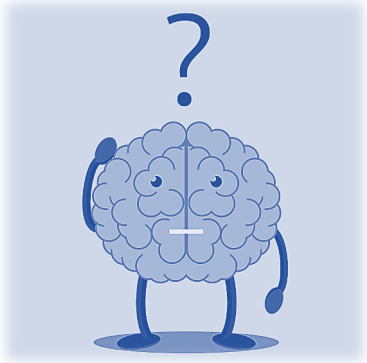
PHENOTYPE NEUROCOMPORTEMENTAL ET QUALITE DE VIE DE L'ENFANT EXTRÊME PREMATURE À L' AGE SCOLAIRE ET QUALITE DE VIE



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PÔLE FEMMES
PARENTS ENFANTS

WHAT DO WE KNOW?

- Survival of Extreme Preterms (EP) ↗
- Disability rates
  - higher than those born at term
  - inversely related to gestational age
- Only 5-10 % have severe disabilities
- **> 50%** EP children have **moderate or mild disabilities at school age**
  - Strong psychosocial and emotional impact on the EP child, the adult and their families
  - Urgent need for a quality of life (QoL) evaluation

Ancel PY. JAMA Pediatrics 2015
Serenius F. JAMA Pediatrics 2016
Van Der Pal de Bruin et al. Early Hum Dev 2015
Breeman et al. Pediatrics 2015

PHENOTYPE NEUROCOMPORTEMENTAL ?

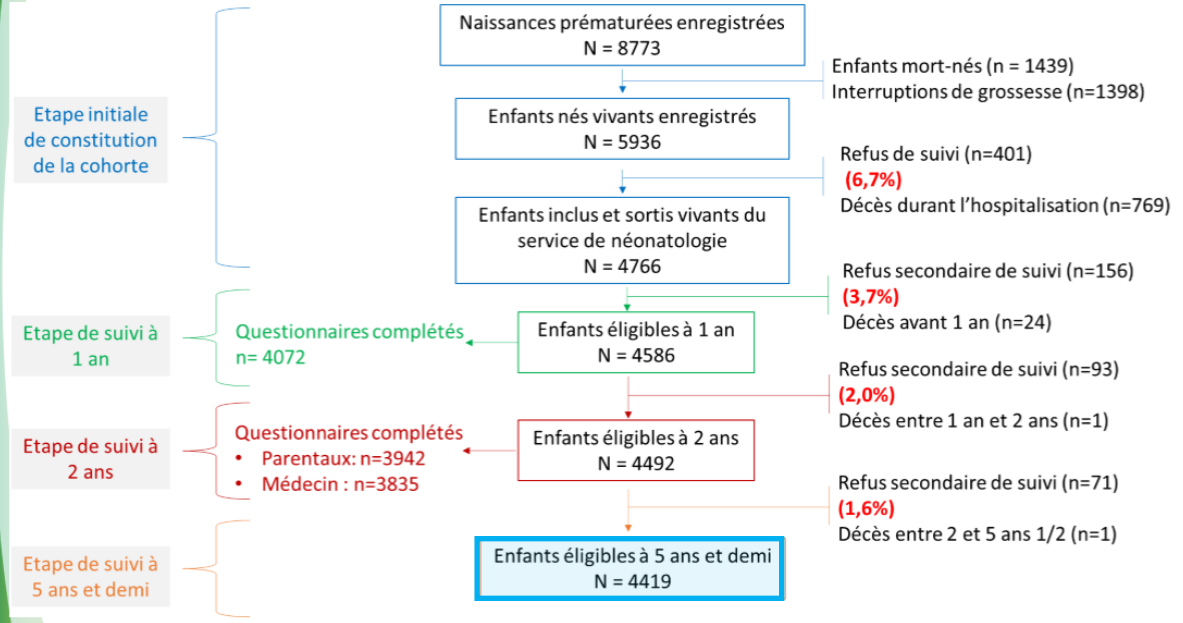
- WHO : Mild and/or moderate disability
- How
  - Individual profile (behavior, motor and cognitive)
  - No false methodology
- WHY
  - Social Impact

EPIPAGE 2

PRINCIPAUX OBJECTIFS

- **Pratiques médicales et organisations des soins**
  - Nouvelles pratiques en obstétrique / néonatologie
  - Bénéfices et effets secondaires de traitements
  - Prise en charge de la prématurité extrême
- **Etiologie de la prématurité et de ses conséquences**
  - Complications de la grossesse
  - Histologie placentaire
- **Devenir à long terme des enfants**
  - Lésions cérébrales
  - Troubles cognitifs spécifiques
  - Problèmes de santé

ETAT D'AVANCEMENT



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epipage2.inserm.fr
PARIS DESCARTES

Table 1. Neuromotor, sensory and cognitive disabilities by gestational age groups. ***V Pierrat BMJ 2020 EPIPAGE study***

	Total 24-31 w	**24-26 w**	**27-31 w**	**Total 32-34 w**		**Term-born**
	n=3254	n=544	n=2710	n=1187	Trend p value	n=592
Overall disabilities††						
No disability	*52.1*	*43.7*	*53.4*	*61.2*	*<.001‡*	81.0
Mild disability	*29.3*	*32.3*	*28.8*	*26.9*		14.5
Moderate disability	*11.6*	*13.6*	*11.3*	*8.5*		3.4
Severe disability	*7.0*	*10.4*	*6.5*	*3.4*		1.1

- Cohorte suédoise EXPRESS
  - 441 NN < 27 SA, 90% suivi à 6,5 ans
  - Comparaison avec 371 NNAT
  - Pas de séquelle: 36%
  - CP: 9,5%
  - Séquelles sensorielles (audit°/visuelles): 2%

Table 2. WISC-IV Scores of Children Born Extremely Preterm and Control Children Born at Term[a]

	Extremely Preterm		Control		Extremely Preterm vs Control	
					Mean Difference (95% CI)	
Variable	Total No.	Mean (SD)	Total No.	Mean (SD)	Unadjusted	Adjusted
FSIQ	371	83.4 (14.8)	367	100.3 (11.7)	16.9 (14.9-18.8)	14.2 (12.1-16.3)[b]
Index scale score						
Verbal comprehension	361	92.1 (14.5)	366	104.0 (11.5)	11.9 (10.0-13.8)	9.3 (7.2-11.3)[b]
Perceptual reasoning	363	89.7 (14.2)	367	104.8 (12.7)	15.1 (13.2-17.5)	12.6 (10.5-14.8)[b]
Working memory	360	78.2 (13.1)	367	90.7 (11.0)	12.5 (10.7-14.3)	11.0 (9.1-13.0)[b]
Processing speed	360	85.0 (14.4)	367	96.9 (12.5)	11.9 (10.0-13.9)	10.8 (8.6-13.0)[b]
	Total No.	No. (%)	Total No.	No. (%)	Odds Ratio (95% CI)	
Index scale score less than the mean −2 SDs[d]						
Verbal comprehension (<80.9)	361	85 (23.5)		8 (2.2)	13.7 (6.6-30.0)	9.3 (4.3-20.3)[c]
Perceptual reasoning (<79.4)	363	91 (25.1)		10 (2.7)	11.9 (6.1-23.2)	9.0 (4.5-18.3)[c]
Working memory (<68.7)	360	94 (26.1)		10 (2.7)	12.6 (6.4-24.7)	8.2 (4.1-16.7)[c]
Processing speed (<72.0)	360	56 (15.6)		9 (2.5)	8.2 (3.9-17.6)	6.1 (2.8-13.2)[c]
FSIQ disability category[d,e]	371		367			
None (FSIQ score ≥88.6)		134 (36.1)		307 (83.7)	1 [Reference]	1 [Reference][c]
Mild (FSIQ score 76.9-88.5)		118 (31.8)		52 (14.2)		
Moderate (FSIQ score 65.2-76.8)		76 (20.5)		7 (2.2)	21.2 (10.2-44.1)	15.6 (7.3-33.5)[c]
Severe (FSIQ score <65.2)		43 (11.6)		1 (0.3)		

PÔLE FEMMES PARENTS ENFANTS

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Table 3. Developmental Coordination Disorder M-ABC2 , by gestational age groups. **Epipage 2 V Pierrat BMJ 2021**

	Total 24-31 w	**24-26 w**	**27-31 w**	**Total 32-34 w**		**Term-born**
	n=3254	n=544	n=2710	n=1187	Trend p value	n=592
Total M-ABC2 score <5th percentile‡	*14.2*	*23.7*	*12.8*	*8.5*	*<0.001*	4.5
By overall disability groups,						
without disability	*4.9*	*10.4*	*4.3*	*2.9*		
with mild disability	*13.9*	*20.9*	*12.8*	*11.3*		
with moderate disability	*35.6*	*46.6*	*33.6*	*28.4*		
with severe disability	*49.4*	*58.3*	*47.3*	*35.5*		

30% OF EPT SCHOOL-AGED CHILDREN, FREE FROM SEVERE DEFICIENCY HAVE A DEVELOPMENTAL COORDINATION DISORDER (DCD) BOLK J, *JAMA PEDIATR* 2018; **172**: 765–774.

Characteristic	No./Total No. (%)		Comparing Extremely Preterm Children With and Without DCD, Adjusted OR (99% CI)[b,c]	*p* value
	Extremely Preterm Children With DCD[a]	Extremely Preterm Children Without DCD[a]		
	Mean Score (99% CI)			
Characteristic	**Unadjusted**	**Unadjusted**	**Adjusted Mean Difference (99% CI)[a]**	***p* value**
No.	85	144		
Cognitive assessment (WISC-IV)[c,e]				
Verbal comprehension	98.6 (10.9)	98.7 (10.9)	−0.88 (−3.2 to 4.9)	.58
Perceptual reasoning	**93.0 (10.0)**	**98.0 (11.3)**	**4.52 (0.6-8.4)**	**.003**
Working memory	**81.8 (9.4)**	**86.0 (9.8)**	**3.2 (−0.4 to 6.7)**	**.02**
Processing speed	**86.0 (9.2)**	**92.8 (12.5)**	**6.0 (2.2-9.9)**	**<.001**
Full-scale intelligence quotient	**88.4 (8.3)**	**93.3 (10.1)**	**3.9 (0.4-7.3)**	**.004**

PÔLE FEMMES PARENTS ENFANTS

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SCHOOL-AGED EPT CHILDREN HAVE MULTIPLE, SPECIFIC NEUROCOGNITIVE/ BEHAVIORAL DISORDERS WHICH ARE OFTEN ASSOCIATED.
"EXPRESS STUDY"

Characteristic	No./Total No. (%)		Comparing Extremely Preterm Children With and Without DCD, Adjusted OR (99% CI)[b,c]	*p* Value
	Extremely Preterm Children With DCD[a]	Extremely Preterm Children Without DCD[a]		
Behavioral problems (SDQ)[d]				
Total behavioral problems	**35/84 (42)**	**27/141 (19)**	**2.71 (1.15-6.37)**	**.003**
Internalizing problems	35/84 (43)	37/141 (26)	1.85 (0.83-4.16)	.05
Emotional problems	18/84 (21)	18/141 (13)	1.98 (0.76-5.14)	.07
Peer relations	15/84 (18)	20/141 (14)	1.10 (0.37-3.30)	.81
Externalizing problems	**29/84 (35)**	**20/141 (14)**	**2.80 (1.10-7.12)**	**.005**
Hyperactivity	**23/84 (27)**	**14/141 (10)**	**3.48 (1.29-9.41)**	**.001**
Conduct	20/84 (24)	23/141 (16)	1.42 (0.58-3.53)	.30
Inattention/hyperactivity (Brown ADD)[d]				
Attentional problems	**32/85 (37)**	**20/139 (14)**	**3.38 (1.39-8.18)**	**<.001**
Combined attentional and hyperactivity problems	**33/85 (39)**	**19/139 (14)**	**3.68 (1.47-9.16)**	**<.001**
Behavioral and social problems (FTF)[d]				
Poor executive function	**24/79 (30)**	**24/135 (18)**	**2.04 (0.87-4.81)**	**.03**
Poor social skills	22/78 (28)	24/135 (18)	1.46 (0.59-3.63)	.28
Perceptual problems	30/78 (39)	33/135 (24)	1.62 (0.72-3.56)	.13
Relation in space	**25/79 (32)**	**24/135 (18)**	**2.06 (0.84-5.04)**	**.04**
Time concepts	25/77 (32)	29/135 (22)	1.61 (0.66-3.08)	.17
Body perception	21/78 (28)	31/135 (23)	1.14 (0.47-2.64)	.75
Visual perception	**30/78 (38)**	**29/135 (22)**	**1.91 (0.82-4.45)**	**.05**

MULTIPLE, SPECIFIC NEUROCOGNITIVE/BEHAVIORAL DISORDERS OFTEN ASSOCIATED
TRUE NEUROBEHAVIORAL "PHENOTYPE" (NBP) OF PREMATURITY WITH CONSEQUENCES ON SOCIAL ADJUSTMENT

- Usually classification disability/no incapacity with FSIQ (Weshler)
  - absence of incapacity,
  - minor disability,
  - moderate disability,
  - severe disability
- FSIQ scores : complex processes involving multiple intellectual and non-intellectual characteristics (attention, emotions, motivation, movement planning, etc.)
- False methodology
  - threshold of ≥89 "normal", low average.
  - dispersion or dissociated subtest value = not reflective of the child's cognitive function
  - Child "normal" with dysexecutive syndrome and/or impaired behavior

SCHOOL-AGED EXTREMELY PRETERM (EPT) CHILDREN WITH MODERATE OR MINOR DISABILITY

- Low severity dysfunctions : ↗ school years into young adult.
- Social adjustment disorders correlated
  - with language
  - and/or executive disorders
  - and/or associated behavioral disorders.
- Topical issue +++: reflects that of the adult the child may become.
- Social adjustment : measured by the quality of life (QoL) evaluation

Korzeniewski SJ, *Dev Behav Pediatr JDBP 2017; 38: 697–705*

But...

- Quality of Life (QoL)
  - Measure of the individual's physical, mental and social well-being via his basic needs: biological, human warmth, work and leisure
  - Subjective measure that changes during the individual's lifetime

WHO 1994

- Evaluation is contingent upon utilization of
  - Standardized and validated generic questionnaires
  - Designed to measure the QoL in the general population
  - Parental or self-evaluation

Quality of life and school age ETP children (without serious sequelae)

- QoL EPT children, has been reduced as compared to a reference children population.
- Independent determinants population's QoL :
  - language comprehension disorders,
  - Visuospatial disorders,
  - Executive disorders and
  - Behavioral disorders

Gire C : *Arch Dis Child* 2019; **104**: 333–339/*Pediatr Res* 2020; **88**: 642–652**.**

OBJECTIVE

- Identify neurobehavioral subgroups in an EPT population free from severe disabilities included in “GPQoL-study”:
  - 1) that shared similar profiles on the measurements of intelligence, executive functions
  - 2) by looking at the distribution of anxiety and behavioral disorders in each group
  - 3) correlating them with a QoL measurement.

TRIAL DESIGN(GPQOL STUDY)

- Cross-sectional multicenter, observational study
  - Between 2012 and 2015
  - 5 French Level III facilities
    - *Marseille Conception, Marseille Nord, Nantes, Nimes and Rouen*
- *Ethics*
  - Trial was approved by the national ethics committee
  - Trial registration number: NCT01675726

INCLUSION CRITERIA(GPQOL STUDY)

- EP child born before 28 week's GA
- Born between 01/01/2004 and 12/31/2007
- Hospitalized after birth in one of the 5 level III participating facilities
- School-aged child (7 to 10 years) at the time of inclusion
- Child capable of answering a French-language questionnaire
- Child whose parents or legal representatives have accepted the study's participation principles and have signed the informed consent

Exclusion criteria (GPQOL study)

- Death after discharge
- Child with severe cerebral palsy, or severe cognitive disability or autism
- Child with blindness or amblyopia, or deafness

ANALYSE DU COMPORTEMENT (SDQ)
QUESTIONNAIRE DES FORCES ET DES DIFFICULTÉS DE L'ENFANT

Les comportements observables dans la vie quotidienne de l'enfant.

- Problèmes émotionnels
  - «A de nombreuses peurs, est facilement effrayé»,
- Troubles de conduite
  - «Se bagarre souvent avec les autres enfants ou les tyrannise»
- L'hyperactivité
  - «Ne tient pas en place ou se tortille constamment»
- Problèmes avec les pairs
  - «Harcelé ou tyrannisé par les autres enfants», et les
- comportements prosociaux
  - «Gentil avec les enfants plus jeunes»).

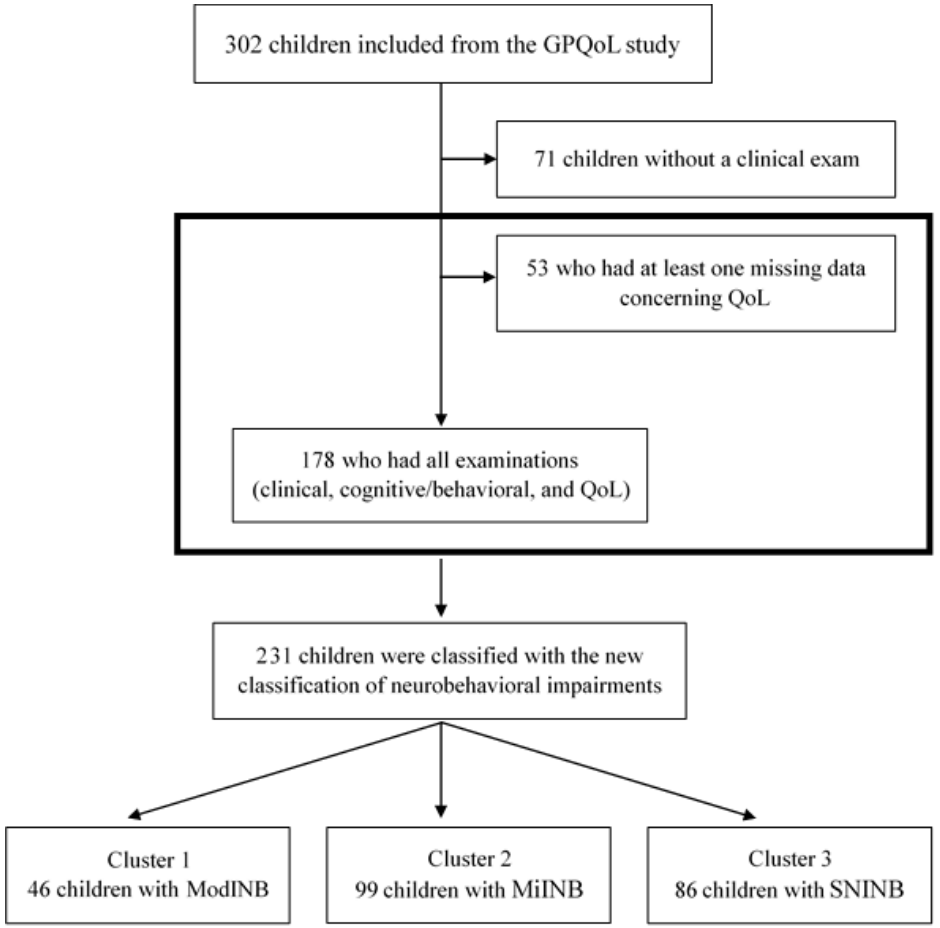
COURSE OF THE STUDY

- A day-long evaluation between 8-10 y
  - Physical examination (Touwen infant neurological examination)
  - Psychometric evaluation (WISC IV, Rey's figure, Nepsy subtests)
  - Comportement (SDQ) et anxieté (STAI)
- QoL evaluation
  - VSP-A
    - French, 35 items, index total score and 9 sub-scor
  - Kidscreen-10
    - European, 10 items, index total score / 100

NEW CLASSIFICATION OF COGNITIVE/BEHAVIORAL IMPAIRMENTS

- CLARA algorithm (Clustering-Large-Applications)
  - constraint being the number of clusters (three in our study).
- The algorithm
  - the most similar subjects within each cluster,
  - and the most differences between the clusters.
  - Distribution by Psychometric evaluation (subtest WISC IV, Nepsy subtests, Rey figure)
  - The data of the anxiety and the behavior are distributed in each cluster.
  - All data were then compared according to the three established neurobehavioral profiles.

Flow Chart

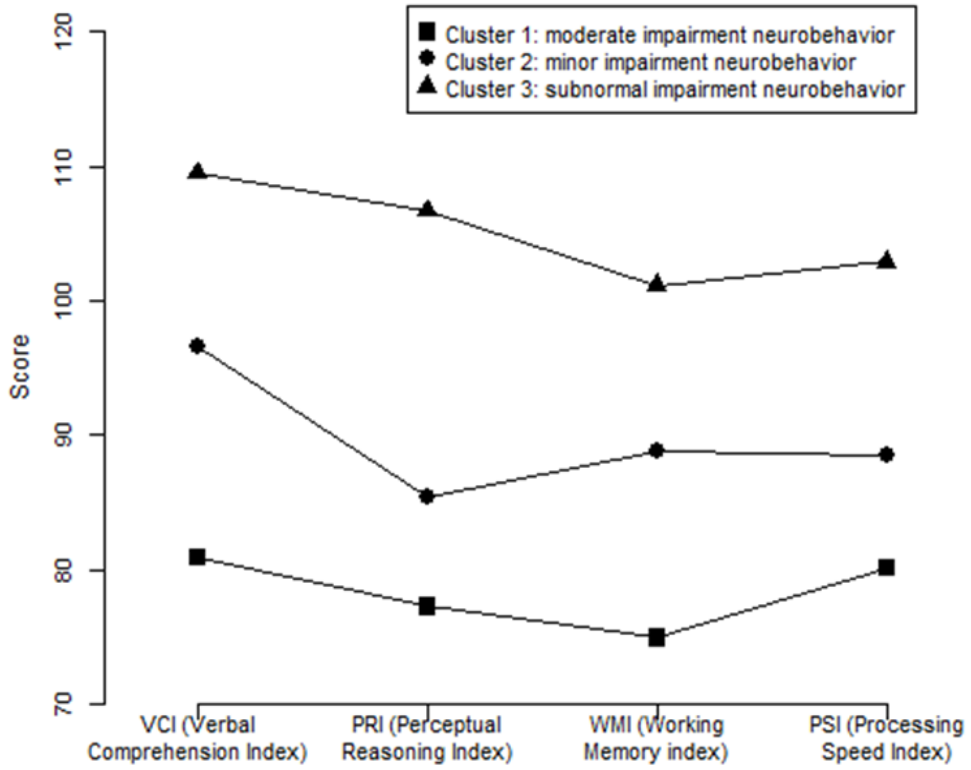

302 children included from the GPQoL study
71 children without a clinical exam
53 who had at least one missing data concerning QoL
178 who had all examinations (clinical, cognitive/behavioral, and QoL)
231 children were classified with the new classification of neurobehavioral impairments
Cluster 1
46 children with ModINB
Cluster 2
99 children with MiINB
Cluster 3
86 children with SNINB

Result (1) :Cognitive/behavioral impairments profiles new classification (231 children three NBP)

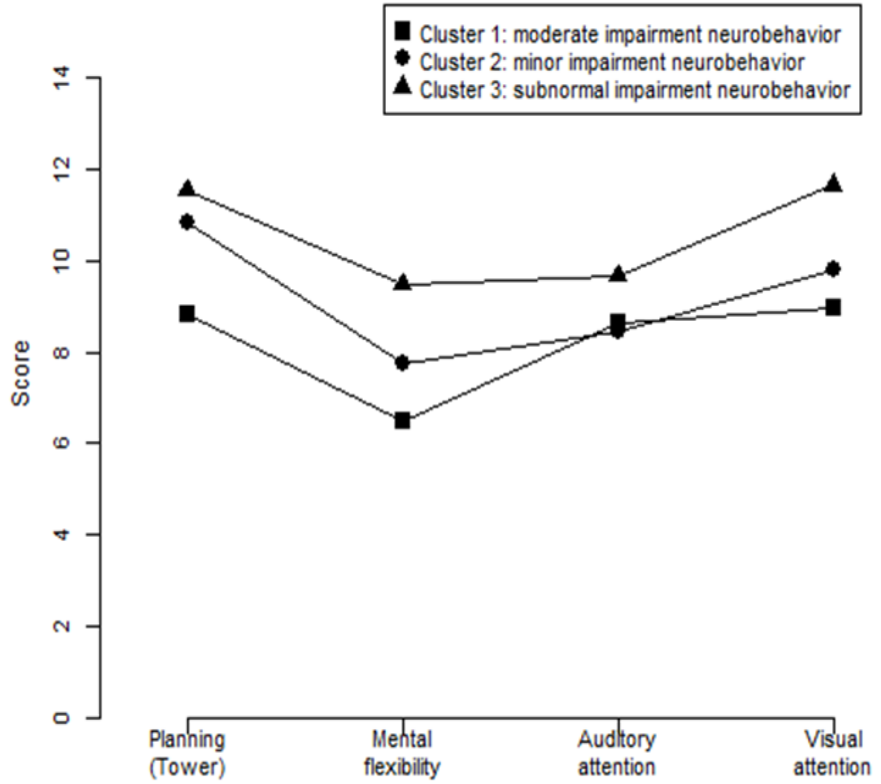
- Cluster-1 (n=46 [20%]), Moderate Impairment NeuroBehavior (ModINB)
  - multiple impairments and behavior troubles ,
  - 95% of executive disorder
- Cluster-2 (n=99 [43%]), Minor Impairment NeuroBehavior (MiINB)
  - less severe multiple impairments and behavior troubles
  - 65% of executive disorder
- Cluster-3 (n=86 [37%]), SubNormal Impairment NeuroBehavior (SNINB),
  - 31% of executive disorder
  - emotional symptoms (score: 3.5 [SDs]=2.56: [slightly below average, therefore pathological])
- Dysexecutive syndrome, behavior and anxiety were :
  - significantly different between the different clusters
  - with a gradient of severity

		Characteristics of Clustered Pooling (N=231)			
		ModINB Cluster 1 (N=46)	MilNB Cluster 2 (N=99)	SNINB Cluster 3 (N=86)	p
Perinatal characteristics					
	GA en WA, mean (SD)	26.13 (0.96)	26.25 (0.82)	26.29 (0.92)	0.607
	Weight in grams, mean (SD)	858.91 (181.77)	878.77 (194.69)	901.31 (171.47)	0.430
	Male, n (%)	20 (43.48)	50 (51.02)	38 (44.71)	0.594
	SGA, n (%)	5 (10.87)	10 (10.10)	1 (1.16)	0.011*
	Multiple pregnancies, n (%)	17 (36.96)	30 (30.30)	31 (36.05)	0.625
	Severe BPD, n (%)	25 (54.35)	46 (47.92)	47 (54.65)	0.613
	Average age of child at the study inclusion, mean (SD)	8.69 (0.65)	8.43 (0.74)	8.39 (0.72)	0.056
Parents' educational level, professional activity and socioeconomic status of family					
	Parents without higher education level, n (%)	29 (74.36)	46 (47.92)	18 (21.43)	<0.001*
	Professional activity of parents, n (%)				0.004*
	Without professional activity	8 (18.60)	7 (7.14)	3 (3.53)	
	Professional activity of one of two parents	16 (37.21)	37 (37.76)	20 (23.53)	
	Professional activity of both parents	19 (44.19)	54 (55.10)	62 (72.94)	
	Professional activity of mother, n (%)	21 (48.84)	63 (64.29)	66 (79.52)	0.002
	Professional activity of father, n (%)	33 (82.50)	82 (89.13)	78 (92.86)	0.243
	Elevated FAS Score, n (%)	21 (45.65)	57 (58.76)	57 (67.06)	0.059
Quality of life[1], mean (SD)					
	VSP-Ae global index (evaluation by the child)	64.38 (12.55)	70.30 (13.07)	70.16 (13.06)	0.029*
	VSP-Ap global index (evaluation by the parents)	64.38 (12.35)	70.66 (10.51)	71.25 (10.61)	0.008*
	Kidscreen global index (evaluation by the child)	68.43 (16.65)	73.26 (17.43)	71.91 (17.30)	0.293
	Kidscreen global index (evaluation by the parents)	62.52 (16.54)	70.16 (14.50)	71.33 (13.39)	0.003*
Neurocognitive assesment[2]					
	WISC-IV[2a], mean (SD)				
	VCI (Verbal comprehension index)	80.93 (9.46)	96.56 (11.75)	109.51 (12.74)	<0.001*
	PRI (Perceptional reasoning index)	77.26 (8.99)	85.41 (9.24)	106.73 (9.94)	<0.001*
	WMI (Working memory index)	74.93 (11.07)	88.85 (9.38)	101.15 (11.41)	<0.001*
	PSI (Processing speed index)	80.15 (8.96)	88.49 (10.75)	102.90 (12.61)	<0.001*
	NEPSY-2[2b], mean (SD)				
	Planification Score (Tower)	8.80 (3.04)	10.81 (2.33)	11.52 (2.43)	<0.001*
	Mental flexibility Score	6.50 (2.27)	7.76 (2.72)	9.48 (2.68)	<0.001*
	Auditive attention Score	8.61 (1.34)	8.45 (1.51)	9.66 (1.73)	<0.001*
	Visual attention Score	8.98 (2.73)	9.78 (3.47)	11.64 (3.03)	<0.001*
	Goodman-SDQ-parents[3], mean (SD)				
	Emotional symptoms	4.05 (2.62)	3.64 (2.37)	3.15 (2.56)	0.136
	Behavioral problems	2.52 (1.99)	1.94 (1.93)	1.64 (1.73)	0.040*
	Hyperactivity/Inattention	5.32 (2.45)	4.89 (2.56)	3.93 (2.74)	0.007*
	Relationship problems with others	2.23 (1.92)	2.17 (1.98)	1.55 (1.77)	0.051
	Prosocial behaviors	8.59 (1.59)	8.61 (1.70)	8.89 (1.42)	0.412
	Total difficulty scores	14.11 (6.39)	12.64 (6.63)	10.27 (5.78)	0.002*
	Anxiety, mean (SD)				
	Spielberg Index (STAIC)[4]	35.30 (8.28)	31.90 (7.71)	32.25 (6.89)	0.035*
Impairment[5]					
	Language delay[5a], n (%)	30 (65.22)	16 (16.16)	1 (1.16)	<0.001*
	Delay in visuospatial integration[5b], n (%)	17 (36.96)	18 (18.18)	0 (0.00)	<0.001*
	Attention deficit disorder[5c], n (%)	15 (32.61)	19 (19.19)	2 (2.33)	<0.001*
	Dysexecutive disorder[5d], n (%)	44 (95.65)	67 (67.68)	26 (30.23)	<0.001*
	Ideomotor dyspraxia[5e], n (%)	14 (30.43)	10 (10.10)	0 (0.00)	<0.001*

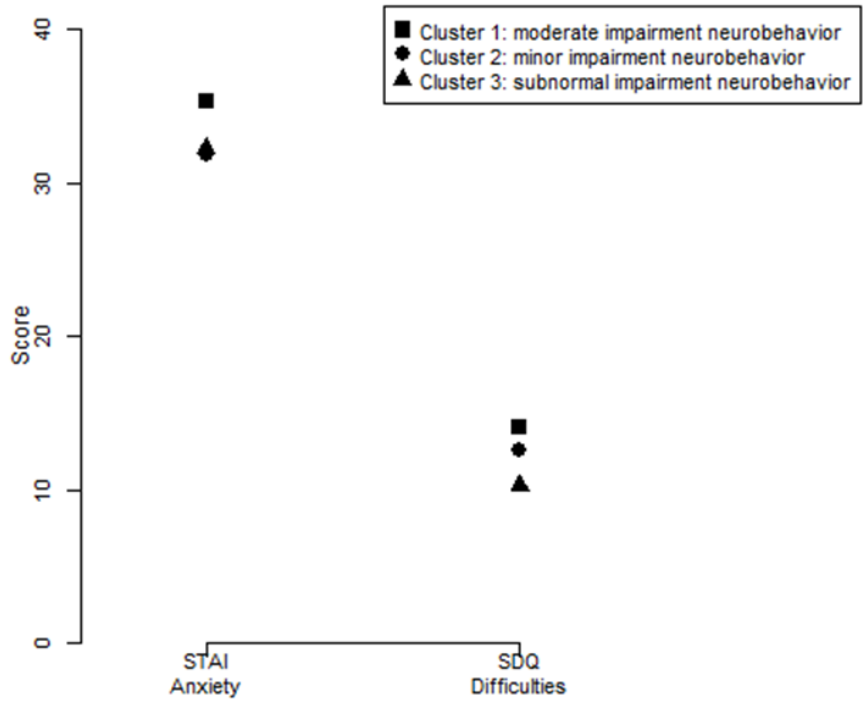
SUBTEST FISQ AND CLUSTER



EXECUTIVE FUNCTION AND CLUSTER (NEPSY)



BEHAVIOR AND CLUSTER



CORRELATION OF NBP AND QUALITY OF LIFE

- The QoL was reduced to the reference population
  - by the parents. : Except relationship with the family and with the teacher,
  - the areas impacted
    - For the children, : 1 self-esteem, 2. relationship with friends, and 3. hobbies.
    - For the parents : 1. psychological well-being, 2. school-work, and 3. general well-being (Table 2).
- Between the clusters (NBP)
  - Significant QoL difference between the clusters in self- and hetero-evaluations.
  - The areas impacted : school-work and self-esteem
- Cluster-3 (SubNoNBP) : reduction in the QoL to the reference population.
  - For the children : 1. relationships with friends, 2. leisure, 3. General well-being.
  - For parental point of view, : 1. psychological well-being, 2. general well-being, and 3. vitality.

	Quality of life between study population vs reference population								Quality of life between three clusters							Quality of life between cluster 3 vs reference population					
	Study population (n=178[a])		Reference population	Difference		*p*	Effect size[3] (ranking)		Cluster 1[c] (n=32)		Cluster 2[d] (n=79)		Cluster 3[e] (n=67)		*p*	Reference population	Difference		*p*	Effect size[3] (ranking)	
	N / mean	SD	Expected Mean	Mean	SD				Mean	SD	Mean	SD	Mean	SD		Expected Mean	Mean	SD			
VSP-A ENFANT[1]																					
Vitality	77.50	19.90	82.46	-4.95	19.96	0.001*	-0.25		77.03	20.90	77.22	19.77	78.06		0.958	82.31	-4.25	19.77	0.083	-0.22	
General well- being	72.61	17.93	78.38	-5.77	18.02	<0.001*	-0.32		68.15	17.56	74.33	17.23	72.72	18.79	0.259	78.42	-5.70	18.73	0.015*	-0.3	3
Relationship with friends	46.89	28.11	58.91	-12.02	28.17	<0.001*	-0.43	2	43.29	24.81	46.70	28.66	48.82	29.14	0.659	58.89	-10.07	29.37	0.006*	-0.34	1
Leisure	62.86	20.52	69.63	-6.77	20.57	<0.001*	-0.33	3	60.16	18.21	63.96	20.81	62.85	21.37	0.679	69.39	-6.54	21	0.013*	-0.31	2
Relationship with family	74.10	19.05	73.19	0.91	19.10	0.528	0.05		74.38	17.33	74.97	18.55	72.94	20.58	0.813	73.00	-0.06	20.77	0.981	0	
School work	76.19	23.50	82.08	-5.88	23.45	0.001*	-0.25		60.94	24.75	78.8	21.87	80.41	22.11	<0.001*	82.16	-1.75	21.98	0.518	-0.08	
Self esteem	74.20	21.33	84.61	-10.41	21.42	<0.001*	-0.49	1	63.54	22.71	74.74	21.39	78.67	19.00	0.004*	84.49	-5.82	19.25	0.016*	-0.3	
Total index	69.19	13.56	75.59	-6.40	13.65	<0.001*	-0.47		63.93	11.5	70.1	13.35	70.64	14.27	0.050	75.51	-4.87	14.31	0.007*	-0.34	
VSP-PARENTS[1]																					
Vitality	69.92	16.15	77.38	-7.46	16.26	<0.001*	-0.46		65.23	16.43	69.86	16.14	72.23	15.77	0.131	77.36	-5.13	15.66	0.009*	-0.33	3
Psychological well being	70.19	20.43	81.34	-11.15	20.50	<0.001*	-0.54	1	70.23	25.58	70.46	19.08	69.85	19.53	0.984	81.19	-11.34	19.57	<0.001*	-0.58	1
Relationship with friends	59.18	20.04	64.53	-5.36	20.15	<0.001*	-0.27		53.45	20.28	59.49	21.28	61.54	18.08	0.169	64.71	-3.17	18.43	0.163	-0.17	
Leisure	52.41	18.32	57.01	-4.60	18.30	0.001*	-0.25		50.13	17.53	54.11	19.03	51.49	17.91	0.512	57.85	-5.36	17.85	0.017*	-0.3	
Relationship with family	77.21	13.65	78.62	-1.41	13.69	0.172	-0.10		75.91	16.08	78.80	13.63	75.96	12.39	0.386	78.51	-2.55	12.32	0.095	-0.21	
Physical well being	75.78	16.18	78.60	-2.82	16.19	0.021*	-0.17		74.28	16.32	76.58	17.03	75.56	15.26	0.789	78.38	-2.82	15	0.129	-0.19	
Relationship with teacher	73.17	18.46	75.16	-1.99	18.67	0.157	-0.11		70.31	19.28	74.26	17.05	73.26	19.76	0.596	75.32	-2.06	19.78	0.398	-0.1	
School work	69.66	20.14	79.80	-10.14	20.18	<0.001*	-0.50	2	60.94	22.17	67.41	18.17	76.49	19.40	0.001*	79.92	-3.43	19.67	0.158	-0.17	
Self esteem	78.93	27.33	88.44	-9.50	27.43	<0.001*	-0.35		62.11	32.14	81.17	24.59	84.33	25.13	<0.001*	88.09	-3.76	25.71	0.236	-0.15	
General well- being	72.72	15.81	80.12	-7.41	15.89	<0.001*	-0.47	3	72.19	18.24	73.20	15.28	72.40	15.42	0.935	79.94	-7.54	15.38	<0.001*	-0.49	2
Total Index	69.61	11.17	75.96	-6.36	11.23	<0.001*	-0.57		64.73	12.38	70.24	10.59	71.19	10.75	0.021*	75.89	-4.69	10.81	0.001*	-0.43	
KIDSCREEN-ENFANT[2]																					
Total index	72.23	17.63	76.87	-4.65	17.74	0.001*	-0.26		67.39	17.7	73.82	17.26	72.66	17.89	0.213	76.78	-4.12	17.92	0.064	-0.23	
KIDSCREEN-PARENTS[2]																					

PÔLE FEMMES PARENTS ENFANTS
Assistance Publique Hôpitaux de Marseille

DISCUSSION 1: PHENOTYPE NEUROCOMPORTEMENTAL ET FE

- *Heeren* study four neurocognitive profile :
  - diffuse impairment (cognitive and executive functions) for moderate and severe profiles,
  - Dysexecutive functions **only** in : “minor profile" .
    - FSIQ was insufficient for moderate or minor cognitive impairment of the EPT
    - impact minimized executive disorders : working memory and mental flexibility,.

Heeren T *Dev Neuropsychol* 2009; **34**: 393–421, *O'Shea TM Early Hum Dev* 2009; **85**: 719–725.

Discussion 1: WMI, PSI, PRI and mental flexibility were always lowering in our different NBP

- PSI, WMI, PRI, mental flexibility and emotional behavior worsening depending on the severity of the NBP.
  - PSI and WM : independent predictors of academic difficulties amongst the very premature-birth preschool children.
  - deficit in WM, and/or attention and/or PSI, impacts other mental processes,
  - cause of later deficit such as speech delay or dysexecutive disorders.
- PSI deficit (dependent on GA) correlated to executive functions:
  - WM (verbal and visuo-spatial),
  - inhibition,
  - cognitive flexibility.
- Correlation between measurement of PSI and/or WM
  - and impulsivity/hyperactivity
  - and attention disorders.

Mulder H ,Arch Dis Child Fetal Neonatal Ed 2010, *Dev Neuropsychol* 2009; **34**: 393–421.

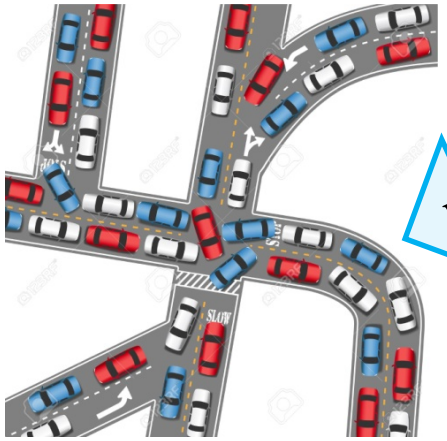
QUE SONT LES FONCTIONS EXÉCUTIVES (FE) ?

- Opérations cognitives qui permettent à l'individu d'adapter son comportement et ses activités aux exigences et fluctuations de l'environnement
- Elles entrent en jeu dès que l'individu est confronté à une situation non routinière (résolution de problèmes)
  - **Planification** ou « Comment faire ? »
  - **Flexibilité** ou « L'art de s'adapter au changement »
  - **L'inhibition** ou « L'art d'ignorer des distractions ou de résister à donner une réponse plutôt qu'une autre »
  - **Mémoire de travail** (MT) ou « L'art de faire »

LES FONCTIONS EXÉCUTIVES EN PRATIQUE…

Inhibition

Flexibilité



Planification

Mémoire de travail

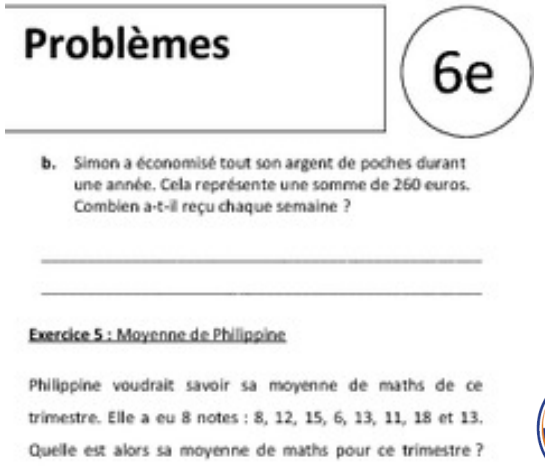
LES FONCTIONS EXÉCUTIVES EN PRATIQUE…

Inhibition

Flexibilité

Planification

Mémoire de travail



Problèmes 6e

b. Simon a économisé tout son argent de poches durant une année. Cela représente une somme de 260 euros. Combien a-t-il reçu chaque semaine ?

Exercice 5 : Moyenne de Philippine

Philippine voudrait savoir sa moyenne de maths de ce trimestre. Elle a eu 8 notes : 8, 12, 15, 6, 13, 11, 18 et 13. Quelle est alors sa moyenne de maths pour ce trimestre ?

PÔLE FEMMES PARENTS ENFANTS

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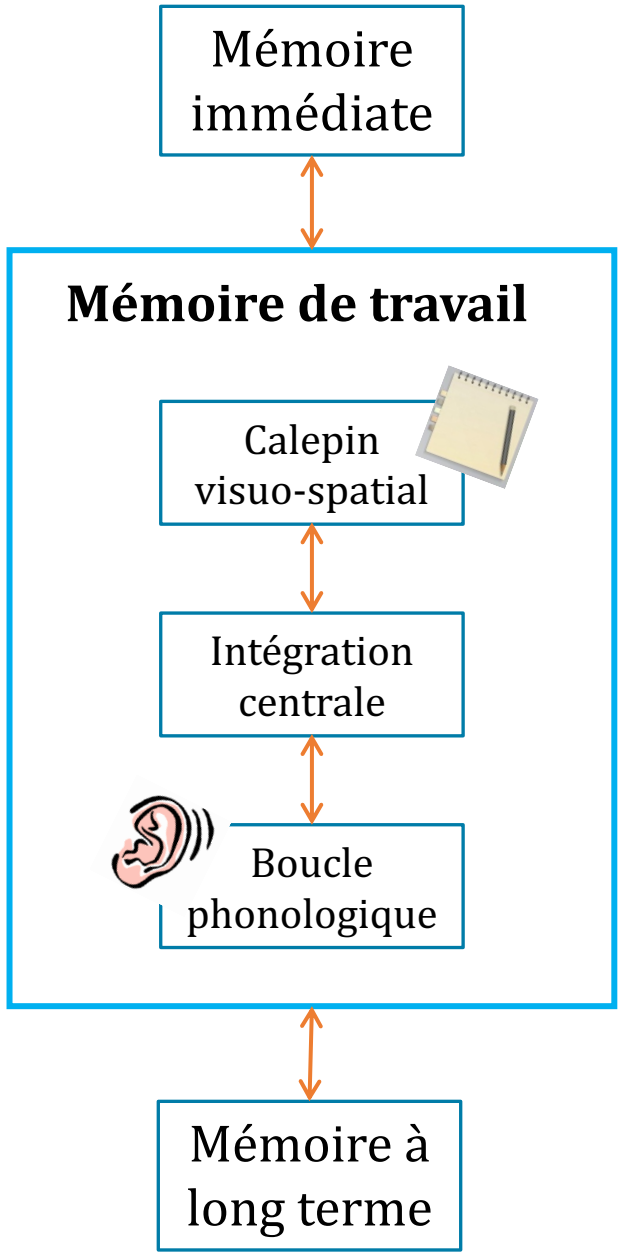

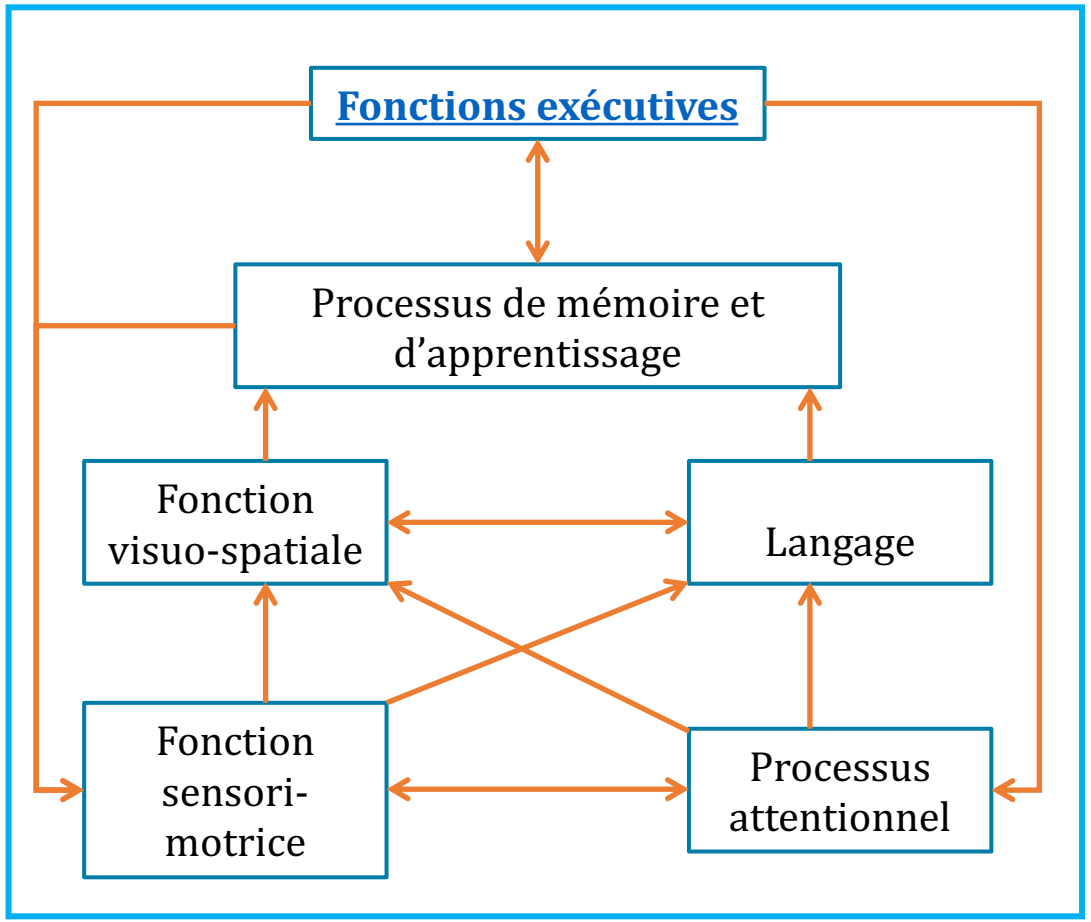

Fonctions sociales, affectives, culturelles, environnementales et socio-émotionnelles

Fonctionnement cognitif global et la réussite scolaire

Test de mesures
WPPSI , WISC
Subtest NePSY

DISCUSSION 3 : SUBNORMAL PHENOTYPE ONLY DYSEXECUTIVE AND EMOTIONAL BEHAVIORAL DISORDERS

- *Johnson* : concept of "behavioral phenotype of premature babies",
  - impact at school-age
  - attention deficit/hyperactivity disorders, social and emotional difficulties, and introversion

Pediatr Res 2011; **69**: 11R–8R , *Early Hum Dev* 2013; **89**: 199–207.

- *Gardner*[20] studied the behavioral and emotional state of VP adolescents
  - 1) from the parents' and teacher's point of view, increase in hyperactivity, relationship problems with peers and emotional disorders,
  - 2) from the point of view of the adolescent, emotional disturbances.

Pediatrics 2004; **114**: 676–682.

Discussion 4 : NBP = diffuse disorder cognitive, motor and behavioral, which influences social adaptation or QoL

- QoL three NBP reduced as compared to the reference population.
- The QoL areas most impacted;
  - for the children's perspective self-esteem, relationship with friends and hobbies,
  - for parent's perspectives psychological well-being, school-work, and general well-being, consistent with our original study.

C Gire Arch Dis Child 2019; **104**: 333–339

- The more the NBP is altered, greater QoL is decreased.
- Decrease in QoL in a "subnormal" NBP :
  - inability of the VP child to manage his/her emotions
  - and with executive dysfunction.

C Gire Pediatr Res 2020; **88**: 642–652.

Discussion (5)

- Review with instruments such as QoL, measurement of social adaptation and behavior,
  - EPTs had poor social adaptation skills early and persistent during childhood and adulthood
  - severity depending on GA, brain abnormalities and socio-economic status.

Ritchie K, *Dev Med Child Neurol* 2015; **57**: 899–918**.**

- NBP of prematurity is due to **cerebral hypo-connectivity,**

- **leading to diffuse structural anomalies similar to autism spectrum disorders**, but with a reduced severity.

Conti E *Front Hum Neurosci* 2015; **9**: 159.

LANGAGE ET PREMATURITE
EXEMPLE DE REPERAGE

- Développement du langage à deux ans est associé au neuro-développement
  - Faible stock lexical (expression)
  - Association
    - Motricité générale et fine
    - Résolution de problème
    - Performance sociale
- Rééducation possible par entrainement

Charlaluk ML. J Ped2019 ; 208 :114-20

CONCLUSIONS

- The prevalence of neurobehavioral disorders currently dominates the EPT's State at school-age.
- Socio-behavioral and emotional capacities associated with :
  - executive functions
  - and educational pathways.
- Knowing the long-term future of EPTs provides :
  - scientifically based, reliable information to parents and
  - improves care by promoting the prevention of these neuro behaviors disorders.
  - from pre-school-age, intervention strategies.
- Tools for “re-educating” executive functions could be integrated into school programs
- Diagnostic method (hypoconnectivity) : MRI, spectro…..

Taylor HG, *J Dev Behav Pediatr JDBP* 2006; **27**: 459–469.Ding S, . *Acta Paediatr Oslo Nor 1992* 2019; **108**: 1237–1244.Escovar E, . *Sci Rep* 2016; **6**: 23011.