ELENA UPDATE

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ELENA WORKSHOP

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A brief definition of Autism…

Complex

Unique

Dynamic

Autism remains a puzzle

Outcome trajectories ?

Risk and protective factors of ASD and its outcome heterogeneity with time ?

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ACAMH THE ASSOCIATION FOR CHILD AND ADOLESCENT MENTAL HEALTH

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Editorial Perspective: Longitudinal research in autism – introducing the concept of 'chronogeneity'

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"Under what circumstances some individuals deviate from their original trajectory to the point that they 'catapult' onto a new trajectory" ?

Studying risk factors

None single factors can explain autism

Rather a combination of multiple factors

An interaction of Genetic and environmental factors

See: EARLI STUDY: www.earlistudy.org

MARBLES study

Challenges in ASD epidemiology

Enhance efforts to describe the epidemiology of ASD over the life course

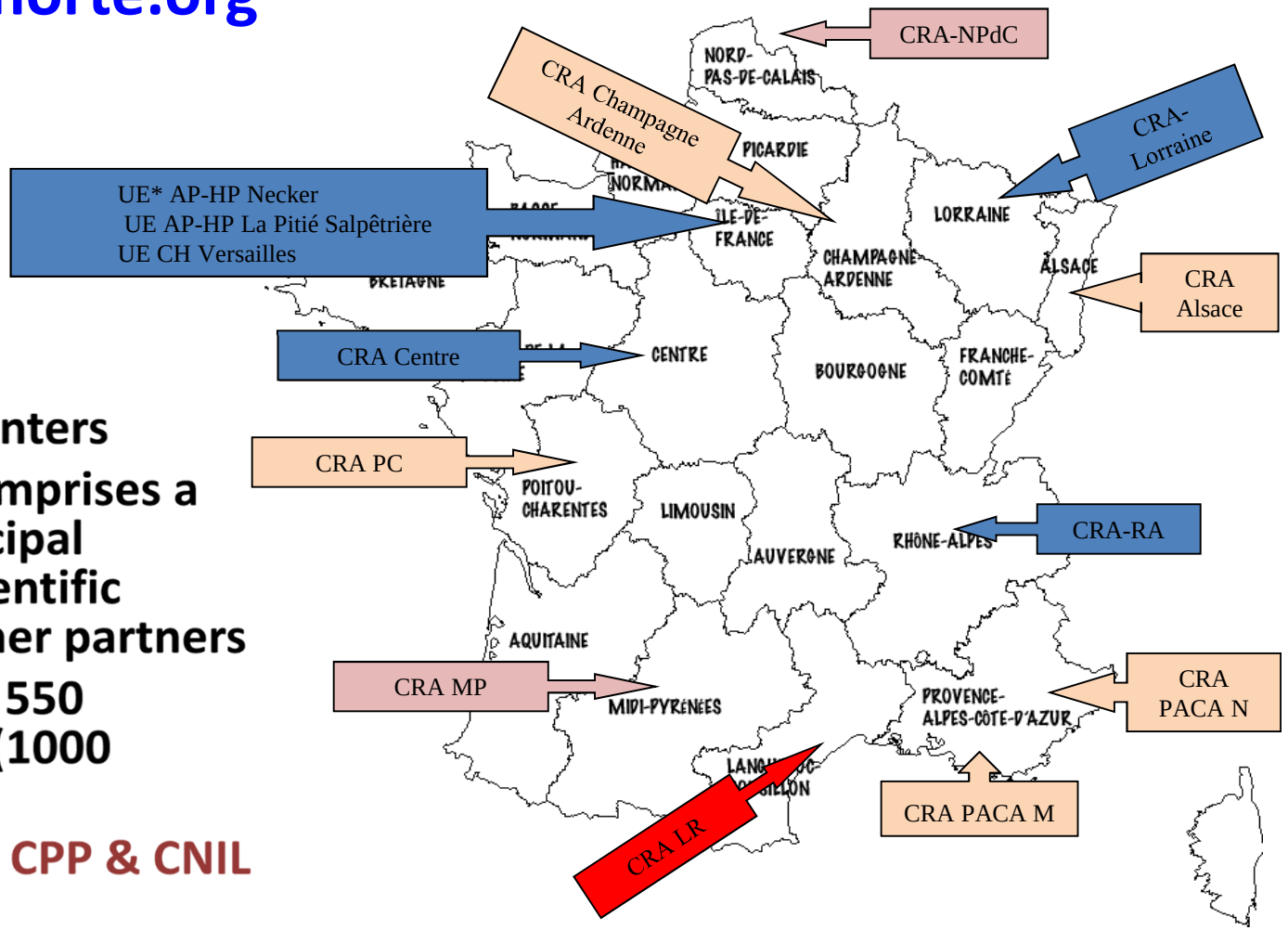
Continue investigation of potentially modifiable risk factors in the field of exposomic.

Use large epidemiologic cohorts of children, containing informative outcome data, relevant biosamples for exposomics and available genomic data

What about ELENA cohort

www.elena-cohorte.org

- **Starting in 2014**
- **A network of 17 centers**
- **The consortium comprises a committee of principal investigators, a scientific committee and other partners**
- **ELENA DATABASE : 550 children recruited (1000 expected)**
- **Study approved by CPP & CNIL**



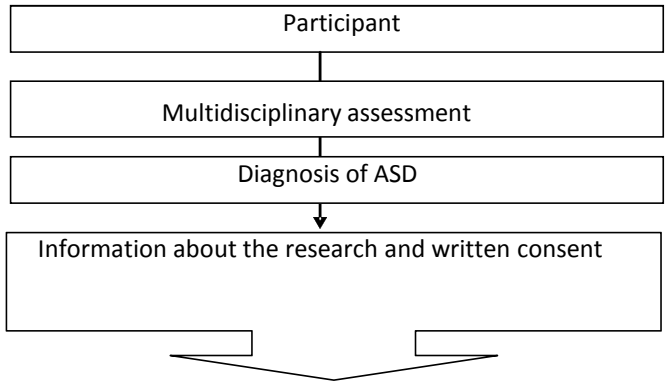
•UE: Unité d'Evaluation

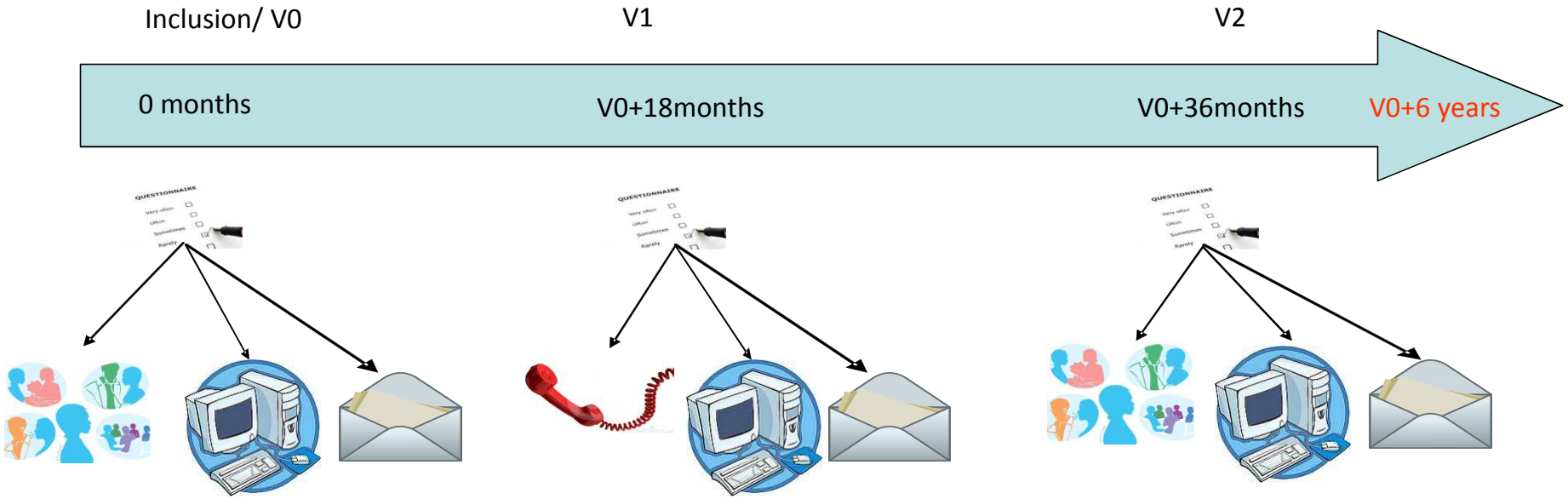
ELENA Aims

- Examine outcome trajectories in children with ASD and how, when, and why some individuals deviate from their group trajectories

- Facilitate communication among researchers studying the longitudinal course of autism and other neurodevelopmental disorders.

ELENA Follow-up schedules





Instruments

INSTRUMENTS	V0	V1	V2
From the multidisciplinary assessment			
VINELAND II	☑	☑	☑
ADI-R	☑		
ADOS1 ou ADOS 2 (Module 1,2,3,4)	☑		☑
IQ (WISC,WAIS…)	☑		☑
EVIP	☑		☑
M-ABC	☑		☑
Medical report	At least once		

Instruments (2)

Parent's Self-report	DIMENSION/ INSTRUMENTS	V0	V1	V2
About children				
	Social interaction disturbances (SRS-2)	☑	☑	☑
	Medical comorbidities	☑		
	Socio-demographic data & interventions	☑	☑	☑
	Sensory Profile	☑		☑
	Anxiety disorders (RC-MAS 2)	☑		☑
	Aberrant behaviors (ABC)	☑		☑
	Psychiatric comorbidities (CBCL)	☑		☑
	Quality of Life (Kidscreen 27)	☑		☑
	ADHD (Conners scale)	☑		☑
About Parents				
	Depression/ anxiety (HADS)	☑		☑
	Coping abilities (WCC-R)	☑		☑
	Parental stress (ISP)	☑		☑
	Parent QoL (Par-DD-QoL)	☑		☑

Cohorte ELENA

ELENA characteristics

	Mean ± Sd
Chronological age (years)	6.1 ± 3.3
Age at first psychiatric advice (months)	32.2 ± 17.9
Age at first diagnosis (months)	57.7 ± 34.0
Age of parents at birth of the child (years)	
Mother	30.8 ± 5.4
Father	33.9 ± 6.3
Vineland 2 (months)	
Communication	67.7 ± 14.4
Socialization	68.2 ± 11.3
Daily Living Skills	72.3 ± 12.7
Best estimate DQ	70.7 ± 28.0
Aberrant behaviors checklist (ABC)	
ABC1 (irritability, uncooperative)	36.1 ± 20.3
ABC2 (lethargy, withdrawal)	29.0 ± 19.5
ABC3 (stereotypy)	33.5 ± 24.6
ABC4 (hyperactivity)	45.2 ± 17.1

Characteristics at BASELINE		**N**	**%**
Chronological age	[2;5 years[	173	47.3
	[5;8 years[	108	29.5
	[8;17 years[	85	23.2
Medical comorbidities (presence)			
	Birth Defects	22	7.0
	Eyes	48	15.4
	Ears	63	20.1
	Nose/throat	35	11.2
	Neck/Back	12	3.9
	Skin	101	33.8
	Pulmonary	41	13.1
	Cardiovascular	16	5.11
	Gastrointestinal	96	32.2
	Genito-urinary	18	5.75
	Endocrine/Metabolic	24	7.8
	Allergic/immunologic	65	21.7
	Neurological	87	30.3
	Genetic syndromes	12	4.7

ELENA : What next ?

1) BIOBANK

DNA & Biomarkers of exposure and response to exposure

2) SIBLINGS

Clinical and developmental profiles

3) BABIES AT RISK OF ASD

(Babies siblings of older children with ASD)

A Biobank :
Why and what to do ?

What do we know about the genetics of autism spectrum disorder (ASD)?

- ASDs are considered genetically-influenced neuro-developmental disorders with evidence pointing to dysfunction at the level of the synapse
- There is extensive genetic heterogeneity and perhaps hundreds of genetic variants involved
- Twin studies support genetic influence BUT not genetic determination

What do we know about environmental factors in ASD ?

- No proof that diagnostic substitution and expanded diagnostic criteria fully account for the massive increase in diagnosis of autism
- A part of the increase may have environmental contributors (Hertz-Picciotto et al, 2009 Epidemiology)
- Low dose, chronic and combined exposures (such as environmental toxins) are known to have potential impact on neurodevelopment and children health

What to target in order to study genetic/environmental causes of ASD ?

- DNA abnormalities **and** biomarkers of exposure in blood, hair and urine (traffic pollutants),
- Physiological parameters (parental age, birth weight, prematurity, and pregnancy complication)
- Style life and nutritional status
- Socio-economical condition

High risk babies studies

BABI Sibs study

Why, who and how ?

Why ?

Research into early onset can get at causal factors

Early symptoms may change with time and be modified/aggravated during development

Possibility of early intervention : with the question of intervention programs for babies at highest risk or that show early signs

Who?

Infants at risk of ASD = babies siblings of older children with autism

Sibling recurrence rates of ASD: between 10 and 20% for non twin siblings vs. 1%

(30% in DZ twins; 32% in multiplex families Ozonoff 2011)

How ?

Prospective design combining precise clinical, genomic and environmental exposure measurements in large datasets

Hundreds of babies followed-up until 3 years

Few studies have reached this stage (ABC; EARLI)

Many questions to solve

- What is the temporal onset of cognitive/behavioral problems in babies who go on to develop ASD
- Do biological abnormalities precede their behavioral abnormalities and are there biological predictors ?
- Are there things we could treat very early that might reduce severity or prevent autism ?
- Are there modifiable risk factors we could prevent ?

STRATEGY PLAN

- WP for ELENA study
  - Genetic/epigenetic
  - Environment
  - Siblings
- Birth cohort of at risk children (BABI)
  - Medical, clinical and developmental follow-up
  - Biobank of DNA and biomarkers of exposures
- Proposal submission : ANR, PHRC? European project ?