduces the environment of the womb. We show that fetal lambs that are developmentally equivalent to the extreme premature human infant can be physiologically supported in this extra-uterine device for up to 4 weeks. Lambs on support maintain stable haemodynamics, have normal blood gas and oxygenation parameters and maintain patency of the fetal circulation. With appropriate nutritional support, lambs on the system demonstrate normal somatic growth, lung maturation and brain growth and myelination.

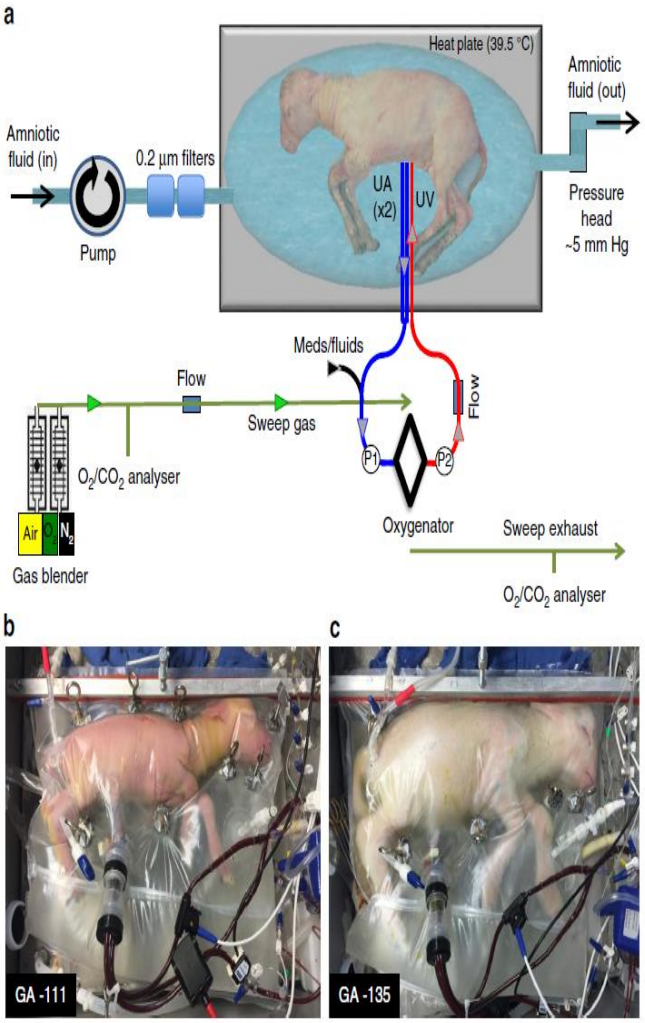


Figure 1 | UA/UV Biobag system design. (**a**) Circuit and system components consisting of a pumpless, low-resistance oxygenator circuit, a closed fluid environment with continuous fluid exchange and an umbilical vascular interface. (**b**) Representative lamb cannulated at 107 days of gestation and on day 4 of support. (**c**) The same lamb on day 28 of support illustrating somatic growth and maturation.

Quelques données récentes…

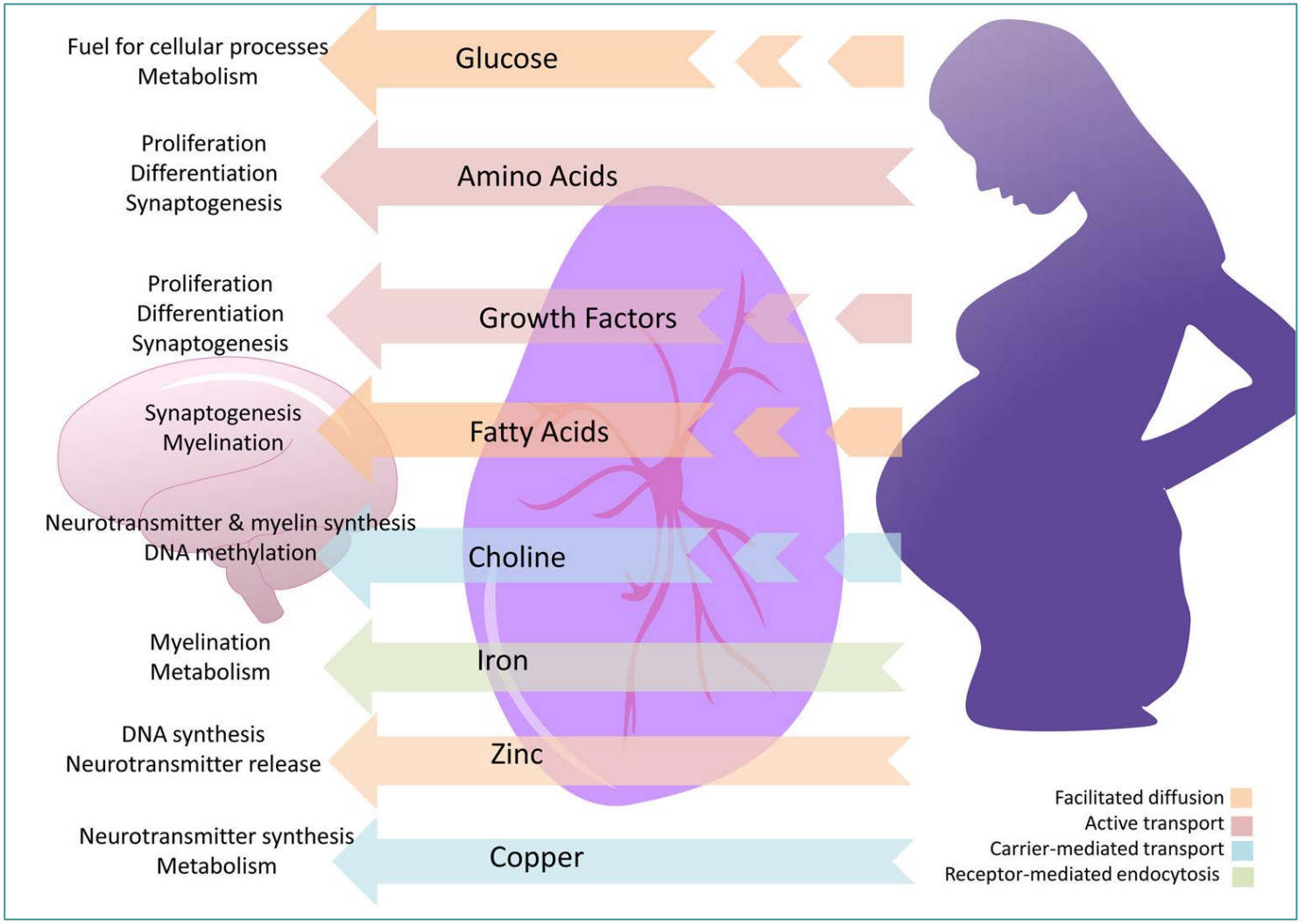
→ Neurologic outcomes of the premature lamb in an extrauterine environment for neonatal development

- Patrick E. McGovern et al. Journal of Pediatric Surgery (55) 10 ; 2115-2123, 2020.

→ The EXTrauterine Environment for Neonatal Development Supports Normal Intestinal Maturation and Development

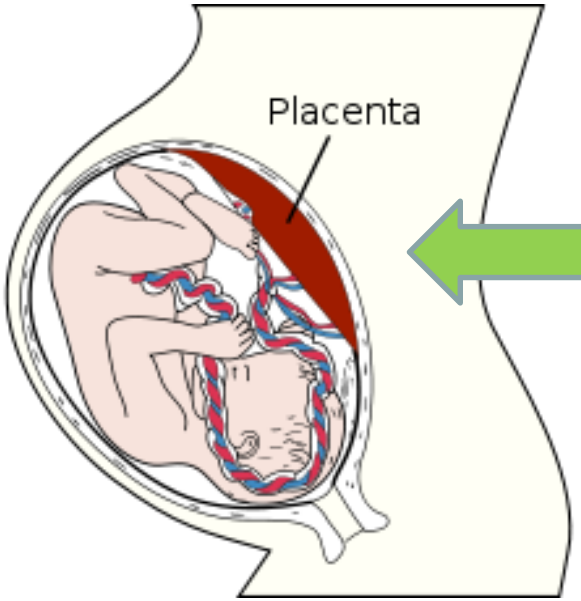
- Heron D. Baumgarten et al. Cellular and Molecular Gastroenterology and Hepatology (10) 3 ; 623-637, 2020.

Le rôle clef du placenta



Nugent & Bale. *Front Neuroendocrinol.* 2015

Peut on parler de complexe Utero Placento Maternel ?



Complexe Utero Placento Maternel

Environnement

RESEARCH PAPER

Epigenetics 8:12, 1321–1329; December 2013; © 2013 Landes Bioscience

The roles of DNA methylation of *NR3C1* and *11β-HSD2* and exposure to maternal mood disorder in utero on newborn neurobehavior

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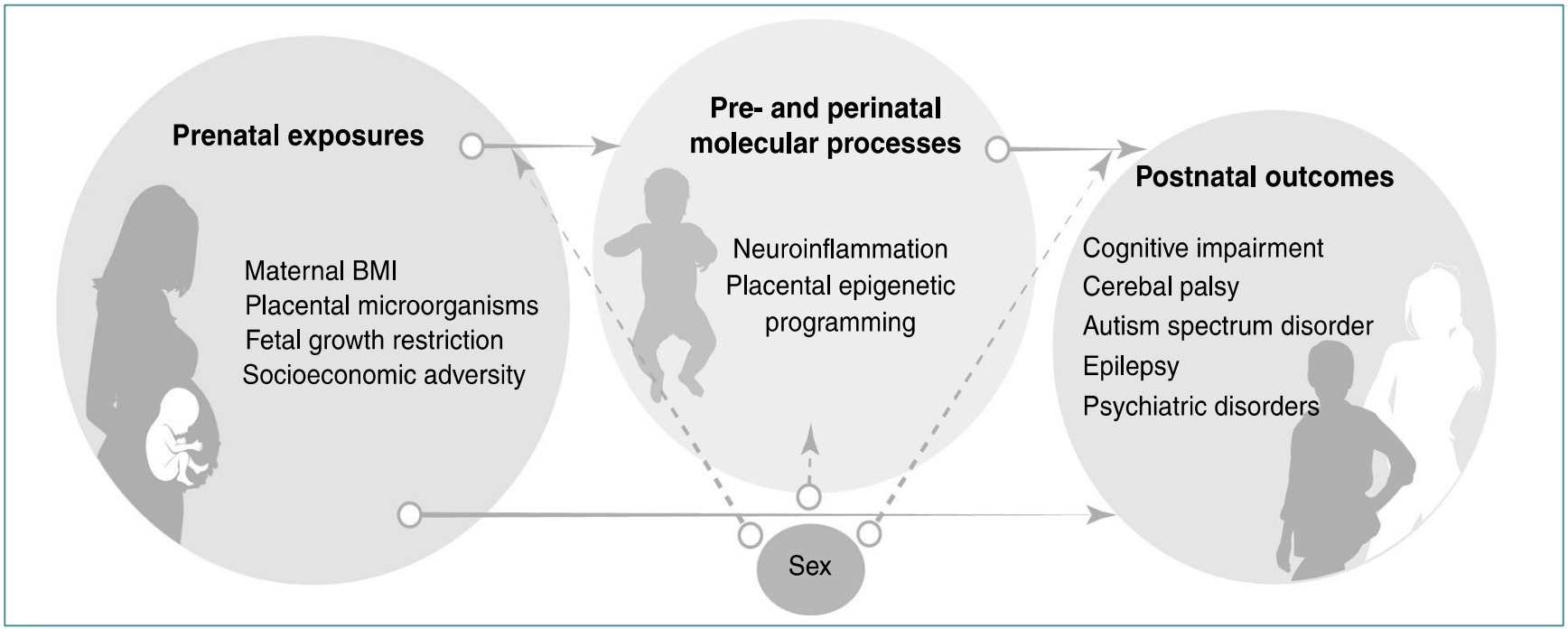
Keywords: DNA methylation, maternal depression, maternal anxiety, newborn neurobehavior

Abbreviations: NNNS, NICU network neurobehavioral scale; HPA, hypothalamic pituitary adrenal axis; ACTH, adrenocorticotropic hormone; GA, gestational age; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age

Exposure to maternal mood disorder in utero may program infant neurobehavior via DNA methylation of the glucocorticoid receptor (*NR3C1*) and 11β-hydroxysteroid dehydrogenase type 2 (*11β-HSD-2*), two placental genes that have been implicated in perturbations of the hypothalamic pituitary adrenocortical (HPA) axis. We tested the relations among prenatal exposure to maternal depression or anxiety, methylation of exon 1F of *NR3C1* and *11β-HSD-2*, and newborn neurobehavior. Controlling for relevant covariates, infants whose mothers reported depression during pregnancy and showed greater methylation of placental *NR3C1* CpG2 had poorer self-regulation, more hypotonia, and more lethargy than infants whose mothers did not report depression. On the other hand, infants whose mothers reported anxiety during pregnancy and showed greater methylation of placental *11β-HSD-2* CpG4 were more hypotonic compared with infants of mothers who did not report anxiety during pregnancy. Our results support the fetal programming hypothesis and suggest that fetal adjustments to cues from the intrauterine environment, in this case an environment that could be characterized by increased exposure to maternal cortisol, may lead to poor neurodevelopmental outcomes.

La boucle est bouclée…



Bangma et al. Pediatrics 2020

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Pour aller plus loin…