I.Mottron, UdM

Symposium Elena
Montpellier 14-15 septembre 2017

Back to prototypes: strategies for a longitudinal cohort

what exactly are we studying when we combine heterogeneous individuals into one "ASD" group, and what might we be *failing* to study by not going deeper into the most frank cases?

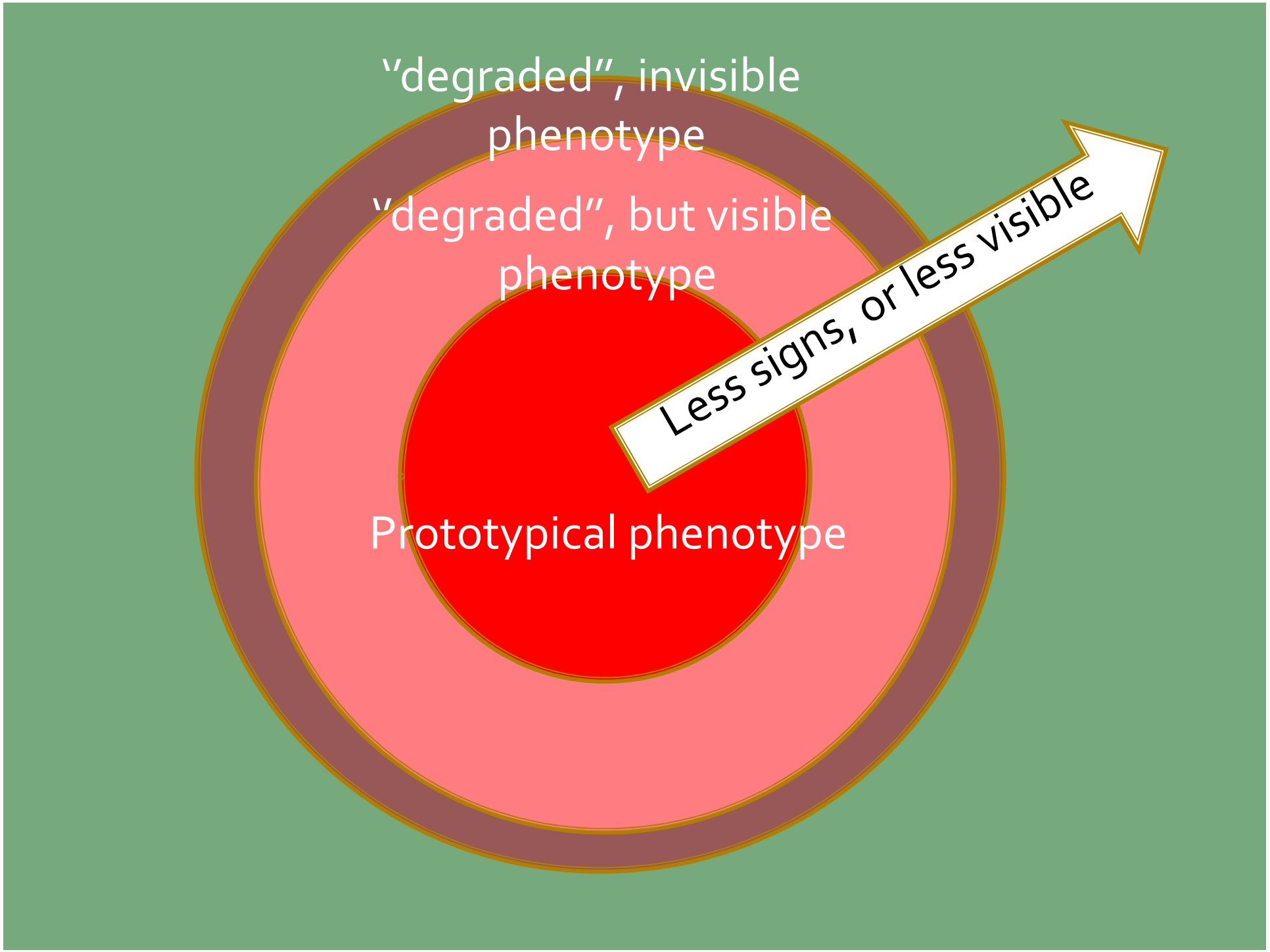
RESEARCH ARTICLE

"Frank" Presentations as a Novel Research Construct and Element of Diagnostic Decision-Making in Autism Spectrum Disorder

Ashley de Marchena and Judith Miller

Consensual, but possibly wrong

- Heterogenity / spectrum is superior to "old" categorical approach
- Spectrum is a good model for autism (eg. rainbow colors/ continuous wavelength)
- Prevalence increases constantly,because autism is "better diagnosed"
- Animal models are informative an prototypical autism
- Prevalence of intellectual disability and epilepsy is increased in autism and reaches 25% of identified cases


"degraded", invisible phenotype
"degraded", but visible phenotype
Prototypical phenotype
Less signs, or less visible

Predictive identification error in presence of a degraded phenotype

- The Mooney figure effect

Figure 1: Mooney or two-tone image (left) and its grayscale source image or "template" (right).

- The more degraded a phenotype is, the more the predictive error due to the prototype distorts what is actually seen, or conflict with others prototypes

- In case acertainent for a cohort, it is a problem, because standardised instruments and criteria are larger than the prototype

noise / signal ratio:
spectrum autism,
Heterogenous phenotypes

Estimated prevalence

"Descending" threshold
for detecting a category

Overinclusive
zone

"true" threshold

Missed degraded
phenotypes

"Ascending" threshold
for detecting a category

Low noise / signal ratio:
prototypical autism
Highly similar phenotypes

Spectrum vs. Prototypical approaches

Spectrum

- Epidemiologicaly oriented
- Psychiatry
- Dimensional
- Large Ns
- Diagnostic Cut-offs would be arbitrary or consensual
- Following blindly current, explicit criteria in diagnosis
- Phenotypically heterogeneous
- High sensitivity, low specificity

- **And trendy**!

Prototypical

- Etiologically oriented
- Neuroscience
- Categorical
- Small Ns
- Diagnostic Cut-offs would reflect a ''natural'' category
- Adding expertise to current criteria (''franck'' autism)
- Phenotypically homogeneous
- High specificity, low sensitivity

- **Old fashioned?**

two types of heterogeneity within DSM-5 autism:

Non-syndromic autism

- High IQ
- No recognizable syndrome
- No epilepsy, macrocephaly
- High sex ratio
- No LDDNM
- Highly similar, but they may be several prototypes

- Plausibly informative on prototypical autism

Syndromic autism

- Low IQ
- Recognizable SyndromeS with identified mutations
- Epilepsy, no macrocephaly
- Low sex ratio
- LDDNM
- Highly dissimilar but may reflext a superficial similarity accoss phenotypes

- Unplausibly informative on prototypical autism

What is the optimal variability to recommand in a cohort?

- If you study a beetle from exacly similar individuals, you may get just males: you will learn how they feed, but not how they breed.
- If you tolerate a certain variation and get male and female individuals, you will learn how the feed and how they breed: **optimal variability**
- If you tolerate a large variation and get one of each type of beetles, you are at risk to miss both their feeding and breeding habits

What can be learnt form protypicality?

- Narrows theoretical constraints on etiological models for autism (eg: does epilepsy, fr. X, and intellectual deficiency should be included in etiological models?)
- Increases constraints on animal models
- Inform on protypical developmental history of autism

What can be lost in a protypicality approach?

- One or several prototypes? The "similarity detection" approach should be iterative and not limited to Kanner's autism
- The women issue: presentation of our cohort

Cohorte de Femmes adultes francophones se reconnaissant sur le spectre de l'autisme au 09/09/2017

- N = 285, Age moyen: 39,6 ans
- Français(e)s : 193 – Canadien(ne)s : 64
  - 107 avec un diagnostic « spectre de l'autisme »; 109 non diagnostiquées; 64 indiquant des démarches en cours
- Age moyen du diagnostic: 35,7 ans

My suggestion for a cohort

- Instead of increasing "spectrum Ns", select 3 protoypical cohorts:

- Prototypical autism
- Protoypical Male Asperger people
- Prototypical self diagnosed autistic Females

research questions adressed using a stratified, prototypical approach: revisiting DSM 5 clinical specifyers

Autism-epilepsy relations

Autism-epilepsy relations

- Context: epilepsy is still a constraint on neurobiological models of autism
- Hypothesis: Epilepsy is associated to syndromic autism only
- Research target: is epilepsy a factor dissociating syndromic from primary autism?
- Impact: inform on delineation between prototypical and syndromic autism

1994 to 2004 papers obtained through Medline database using 'autism' + 'epilepsy' entry (n=230)

- ***Exclusion criteria:*** 'reviews' (n=74), irrelevant (e.g.: therapeutic; n=84)
- ***Inclusion criteria:*** (N= 71) New studies including participants with autism + epilepsy, with or without another clinical entity

Autism and epilepsy comorbid with:	Number of articles
Cerebral lesions	8
Biochemical anomaly	21
Rare genetic syndrome	29
Chromosomal anomaly	8
Autism and epilepsy without other anomaly	8
TOTAL	71

Our incidence data

Epilepsy in a population of 220 PDD with an IQ above 50 (AD: 92; AS: 75; PDDNOS: 58): **12 / 220) =** 5.4 %

- in PDD, IQ above 70: 10/ 188 = 5.31 %
- in PDD, IQ above 85: 5/149 = 3.33 %

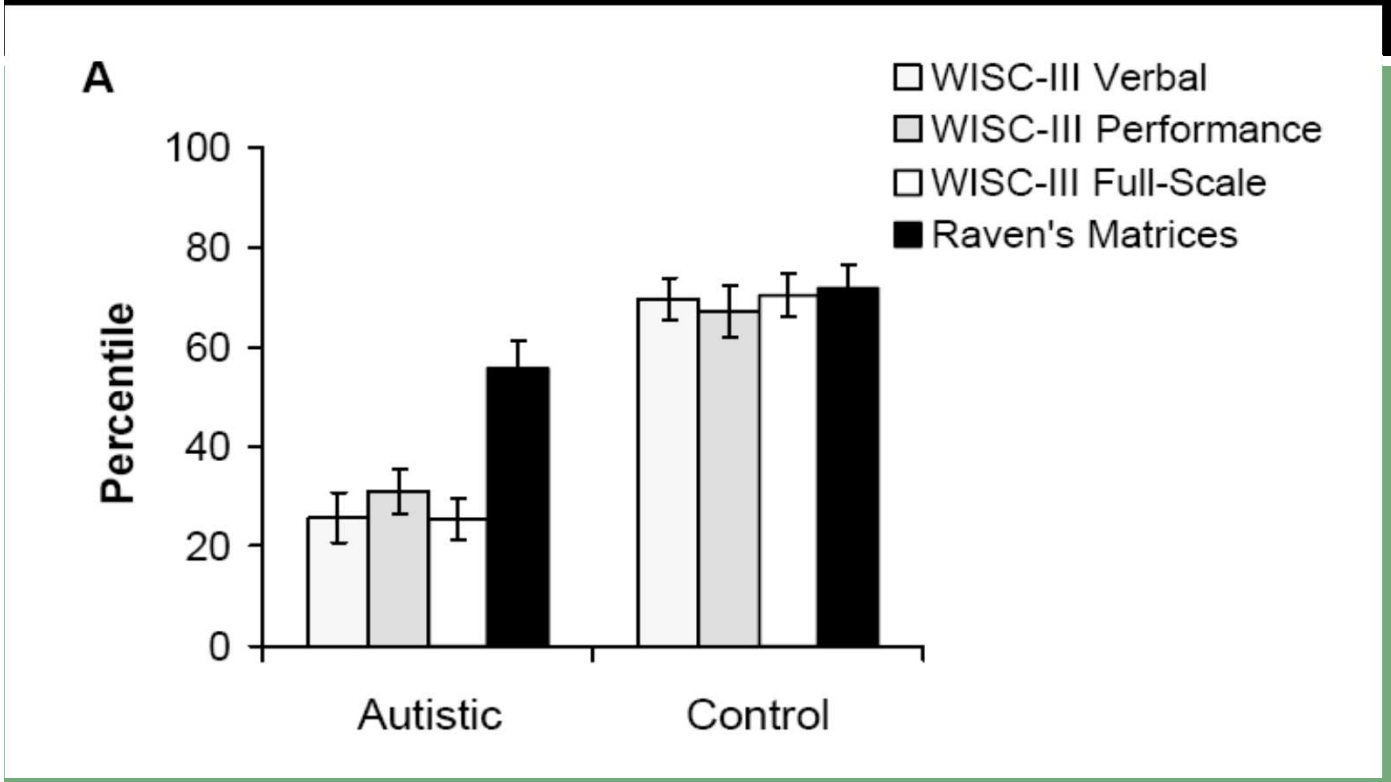
Etiology of epilepsy in a sample of 220 persons with PDD

- Cerebral lesion: 8/12
- Rare genetic disease: 1/12

- Essential 3/12 (1.3 %) (PDD-NOS: 2, Asperger. 1)

Autism-intelligence relations

Niveau Raven vs Niveau Wechsler



38 enfants autistes,
24 enfants typiques

PSYCHOLOGICAL SCIENCE

Research Report

The Level and Nature of Autistic Intelligence

Michelle Dawson,[1] Isabelle Soulières,[1,2] Morton Ann Gernsbacher,[3] and Laurent Mottron[1,2]

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OPEN ACCESS Freely available online

PLoS one

The Level and Nature of Autistic Intelligence II: What about Asperger Syndrome?

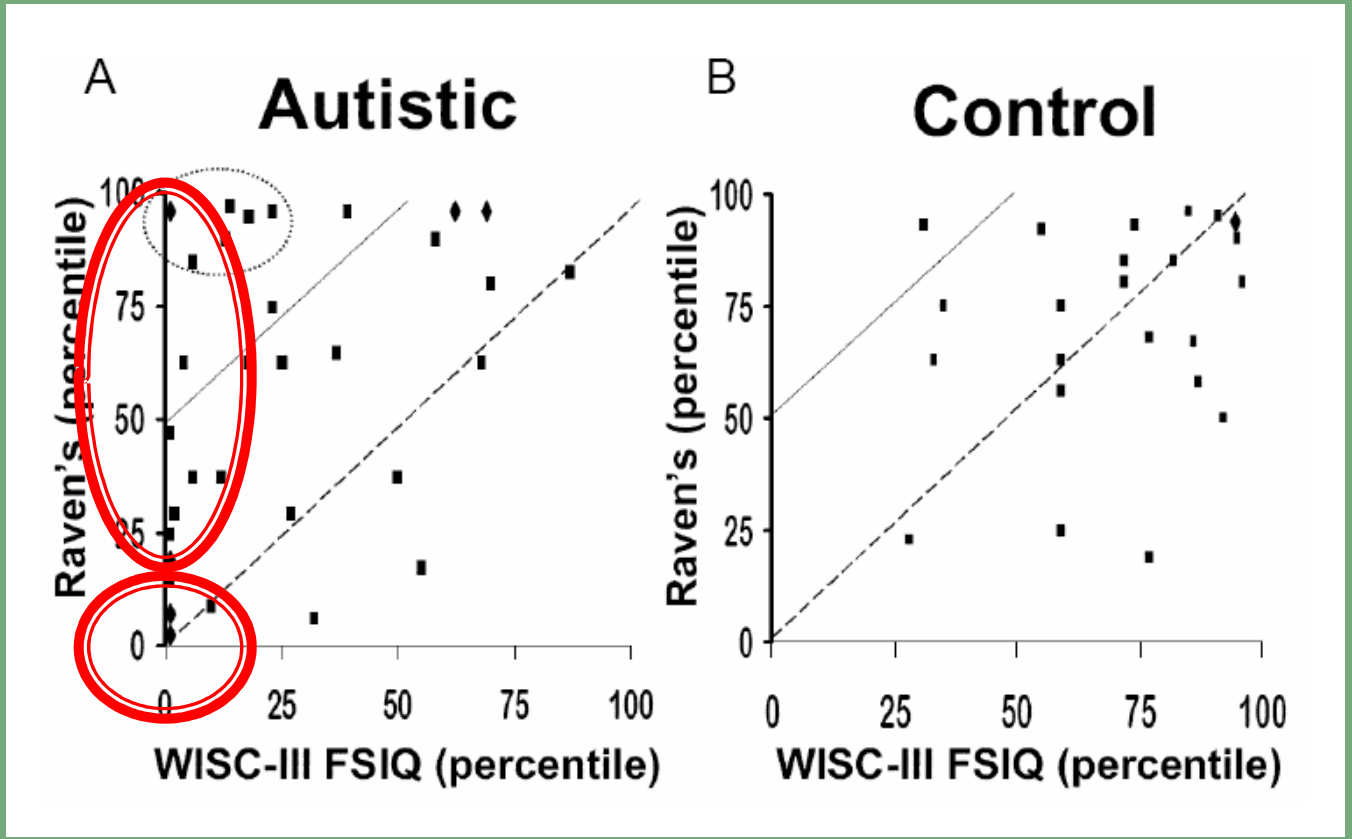
Isabelle Soulières[1,2]*, Michelle Dawson[1], Morton Ann Gernsbacher[3], Laurent Mottron[1]

1 Centre d'Excellence en Troubles Envahissants du Développement de l'Université de Montréal (CETEDUM), Montréal, Québec, Canada, **2** Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, United States of America, **3** Department of Psychology, University of Wisconsin-Madison, Madison, Wisconsin, United States of America

Vraie et fausse DI

Fausse DI

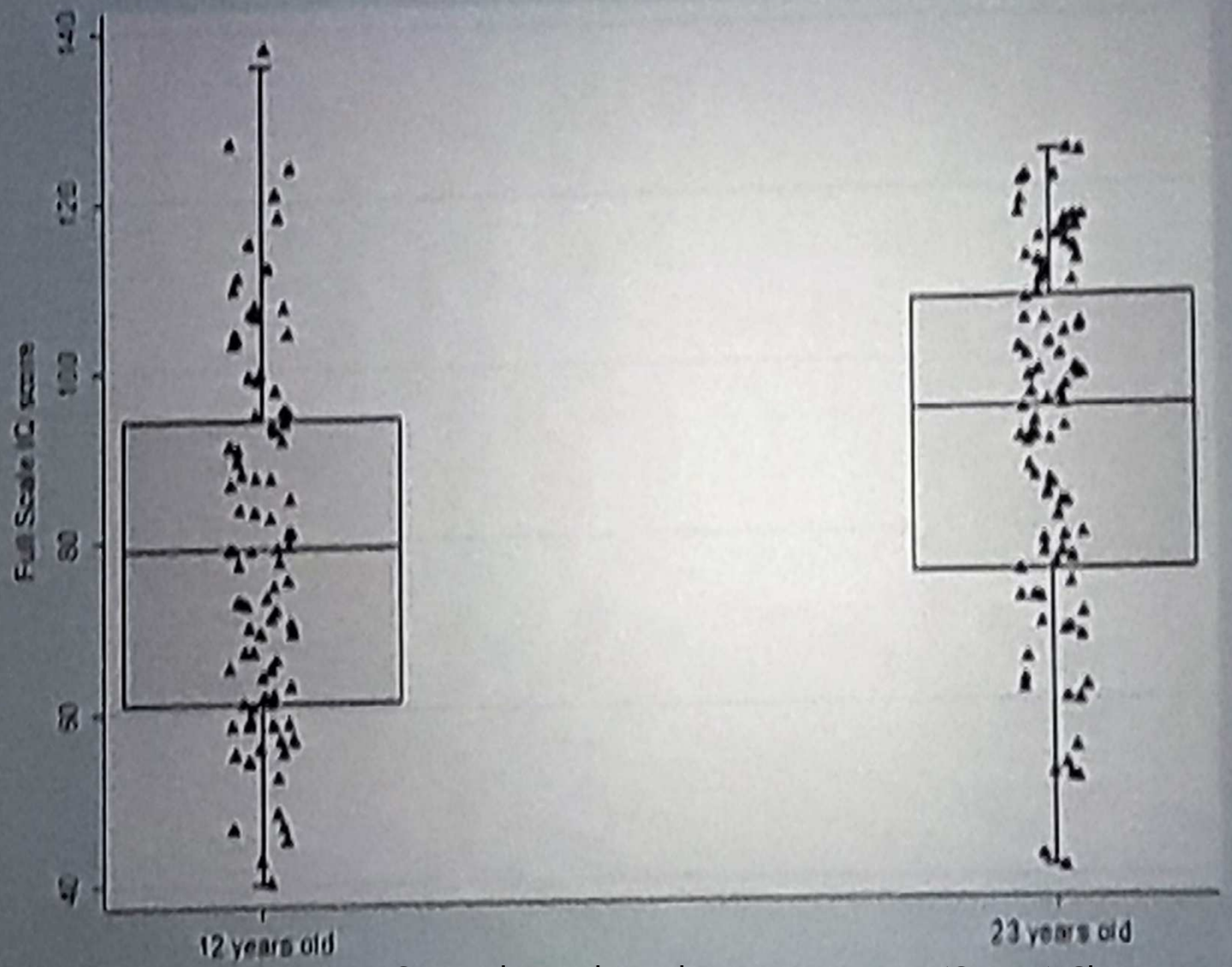
Vraie DI



Is there a trend for increasing IQ w. age, or only verbal one?

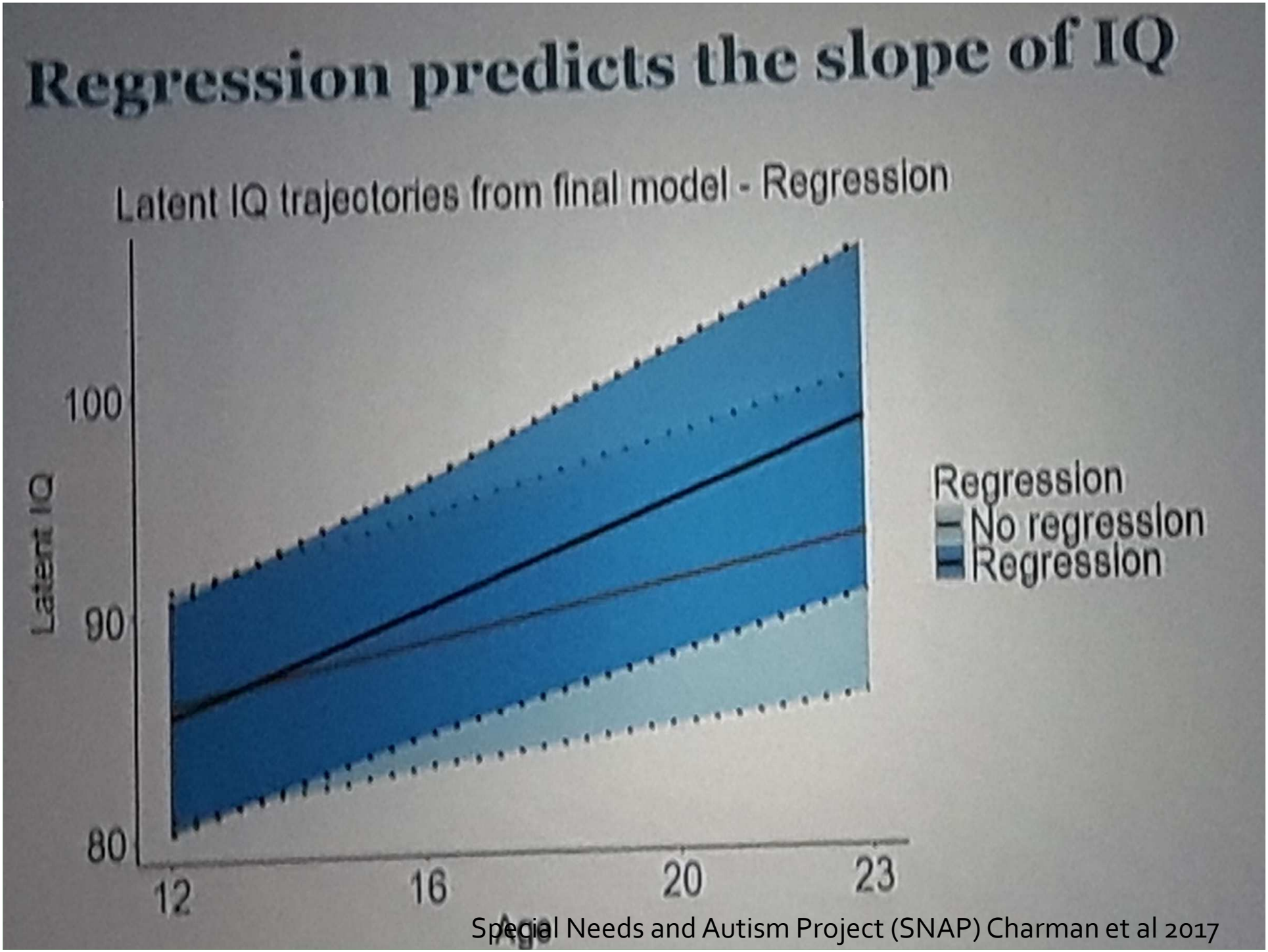
- Context: Discrepancy between RPM and Wechsler
- Hypothesis : increased compliance to testing and increased exposition to complex materials w. age will result in increased measured intelligence, even non verbal
- Research target: specify the level and nature of autistic intelligence in prototypical and syndromic autism
- Impact: inform on delineation between prototypical and syndromic autism, and influence intervention programs.

Full scale IQ – 2 timepoints (n = 93)



Special Needs and Autism Project (SNAP) Charman et al 2017

Regression predicts the slope of IQ

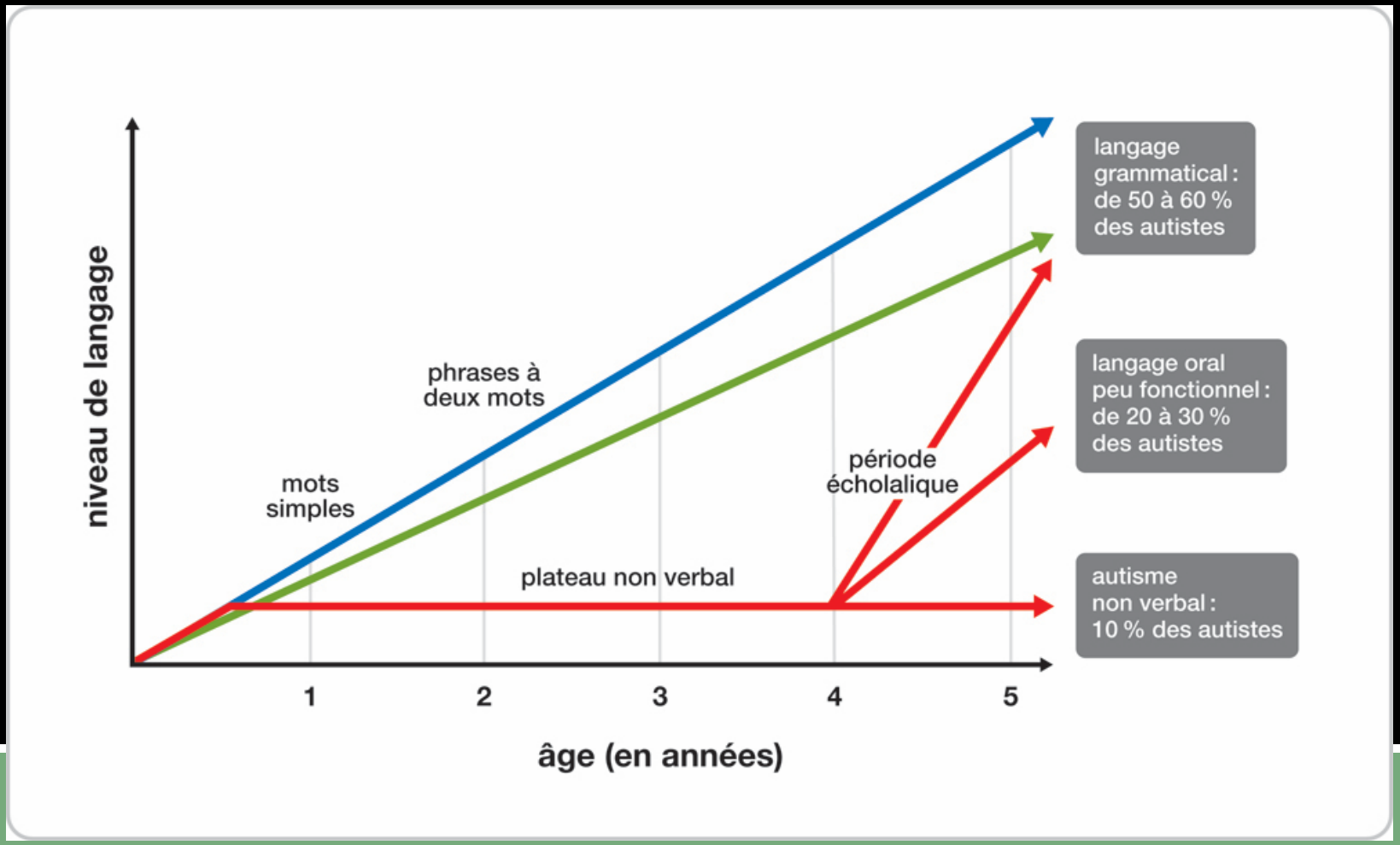


Special Needs and Autism Project (SNAP) Charman et al 2017

Autism-language relations

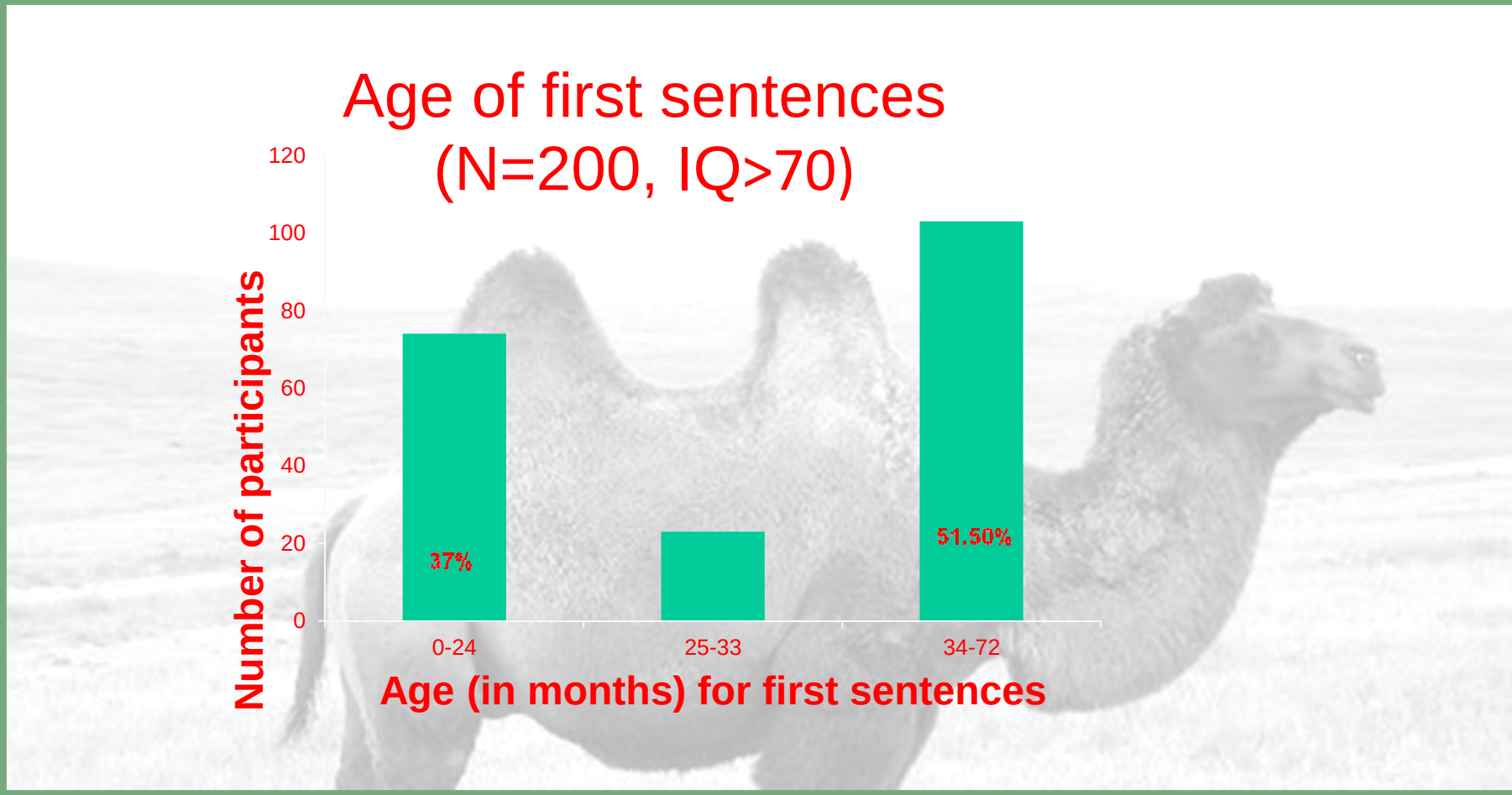
The bayonette-shaped speech development in prototypical autism

- Context: uncertainties on the specificity of speech learning curve in SLI vs. Autism
- Hypothesis : absence of speech, followed by Prizant sequence, caracterizes prototypical autism
- Research target: add a specified speech developmental profile to known signs of prototypical autism
- Impact: Characterize speech prognoses in prototypical situations, and influence interventions


niveau de langage
phrases à deux mots
mots simples
période écholalique
plateau non verbal
langage grammatical : de 50 à 60 % des autistes
langage oral peu fonctionnel : de 20 à 30 % des autistes
autisme non verbal : 10 % des autistes
1
2
3
4
5
âge (en années)

Autism- Asperger relations

Bimodal distribution of speech onset (two-words sentences)



Within non-syndromic autism: Two distinct (?) profiles

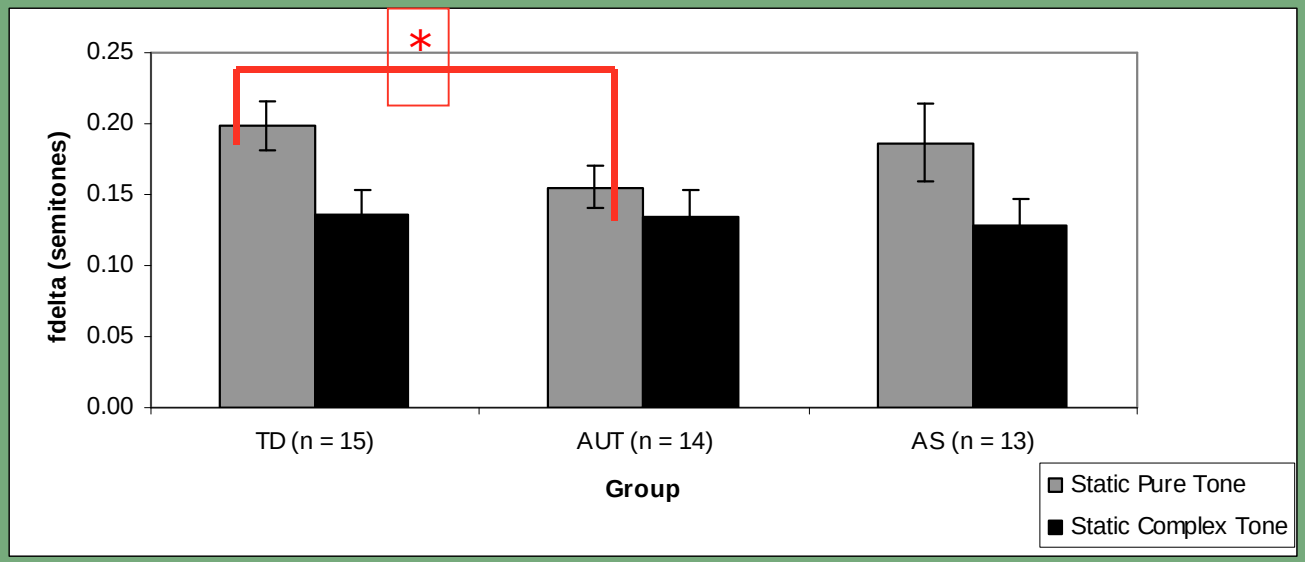
Autism = AS-SOD

- Speech Onset Delay (SOD)
- Strength in non verbal reasoning (Raven)
- Perceptively defined interests
- Hyperlexia

Asperger = AS-NoSOD

- Early speech
- Strength in verbal reasoning (similitude)
- Thematically defined interests
- Early reading

Superior pitch perception in AS-SOD only



Contents lists available at ScienceDirect

Neuropsychologia

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

Enhanced pure-tone pitch discrimination among persons with autism but not Asperger syndrome

Anna Bonnel[a,b,c], Stephen McAdams[d], Bennett Smith[d], Claude Berthiaume[c], Armando Bertone[a,b,c], Valter Ciocca[e], Jacob A. Burack[a,b,c], Laurent Mottron[b,c,*]

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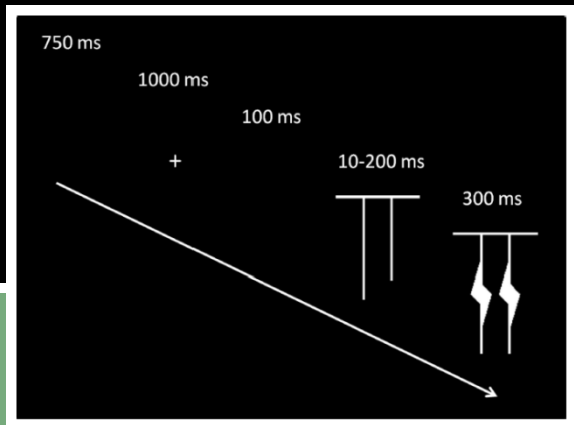
Neuropsychologia

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

Auditory discrimination and auditory sensory behaviours in autism spectrum disorders

Catherine R.G. Jones[a], Francesca Happé[b], Gillian Baird[c], Emily Simonoff[d], Anita J.S. Marsden[e], Jenifer Tregay[e], Rebecca J. Phillips[e], Usha Goswami[f], Jennifer M. Thomson[f], Tony Charman[a,*]



Journal of Abnormal Psychology

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The Level and Nature of Autistic Intelligence III: Inspection Time

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Superior visual inspection in AS-SOD only

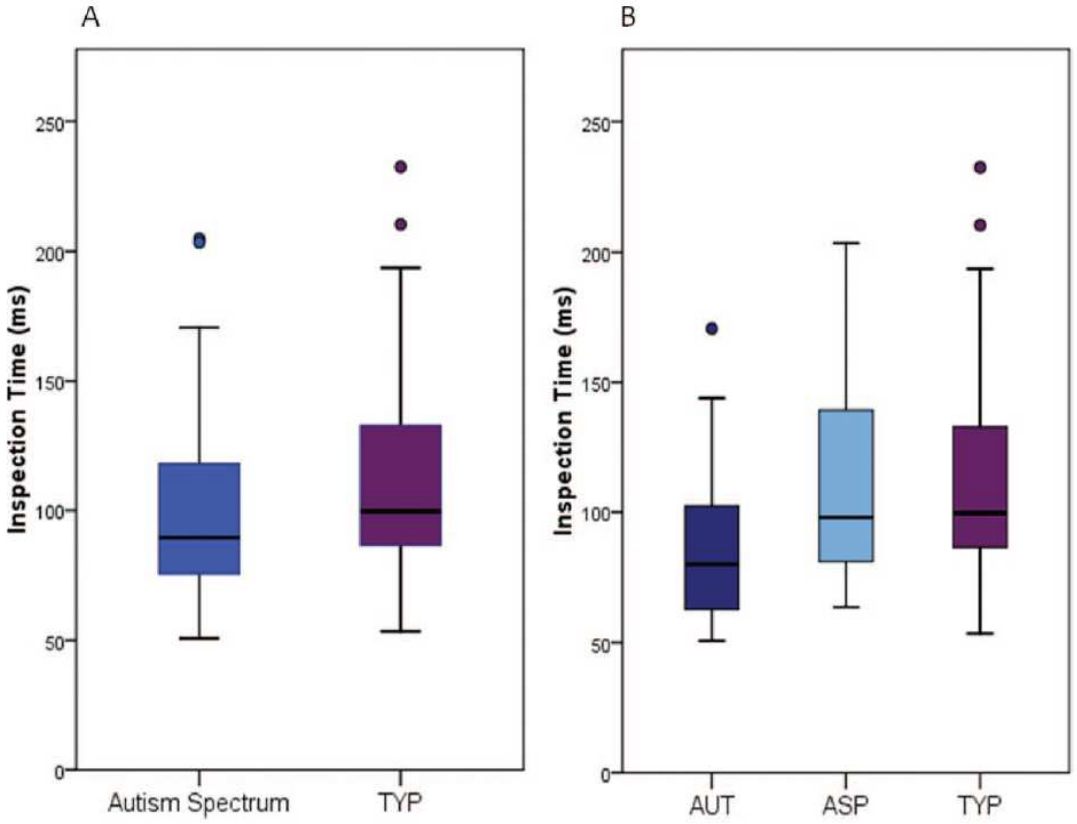
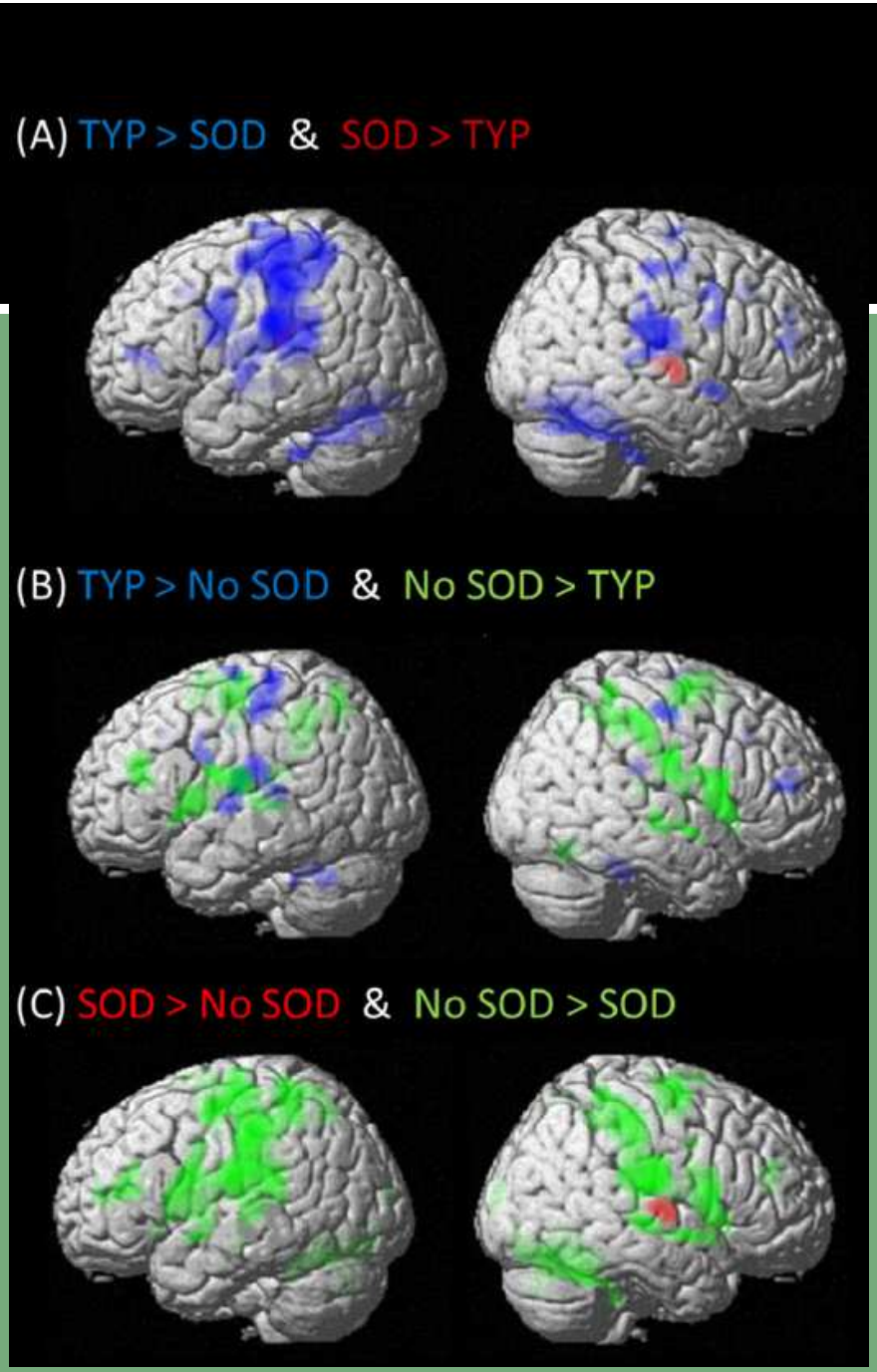


Figure 2. Inspection time distribution for (A) autism spectrum (n = 42) and typical (n = 30) groups; (B) autistic (n = 18), Asperger (n = 17) and typical (n = 30) groups. Error bars represent 1.5 standard deviation.



Cortical reallocations may account for autistic heterogeneity

Journal of Psychiatric Research 68 (2015) 285–292

Contents lists available at ScienceDirect

Journal of Psychiatric Research

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

Speech acquisition predicts regions of enhanced cortical response to auditory stimulation in autism spectrum individuals

F. Samson [a, b, *], T.A. Zeffiro [c], J. Doyon [d, e], H. Benali [e], L. Mottron [b]

If we target new findings, our research questions and methodology should differ from what is done elsewhwere