From early signs to an early diagnosis in ASD

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Topics

ASD before 24 months

Recent findings in early diagnosis in ASD

Recent findings in early intervention

implications
Autism

Qualitative impairments are correlated with developmental level before 36 months.

- Social interaction
- Communication
- Unusual, repetitive behaviors and restricted interests

[Image of children in a classroom setting]
Epidemiology

1/100 for ASD
3 à 4 boys/1 girl

• A Real Major Public Health concern

International Consensus:

Neurodevelopmental disorders
Phenotypic Heterogeneity
Aetiologic Heterogeneity
**Diagnosis: rising**

By some counts, autism diagnoses have climbed steadily since the 1970s. Some research has found explanation for more than half of the rise (right).

An enlarged spectrum : ASD

*Nature, nov. 2011*
Autism Spectrum Disorder (ASD)

Social Interaction

Low IQ
Non-verbal

High QI
Verbal
Autism spectrum disorders

Unlike in typical development, predispositions to orient to, and engage with people are absent or impaired.
From Smell to Faces

The basis of social behavior

Ability to recognize a specific individual

Non-primate mammals

SMELL

Primates

monkeys & human

Eyes & VOICES
« Eye Tracking »

Pelphrey et al., 2002
15 mo-old with autism

A. Klin et al., 2008, 2013
INMED/TINS special issue

Autism, the superior temporal sulcus and social perception

PET

Zilbovicius et al, 2000
Meresse et al, 2005
Duschenay et al, 2011

aMRI

Boddaert et al, 2004
37 ASD, 22 MR, 51 controls : 14-42 months
Si 69% time of de fixation on geometric figures : 100% prediction for ASD
Why is it important to diagnose early ASD

- Mean age of autism diagnosis: 34-61 months
- Mean age of parental concern: 18-19 months
  - 30-50% report concerns before 12 months

AAP (2001): screening at 18 and 24 months

Earlier detection → Earlier diagnosis → Earlier intervention

better outcomes
Born to Change!
Cerebral plasticity—critical period

Structural organisation = functional learning

Figure 3. - Coupe histologique transversale au niveau du cortex moteur chez des nouveau-nés humains décédés à la naissance, à 15 mois et à 2 ans. On notera que le nombre des neurones reste approximativement le même, mais que la richesse des arborisations dendritiques va croissant (d’après Scholl).
Transactional model of development in ASD

Biological level

Brain

development

sX1 sx2 sx3 sX4 symptom level

social environment changes
• Learning and memory associated with multilevel brain changes

• Both dendritic development and pruning are strongly influenced by the use or disuse

• Behavioral treatments cause changes in brain structure, function and organization in brain

Keller et al, 2009; Spironelli et al, 2010
synthesis

- Brain development and skill acquisitions are influenced by both genetic and experience.
- Environmental influences can moderate the development of inherited tendencies in children.
- The early years of life are an important time for active brain development and organization.
- Provision of positive experiences in early life is more effective and less costly than corrective intervention at later ages.
Diagnostic

- Provide access to resources for parents
- Increase parenting efficacy
- Reduce negative attributions
Questions

• How early can we identify autism in babies?

• What are the earliest signs of autism?
Challenges for very early diagnosis

• Increased behavioral variability at young ages

• Overlapping symptoms with other developmental disorders

• Different patterns of symptoms in the first 18 months
Typical development

Before 6 months
- Looking at faces
- Smiling at others
- Cooing

6-12 months
- Responding to name
- Babbling
- Playing social games
- Displaying bright affect

12-18 months
- Pointing
- Using single words
- Using gestures
- Imitating
- Interest in other children
Typical signs in ASD

- Eye contact
- Response to name
- Gestures
- Showing
- Imitation
- Pretend play
- Joint attention

Repetitive behaviors
- Spinning or lining up

Stereotyped behaviors
- Flapping
- Walk on tip toes

Sensory behaviors
- visual examination
- feeling material
How to identify early signs?

retrospective method

1- family movies, but heterogeneity, not really adapted for research à la recherche, non standardised situations

2- parents interview: memory bias et forward telescoping

3- diagnostic tools (ADI-R) : Training, memory
Symptom onset: patterns

The traditional view:

• Early onset: differences in development in the first year of life

• Regression: achievement of early milestones followed by loss of skills
Prospective method: Studying children at high risk, siblings (TSA: 1-20%)

Intermediate phenotypes on a 24 months period, gradual beginning

Patterns of symptoms

Early onset and regression....

- Lack of response to name
- No good eye contact
- No Joint attention
- No emotional behaviors sharing
- No imitation

between 12 et 24 months :

most strongest pattern of « early onset »

Sib baby approach

• *AOSI Autism Observation Scale For Infants*
  ◊ Visual tracking
  ◊ Eye contact
  ◊ attentional disengagement
  coordination of eye gaze and action
  ◊ imitation
  affective response
  ◊ Social communicative behaviors
  ◊ sensory motor behaviors
  ◊ Orienting to name
  ◊ social smiling
  ◊ Behavioral reactivity
  ◊ social interest

No differences at 6 months but 12
12 months

Earliest age where clinical differences can be reliably detected in some ASD cases
Regression

- Average onset: 19-21 months
- Gradual course
- Both loss of acquired skills (language, social and onset of stereotypies and other symptoms of ASD)

New vision

- Autism emerge over time
- Signs of autism are not present at birth in many children
- Loosing skills is much more common than previously thought
- Regression often subtle, gradual and difficult to observe in real time and capture via parent report

Gradual deceleration and disengagement in early profil

Ozonof et al., 2010
Screening tools

Modified Checklist for Autism in Toddlers M-CHAT
18-24 months

Robins et al, 2001

- Short Questionnary for parents (23 items)
- Sensibility 85%
- Specificity 65%
- Easy to use
2- does your child take an interest in other children

7- does your child ever use his/her finger to point to indicate interest in something

9- does your child ever bring objects over to you to show you something

13- does your child imitate you (if you make a face)

14- does your child respond to his/her name when you call

15- If a point at a toy across the room, does your child look at it
Positive screening: 3/23 or 2/6 critical items

Interview with the parents, if concerns:

Diagnostic center

www.firstsigns.org/downloads/m-chat.pdf
Infant toddler checklist of CSBSDP (Wetherby et al, 2001)

Useful for children less than 18 months with concerns with

- social and communication deficits
- Risk factors (sibling/family members with ASD)

Sensitivity 0.78

Spécificity 0.84

www.brookespublishing.com downloadable
The One-Year Well-Baby Check-Up Approach: general population

The Communication and Symbolic Behavior Scales Developmental Profile Infant-Toddler Checklist

- At 12 months, children seen again at 36 months…
- Pediatricians
- Good positive predictive value: 0.75
- 24 items, 3 domains: social communication and emotions, langage (expressive et receptive), symbolic symbolic behaviors
- Duration: 5 mn
- Rating: 2 mn

Questions remaining....

Reliability and Stability of the diagnosis
Under 24 months

Why some kids improve spontaneously?
Early Start Denver Model (ESDM)

- développemental and behavioral treatment
- Parents training
- 20 à 25h /week, with the child and parents (at home)
- Duration : almost 2 years
- Children under 4

Improvement in language, socialisation, cognitive functions

(Vismara et al, 2008; Dawson et al, 2010)
Dawson et al, 2010

mullen scales

VABS

Standard score

ESDM
A/M

Baseline  Time 1  Time 2

Baseline  Time 1  Time 2

Dawson et al, 2010
What to do….

• Infant with risk signs should be offered interventions for symptoms and not wait for definitive diagnosis

• Development of treatment is an urgent priority

• Continued search for markers that identify risk before the onset of behavioral signs

• Screening for autism needs to be done on multiple times in first years to be sure that we pick up children that might have developed latter signs
Road blocks

- Limited knowledge of early signs
- Limited use of formal ASD screening tools
- Long wait for diagnostic evaluation
- Limitated availability of ASD specialized services and providers
Looking for biomarkers

Interventional methods and measures of change
Early Diagnostic Biomarker

• Longitudinal studies with very young children
• Sib studies
Eye-tracking/EEG
Change biomarker?

Eye tracking:
- semi naturalistic situations
- visual preference
- joint attention
multimodal MRI

1) Clinical MRI
2) Anatomical MRI
3) DTI
4) fMRI
5) ASL - CBF
Changing developmental trajectories

« Non – Social » Expertise

social

Expertise

April 1926

1 2 3
4 5 6 7 8 9 10
11 12 13 14 15 16 17
18 19 20 21 22 23 24
25 26 27 28 29 30