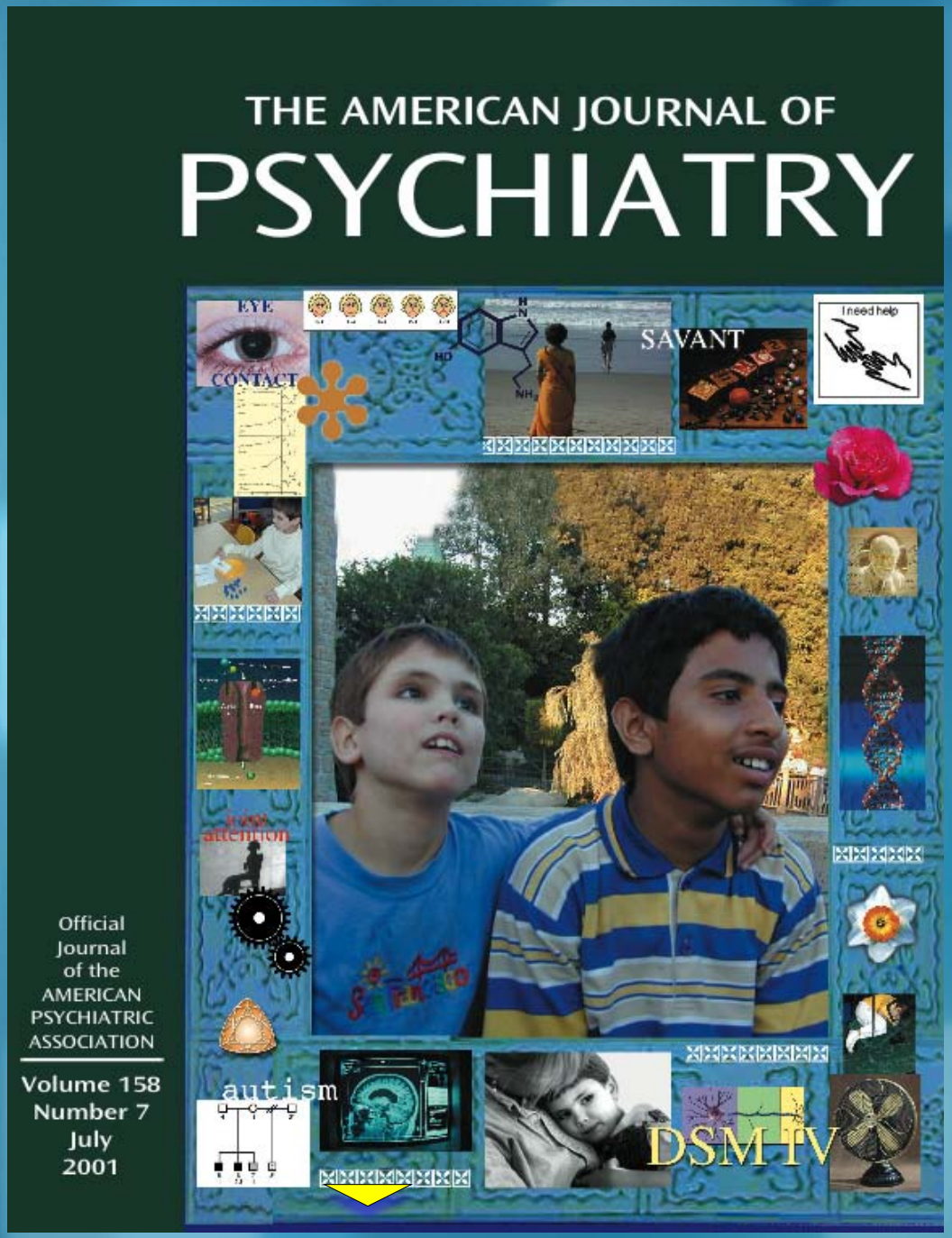
The Forgotten Half of Autism:

Nonverbal and Low-Communicating Individuals with Autism

Portia Iversen
July 9, 2013

For the Interagency Autism Coordinating Committee, NIMH



Timeline 1995:
The Cure Autism Now Foundation is established to promote and fund autism research.

1997

Cure Autism Now establishes the Autism Genetic Resource Exchange (AGRE)

2000

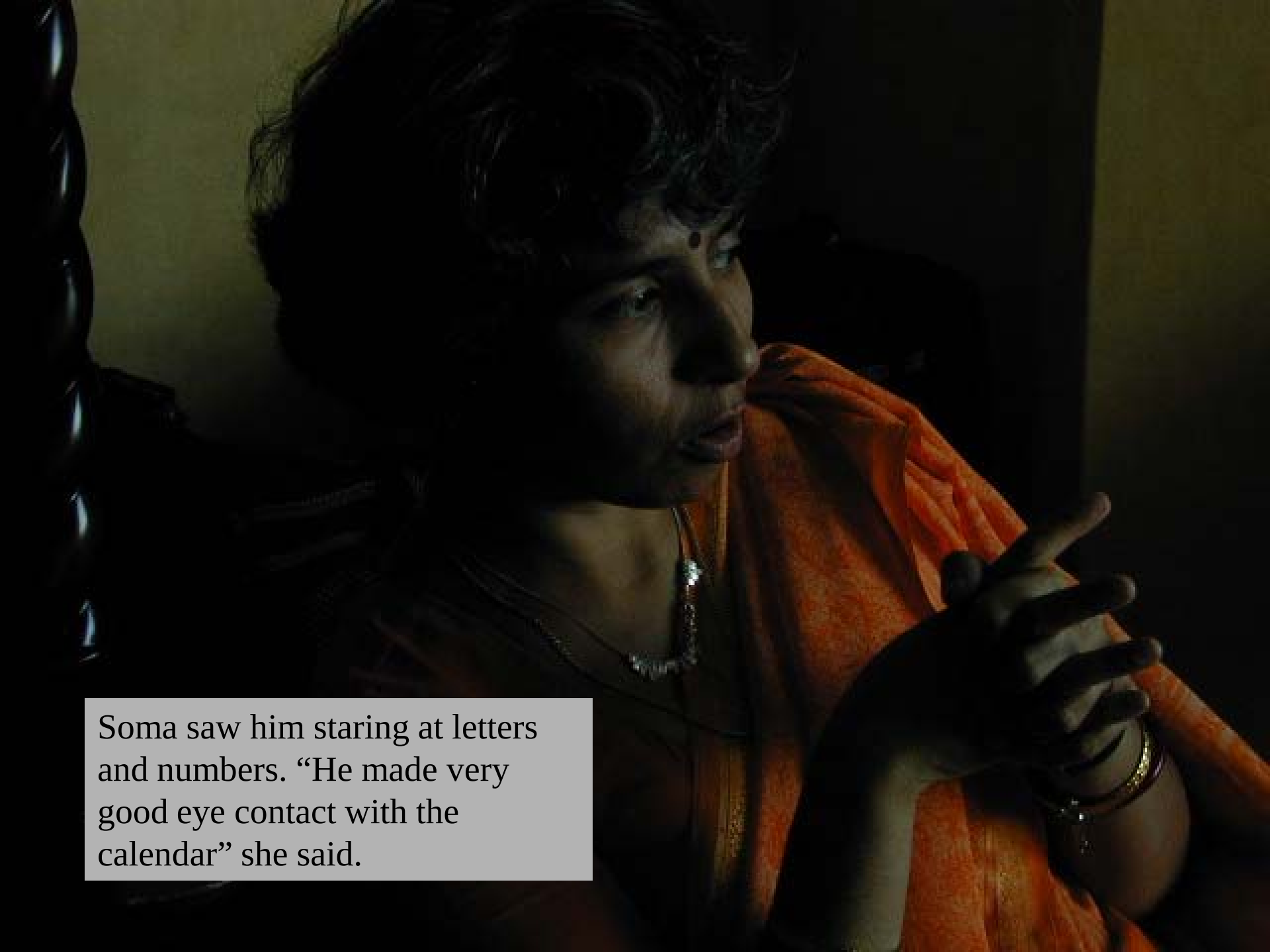
Cure Autism Now establishes the International Meeting For Autism Research (IMFAR)

2000

Cure Autism Now establishes the Innovative Technology for Autism (ITA) initiative

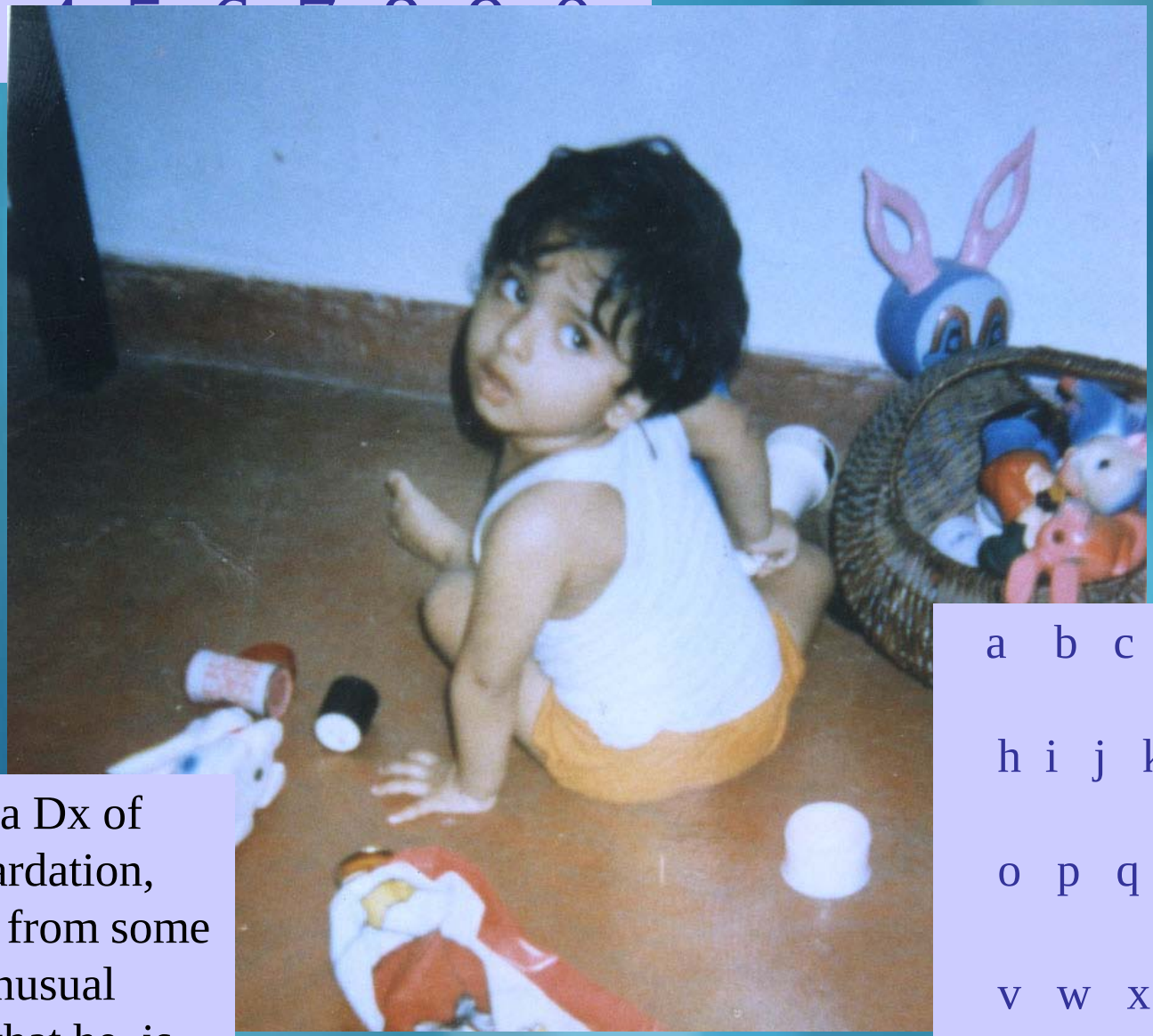
VIDEO:
Dov 4 mo. – 13 yrs

2001



Soma saw him staring at letters and numbers. “He made very good eye contact with the calendar” she said.

1 2 3



a b c d e f g

h i j k l m n

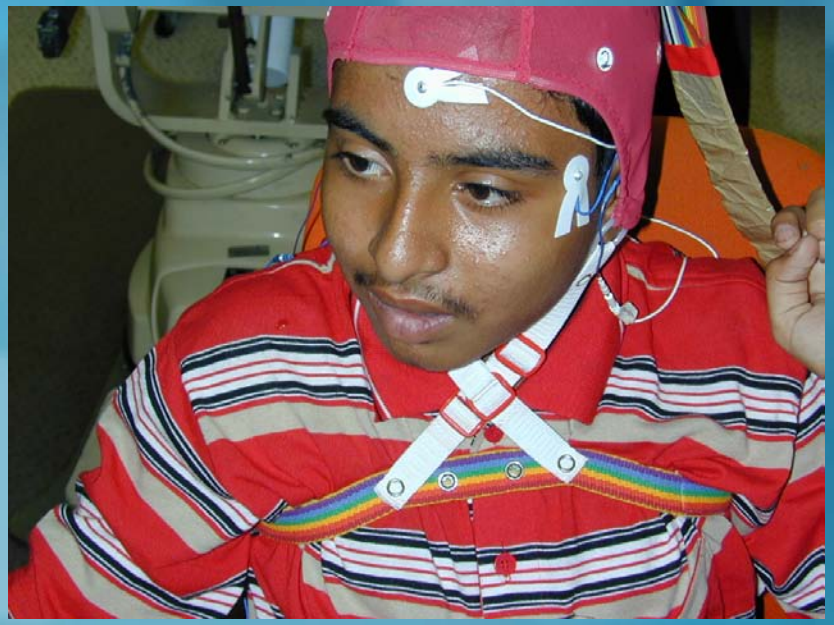
o p q r s t u

v w x y z

In spite of a Dx of mental retardation, Soma sees from some of Tito's unusual activities, that he is capable of learning.

Over several years Soma develops her method which consists of constant verbal, visual and motor prompts to keep Tito’s attention - eventually she succeeds in she teaching Tito to point at letters, spelling out words.

Some of the labs Tito visited...



UCSF: Merzenich, Bonneh, Houde, and others

UCSD: Courchesne, Ramachandran & Hirstein

UCLA: Zaidel, Kaiser

Stanford: Gillette

George Town U: Eden

Adaptation to one dominant sensory mode

Vision Dominant
(Temple)

Auditory Dominant
(Tito)

Screens out other senses to reduce overload

Is Tito one in a million?

“Listening…”

PORTIA IVERSEN

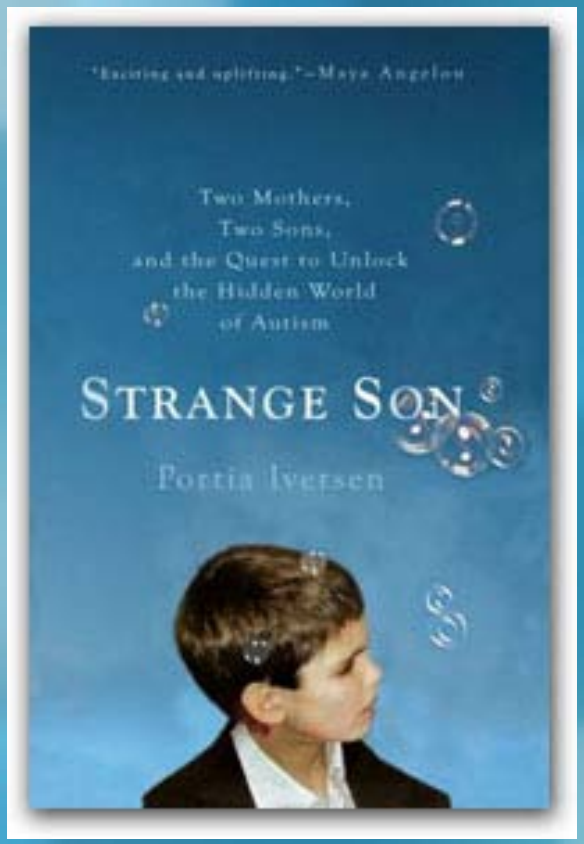
Strange Son

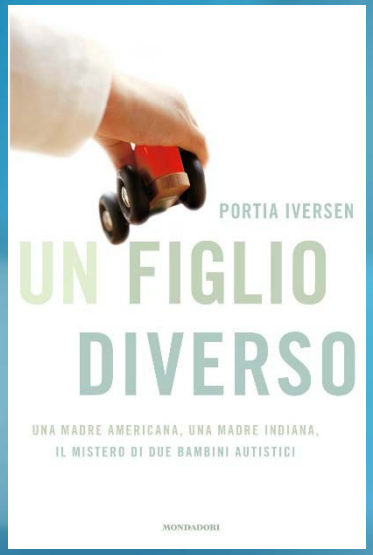
Two Mothers, Two Sons

and the Quest to Unlock

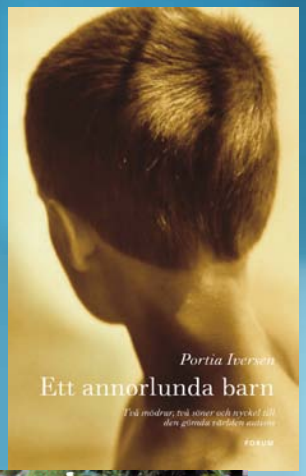
the Hidden World of Autism

2007




PORTIA IVERSEN
UN FIGLIO DIVERSO
UNA MADRE AMERICANA, UNA MADRE INDIANA,
IL MISTERO DI DUE BAMBINI AUTISTICI
MONDADORI


엄마가 지켜줄게
포서 아이버슨
Strange Son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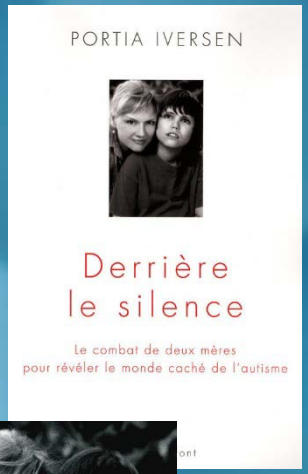
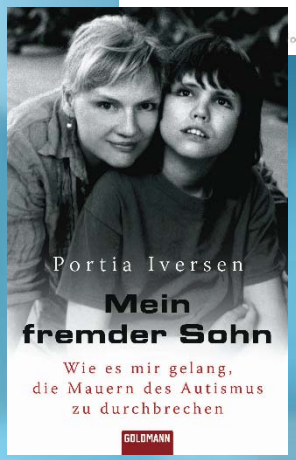
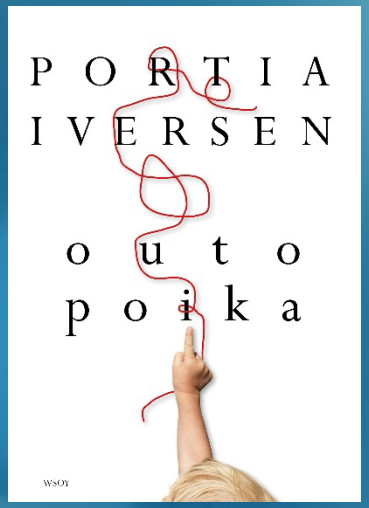

PORTIA IVERSEN
Derrière le silence
Le combat de deux mères pour révéler le monde caché de l'autisme


奇蹟的孩子
STRANGE SON
Two Mothers, Two Sons, and the Quest to Unlock the Hidden World of Autism
一段開啟
封閉心靈的旅程


Portia Iversen
Mein fremder Sohn
Wie es mir gelang, die Mauern des Autismus zu durchbrechen
GOLDMANN


PORTIA IVERSEN
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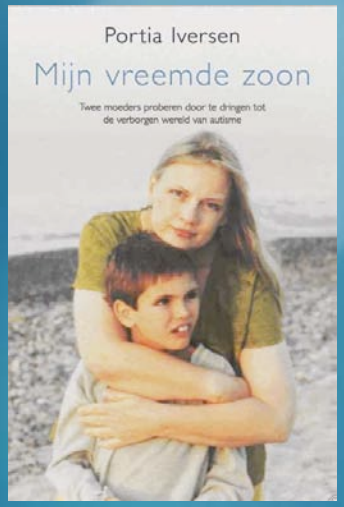
Portia Iversen
Mijn vreemde zoon
Twee moeders proberen door te dringen tot de verborgen wereld van autisme


ぼくは考える木
自閉症の少年詩人と探る脳のふしぎな世界
ポーシャ・アイバーセン
小川敏子[訳]
早川書房


בן מוזר

VIDEO: When World’s Collide

“Clearly words like "nonverbal" and "low functioning" just don't cut it. Watching Temple Grandin stumped by Tito's use of language is just amazing. What I am trying to understand is how many Titos are out there in this "nonverbal" population.

But at a more basic level, this calls into question some of our basic models of verbal communication as a proxy for sociality.”

- Tom Insel

The Problem:

Literature search reveals:

No standardized terminology or taxonomy for ‘nonverbal’ phenotype therefore cannot assess what research has been done.

No distinction between these phenotypes:

- functionally nonverbal (low-communicating)
- physically nonverbal (speech praxis)
- cognitively nonverbal (mental retardation)

Example:

Searching the IACC Autism Spectrum Disorder Research Portfolio Analysis (2010):

Using the terms “nonverbal” and non-verbal”

Out of 139 projects listed, only 13 actually have anything to do with nonverbal autism.

How many are there?

•The percentage of the ASD population that is nonverbal or low-communicating is unknown.

• Best guess is 25% are nonverbal (cannot speak) and *at least* 25% can physically speak but don't have functional language.

•That means we are talking about 25 – 50% of the spectrum.

Yet almost nothing is known about these individuals, they are not included in research and the most basic questions remain unanswered.

While autism research and the development of interventions has increased dramatically over the past 20 years -- **our understanding of nonverbal autism has remained unchanged**.

This is not acceptable.

Rethinking the Model of Nonverbal Autism:

Recent autism genetic research (ie role of CNVs, common and rare variants, Sebat, Wigler, etc) suggests tremendous heterogeneity in the etiology of ASD.

This upends the traditional spectrum model that says autism is a disorder that ranges from severe to mild, though some subgroups will likely fit a spectrum model certainly not all will.

ORIGINAL ARTICLE

Array-based comparative genomic hybridisation identifies high frequency of cryptic chromosomal rearrangements in patients with syndromic autism spectrum disorders

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13 July

Sciencexpress Report

Strong Association of De Novo Copy

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30. The research at the University of Iowa was supported by NASA through contract 1279973 with the Jet Propulsion Laboratory.

Supporting Online Material

www.sciencemag.org/cgi/content/full/1138562/DC1
SOM Text
Figs. S1 to S8
References

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Strong Association of De Novo Copy Number Mutations with Autism

Jonathan Sebat,[1]* B. Lakshmi,[1] Dheeraj Malhotra,[1]* Jennifer Troge,[1]* Christa Lese-Martin,[2] Tom Walsh,[3] Boris Yamrom,[1] Seungtai Yoon,[1] Alex Krasnitz,[1] Jude Kendall,[1] Anthony Leotta,[1] Deepa Pai,[1] Ray Zhang,[1] Yoon-Ha Lee,[1] James Hicks,[1] Sarah J. Spence,[4] Annette T. Lee,[5] Kaija Puura,[6] Terho Lehtimäki,[7] David Ledbetter,[2] Peter K. Gregersen,[5] Joel Bregman,[8] James S. Sutcliffe,[9] Vaidehi Jobanputra,[10] Wendy Chung,[10] Dorothy Warburton,[10] Mary-Claire King,[3] David Skuse,[11] Daniel H. Geschwind,[12] T. Conrad Gilliam,[13] Kenny Ye,[14] Michael Wigler[1]†

We tested the hypothesis that de novo copy number variation (CNV) is associated with autism spectrum disorders (ASDs). We performed comparative genomic hybridization (CGH) on the genomic DNA of patients and unaffected subjects to detect copy number variants not present in their respective parents. Candidate genomic regions were validated by higher-resolution CGH, paternity testing, cytogenetics, fluorescence in situ hybridization, and microsatellite genotyping. Confirmed de novo CNVs were significantly associated with autism ($P = 0.0005$). Such CNVs were identified in 12 out of 118 (10%) of patients with sporadic autism, in 2 out of 77 (3%) of patients with an affected first-degree relative, and in 2 out of 196 (1%) of controls. Most de novo CNVs were smaller than microscopic resolution. Affected genomic regions were highly heterogeneous and included mutations of single genes. These findings establish de novo germline mutation as a more significant risk factor for ASD than previously recognized.

ASD was needed. We have performed high-resolution genomic microarray analysis on a sample of 264 families to determine the rate of de novo copy number mutation in unaffected and affected children.

Our study focused on a sample of 264 families, including 118 "simplex" families containing a single child with autism, 47 "multiplex" families with multiple affected siblings, and 99 control families with no diagnoses of autism. The majority of patients came from the Autism Genetic Resource Exchange (AGRE) and from the National Institute of Mental Health (NIMH) Center for Collaborative Genetic Studies of Mental Disorders. Additional families were obtained through the authors (T.C.G., J.S.S., J.B., and D.S). Efforts were made at all of the collecting sites to exclude cases of syndromic autism (i.e., those with severe mental retardation or other congenital anomalies) and to exclude known cytogenetic abnormalities. Identities of all subjects and their parents were coded so that analysis could be done blind to affected status while maintaining knowledge of

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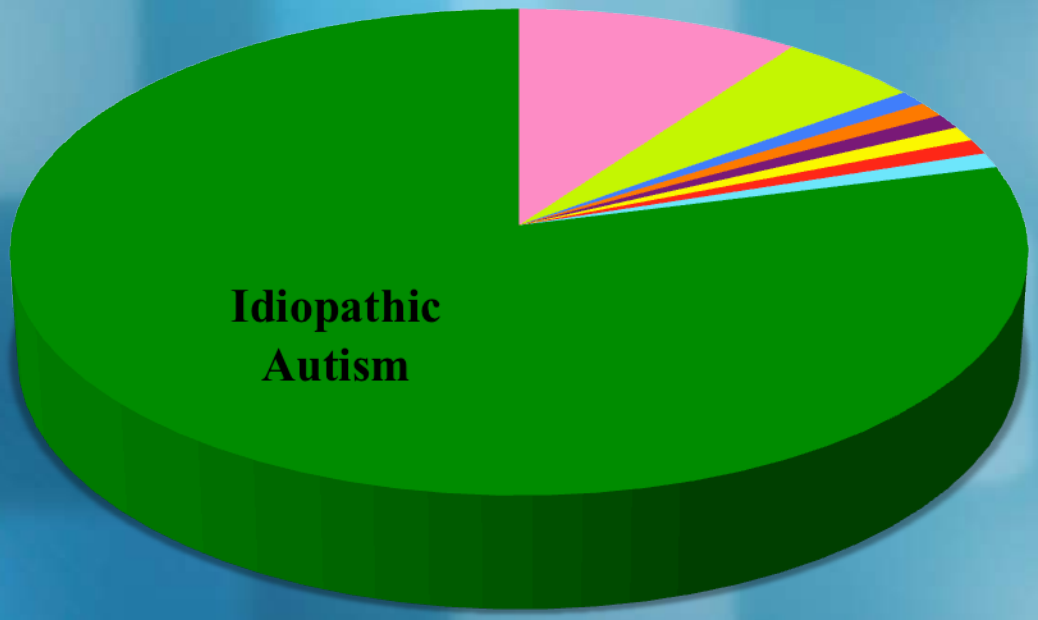
Known causes of 10 – 25% of Autism



- De Novo CNVs, cytogenetic, epigenetic
- Single Mendelian Gene Defects w/ Major Effect (ie Tuberous Sclerosis)
- 100+ Rare Single Gene Mutations
- Chromosomal Cytogenetic Abnormalities (ie Angelman/PraderWillie)
- X-linked traits (ie Rett, Fragile X)
- Detectable Brain malformation (ie Chiari Malformation)
- Nongenetic causes (ie congenital Rubella)
- Documented Environmental Causes
- "Real" Autism (Ideopathic)

The Current Model

Deficits in language and communication

Deficits in social interaction

Restricted and repetitive behaviors

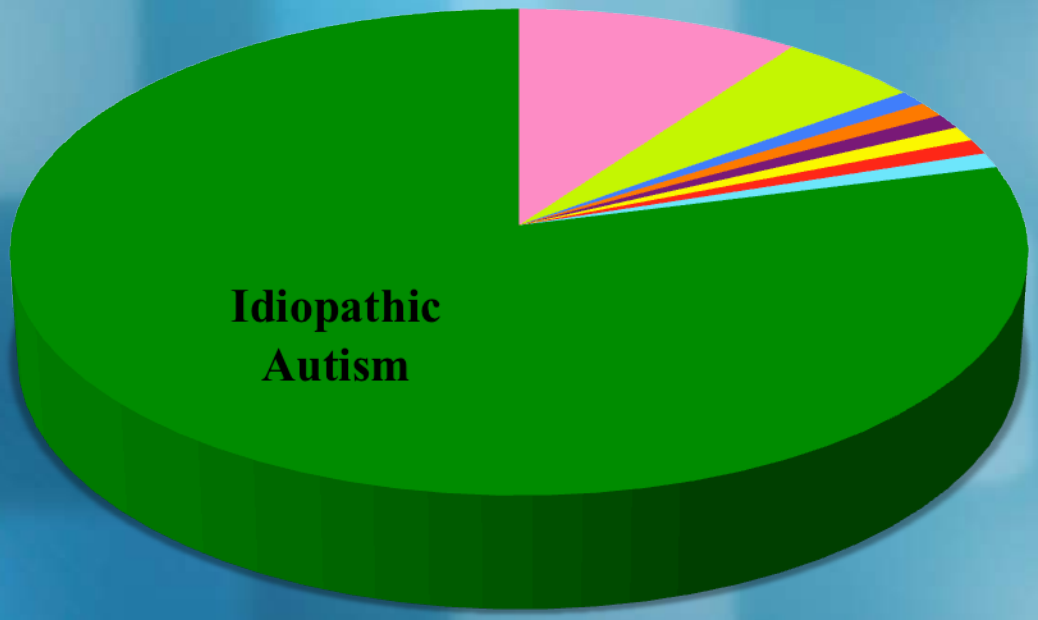
Obsessive, compulsive behaviors

"Autism is a spectrum disorder ranging from mild to severe."

High Functioning Autism: Verbal, average IQ, less severe behavioral and motor symptoms

Low Functioning Autism: Nonverbal or verbal without functional language, mental retardation, more severe behavioral and motor symptoms

Known causes of 10 – 25% of Autism



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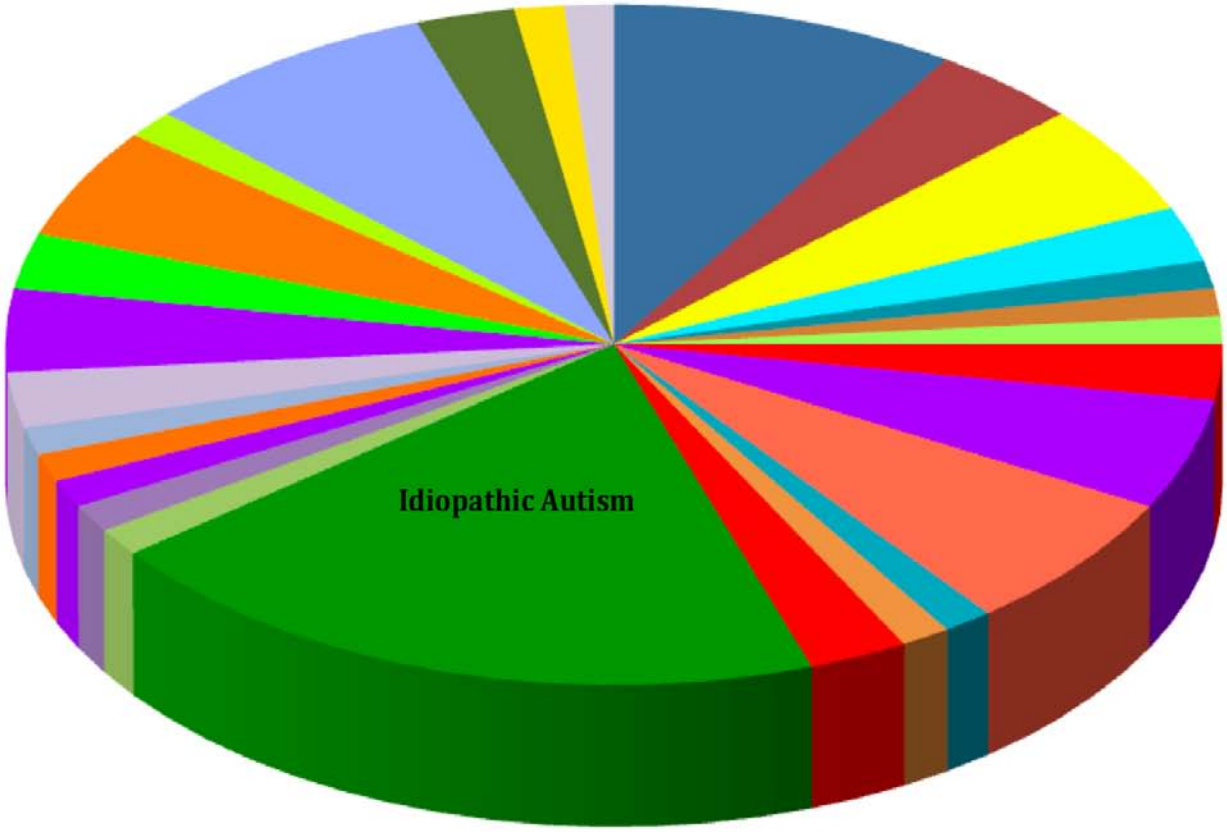
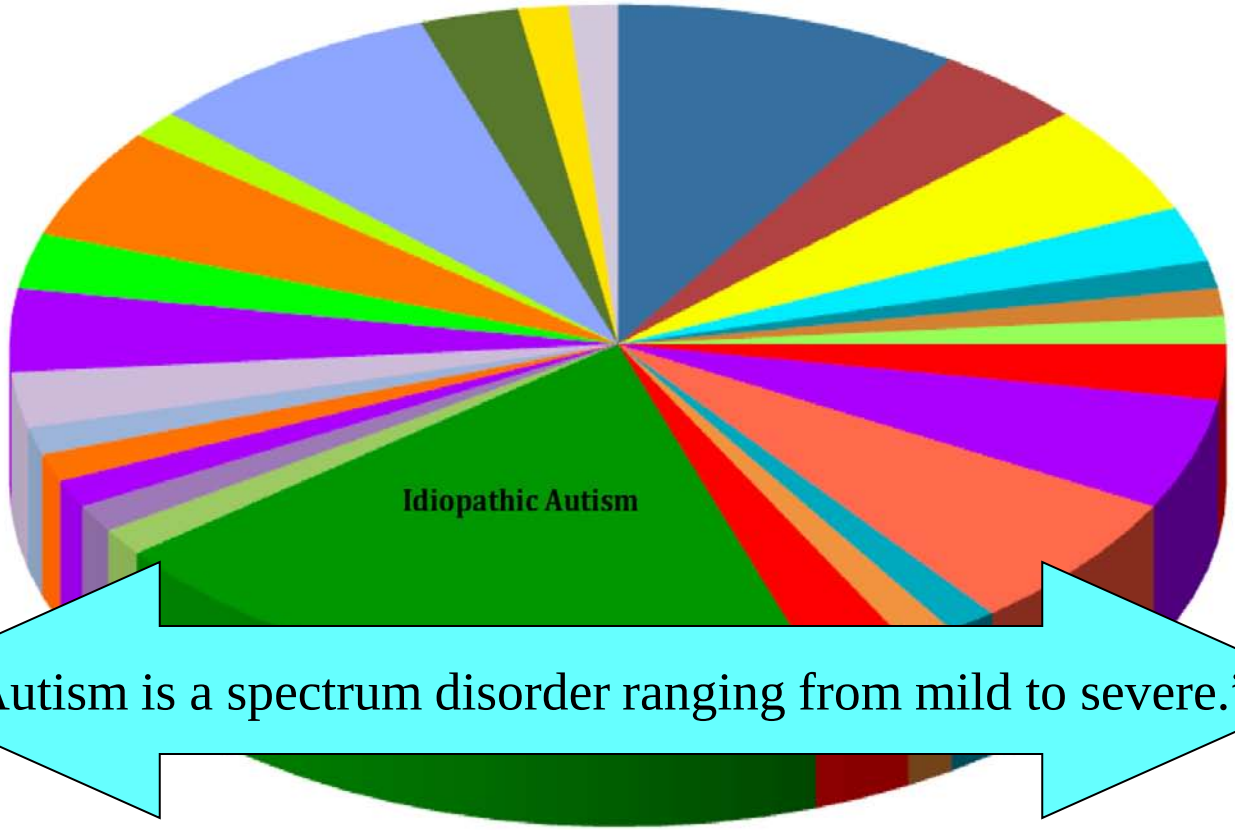
Known Causes of 78% of Autism



Known Causes of 78% of Autism



"Autism is a spectrum disorder ranging from mild to severe."

Rethinking the Model:

The nonverbal subgroup is likely to be very heterogeneous.

The nonverbal subgroup is probably not *only* the more severe form of ‘Idiopathic Autism’ but rather a mixture of disorders some that include MR and some that do not, all of which are lumped into the ‘severe’ end of the spectrum by virtue of their profound inability to communicate and severely autistic behaviors.

Rethinking the Model:

Therefore we can no longer equate the absence of communicative ability and presence of “low-functioning” behaviors with the absence of intrinsic cognitive ability.

Lack of expressive language may not mean absence of receptive language…or intelligence.

How many nonverbal children are receiving a life-long diagnosis of mental retardation if they are not speaking by the age of five years old?

Some Key Questions:

- What methods or tools can we develop or adapt to determine if ***receptive language*** is intact in this population?
- What kinds of skills can be taught that would allow us to test cognition in this population?

  (ie pointing)
- What cognitive measures can be developed or adapted for use with this population and how?

2 examples of research that could begin to answer some basic questions about nonverbal autism:

- Barry Gordon’s research assesses receptive vocabulary knowledge in low-functioning autism by eye movements, pupillary dilation, and event-related potentials.

- John Connolly uses cognitive event-related brain potentials (ERPs) recorded in a structured protocol to evaluate cognitive function in non-verbal individuals with autism, including individuals with autism who use alternate means of communication. These methods were originally developed for assessing brain-injured people who have received diagnoses of "vegetative state" and "locked-in" syndrome, and are expected to provide a rigorous means of demonstrating speech comprehension at different levels of sophistication and related cognitive functions.

VIDEO:
Dov’s Preparation for his Bar Mitzvah