Making Sense of Autistic Spectrum Disorders

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Los Angeles County Office of Education

January 17, 2014

Outline

Etiology, Epidemiology, and Quackery [10:30 -12:00]

- > The autism "explosion
 - · Where did it come from? What does it mean?
 - · Impact of DSM5
- Causes of ASD: Proven, unproven, and disproven
 - · Genetics, and why you should care about it
- · The signs and symptoms of quackery

LUNCH [12:00 - 1:00]

The ASD "Explosion"

- Are we in an epidemic?
- If so:
 - Is there a smoking gun?
 - Are there preventive or therapeutic measures?
- If not:
 - Where did all these kids come from?
 - Where are the "missing" adults?

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DEFINITIONS

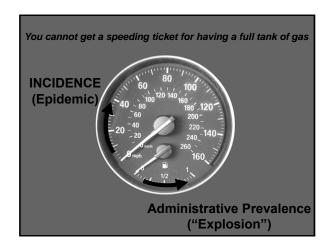
- Incidence
- Prevalence
- Epidemic
- "Explosion"

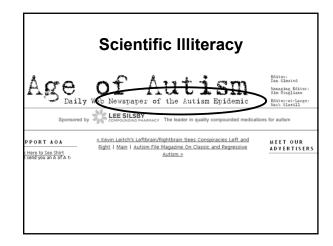
Incidence = Rate

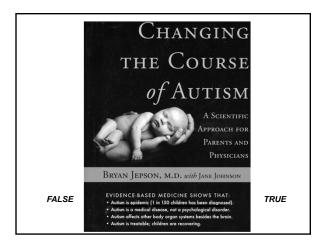
- The number of new cases of a disorder, over a specified period of time, in a defined population
 - New cases of Influenza / 100,000 persons / wk
 - Incidence of ASD =
 - Birth rate of newborns who will have ASD +
 - · Attack rate of autistic regression among children
 - The Incidence of ASD is Unknown

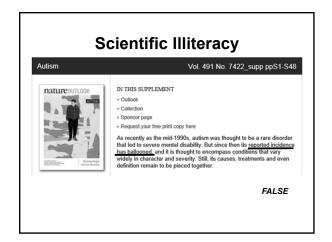
Prevalence = Proportion

- The percent of the population that is affected, at one point in time
 - The % of people with the Flu at a given time
 - The % of people with ASD
- We do not know the prevalence of ASD. What we know is the number of children being served with a diagnosis of ASD (the "administrative prevalence").









What difference does it make?

- If we are really in an epidemic:
 - Is there a smoking gun?
 - Immunizations
 - Mercury
 - Other?
 - Is there a cure or preventive measure?

Known Causes of **↑** Administrative Prevalence of ASD

- > Broadening diagnostic criteria
- Broadening Federal service & reporting requirements
- · Diagnostic substitution
- Broadening ascertainment methods

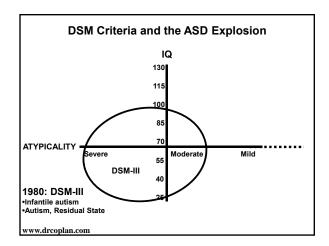
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Relationship between *diagnostic criteria* and apparent prevalence

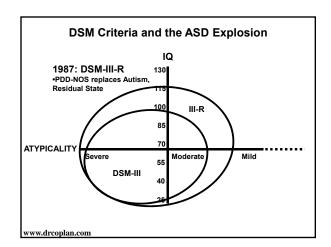
What is the prevalence of "Tall Stature"

- If the cutoff for "Tall" = 7 feet?
- If the cutoff for "Tall" = 6 ft 10"
- If the cutoff for "Tall" = 6 ft 6"
- If the cutoff for "Tall" = 6 ft
- Etc.....

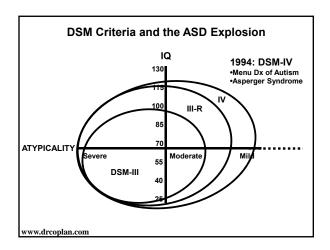
DSM III		
Yr	Event	Comment
1980	DSM-III: First appearance of: •Infantile autism •Autism-residual state: Children who once met criteria for infantile autism but no longer do.	6 mandatory, severe criteria for Dx of autism, including: •Pervasive lack of responsiveness to other people •Gross deficits in language development •Bizarre responses to various aspects of the environment

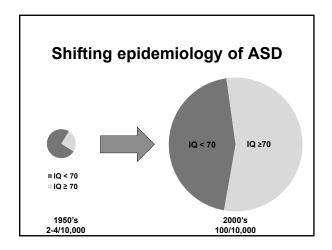


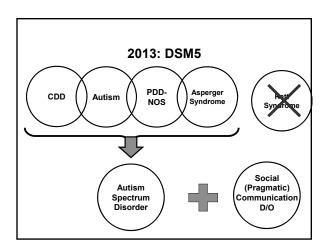
DSM III-R		SM III-R
Year	Event	Comment
1987	DSM-III-R: •"Infantile autism" replaced by "Autistic Disorder" •"Autism-Residual State" replaced by PDD-NOS	PDD-NOS encompasses children who never met full criteria for Autism, as well as children who once met such criteria but improved over time.
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DSM IV		
Year	Event	Comment
1994	DSM-IV: *Three Domains *Social *Language *Repetitive Behavior *Menu of qualifying symptoms* *Asperger's Disorder first appears *"No gross delay in language"	6 of 12 milder criteria, such as: •Lack of spontaneous seeking to share achievements with other people •Difficulty sustaining a conversation •Lack of varied social imitative play •Persistent preoccupation with parts of objects
	* "Polythetic" approach	







Autism Spectrum Disorder

Two Clinical Domains (vs. 3 in DSMIV, and 4 in Kanner)

- A. Deficits in Social Communication and Interaction
 - Combines Social & Language domains
- B. Restricted, Repetitive, Behaviors, Interests, and Activities

DSM5 - ASD

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following,* currently or by history (examples are illustrative, not exhaustive):...

* Doesn't say "all" of the following; intent unclear

Social Communication & Interaction

 Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.

Social Communication & Interaction

 Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.

Social Communication & Interaction

 Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.

DSM5 - ASD

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive)...

Restricted, repetitive patterns of behavior, interests, or activities

 Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypies, lining up toys or flipping objects, echolalia, idiosyncratic phrases)

Restricted, repetitive patterns of behavior, interests, or activities

 Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day)

Restricted, repetitive patterns of behavior, interests, or activities

 Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests)

Restricted, repetitive patterns of behavior, interests, or activities

 Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain / temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement) "Because symptoms change with development and may be masked by compensatory mechanisms, the diagnostic criteria may be met based on historical information, although the current presentation must cause significant impairment.

- C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).
- D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
- E. These disturbances are not better explained by intellectual disability or global developmental delay.

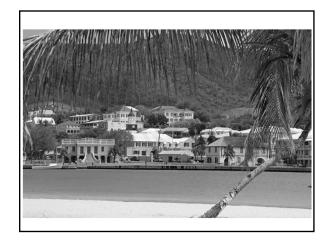
Note: Individuals with a well-established DSM-IV diagnosis of autistic disorder, Asperger's disorder, or PDD-NOS should be given the diagnosis of ASD. Individuals who have marked deficits in social communication, but whose symptoms do not otherwise meet criteria for ASD, should be evaluated for social (pragmatic) communication

ASD vs. Social (Pragmatic) Communication D/O

Communication B/C		
Symptom Domain*	Autism Spectrum D/O	Social (Pragmatic) Communication D/O
Social and Language	✓deficits in social-emotional reciprocity ✓nonverbal communication, and ✓ maintaining / understanding relationships	"Deficits in social communication result[ing] in functional limitations in effective communication, social participation, development of social relationships, academic achievement, or occupational performance"
Restricted, repetitive patterns of behavior, interests, or activities	✓Stereotypad or repetitive motor movements, use of objects, or speech ✓Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior ✓Highly restricted, fixated interests that are abnormal in intensity or focus ✓Hyper- or hyporeactivity to sensory input (at least 2 out of 4)	NO

DSM5: ASD vs. Social Communication D/O

"Current absence of symptoms would not preclude a diagnosis of autism spectrum disorder, if the restricted interests and repetitive behaviors were present in the past. A diagnosis of social (pragmatic) communication disorder should be considered only if the developmental history fails to reveal any evidence of restricted/repetitive patterns of behavior, interests, or activities"





Autism in DSM-5: progress and challenges

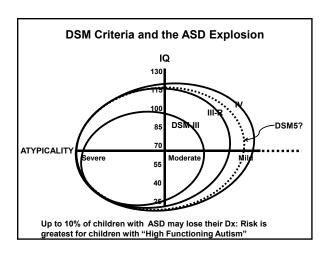
Fred R Volkmar* and Brian Reichow

- DSM-IV: 3 categories (Language, Social, Repetitive Behavior) and a menu of qualifying criteria within each category gave >2,000 combinations of criteria that would yield an autism diagnosis
- Combining Social and Language into one category, and requiring 3 out of 3 criteria to be met for Repetitive Behavior results in many fewer potential combinations
- "Despite the name change to Autism Spectrum Disorder, the concept actually proposed is apparently more restricted than the DSM-IV approach"

Autism in DSM-5: progress and challenges

Fred R Volkmar* and Brian Reichow

- "The impact is probably greatest among the most cognitively able cases and those with less classic autism presentations;" up to 10% may lose Dx of ASD
- Impact will be greatest in settings where reliance is placed exclusively on testing, w/o diligent review of early developmental history





"Implications for School Psychology"
Stephen E. Brock & Shelly R. Hart
"Ultimately, we ask the question as school
psychologists: What does this mean for
us?...The short answer is: Nothing...

The work of school psychologists is, and always has been, *informed* by DSM. DSM has never been a controlling authority....



"The simple presence of a DSM diagnosis for a student we serve can and should direct our attention, but it never should direct our action.

The education codes and regulations that do direct our action (i.e. IDEA) require clear evidence of an adverse effect on educational functioning, and, as a result, some might argue are more restrictive in this setting than DSM*..."

(* Some of us would beg to differ: Anxiety w/o academic failure, e.g.)

Known causes of ♠ prevalence of children with a Dx of ASD

- Broadening diagnostic criteria
- ➤ Broadening Federal service & reporting requirements
- · Diagnostic substitution
- Broadening ascertainment methods

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	Changes in F	ederal Law - 1
Year	Event	Comment
1975	Congress enacts Public Law 94-142: Education for All Handicapped Children (EAHC)	First Federal law requiring the States to provide free and appropriate public education (FAPE) to "all children >5 yrs old, regardless of disability"
		But

"Handicapping Conditions" (PL 94-142; 1975)

- · Mentally Retarded
- Learning Disabled
- Speech impaired
- Hearing / Vision Impaired
- Seriously emotionally disturbed
- · Orthopedically impaired
- Multi-handicapped
- Other health impaired

Where is autism?

Changes in Federal Law - 3		
Year	Event	Comment
1990	Congress Amends PL 94-142 again (PL101- 476)	•Renamed Individuals with Disabilities Education Act (IDEA) •Includes Autism & Traumatic Brain Injury (TBI) as "eligible disabilities" under the scope of the law

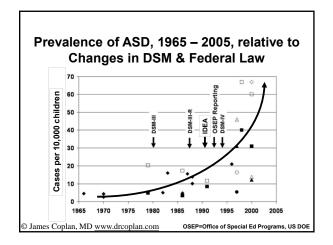
Prior to 1990, according to Federal regulations, *Autism did not exist*.

Year	Event	Comment
1991	US Department of Education, Office of Special Education Programs (OSEP) requires reporting of autism by the States, starting in 1992.	Coincides with implementation of Part B (3 to 5 yr olds) & Part H (birth to 3) of PL 99-457

Impact of Federal Law & Regulations

- El & 3 to 5 Services begin: 1986
- Autism recognized as a fundable D/O:1990
 - Re-classification of children already in the system (diagnostic substitution)
 - Correct classification of new children with autism entering the system
- Reporting autism to US DOE required: 1992

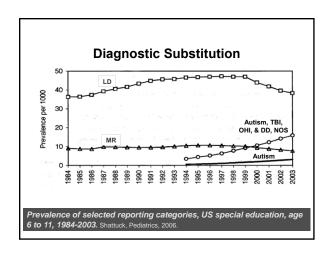
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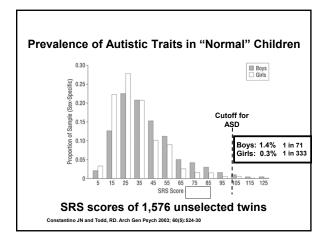
Ascertainment Methods for ASD

- Old: Count already-identified cases
 - School data
 - Medical clinics
- New: Search for unrecognized cases
 - Population Screening (El, ACA, etc.)
- Ascertainment Bias?

Population Screening

- Subjects
 - Missouri Twin Study
 - 788 twin pairs, age 7-15
 - No identified developmental disorder
- Methods
 - Social Responsiveness Scale (SRS); mother = informant (97%)

Constantino JN and Todd, RD. Arch Gen Psych 2003; 60(5):524-30





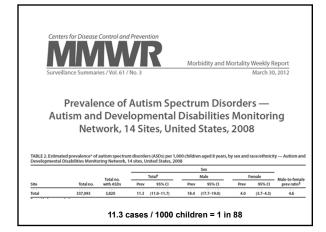
Autism-Related Conditions

http://www.hhs.gov/autism/factsheet-aca-autism.html

 New health insurance plans or insurance policies must cover preventive services without costsharing, including autism screening for children at 18 and 24 months

Ascertainment Bias

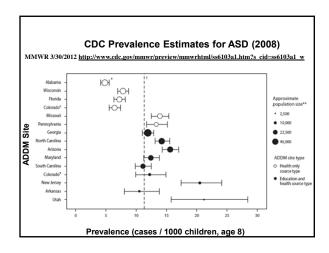
- Differential ascertainment
 - By race
 - By geographic region
 - By socioeconomic status

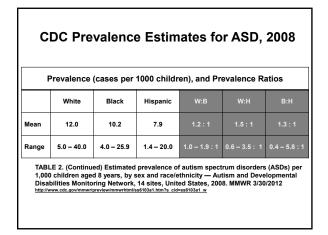


CDC Prevalence Estimates for ASD, 2008

- Autism and Developmental Disabilities Monitoring Network (ADDM)
 - 14 Sites (Universities, State Depts of health; not demographically representative of the US as a whole)
- · Data sources:
 - Healthcare organizations (general & specialty)
 - Schools (some sites)
- N = 337,093 children, age 8
- 3,820 met surveillance case criteria for ASD
 - $-\,$ 79% had a pre-existing Dx of ASD in their records
 - 21% had no ASD Dx in their records

Prevalence of Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, March 30, 2012 / 61(SS03);1-19 http://www.cdc.gov/mmyr/preview/mmyrhtml/ss6103a1.htm?s_cid=ss6103a1_w





Socioeconomic Inequality in the Prevalence of Autism Spectrum Disorder: Evidence from a U.S. Cross-Sectional Study

Durkin MS, Maenner MJ, Meaney FJ, et al. 2010 PLoS ONE 5(7): e11551.

Prevalence increased with increasing SES* in a dose-response manner, with prevalence ratios relative to medium SES of 0.70 for low SES, and of 1.25 for high SES, (P<0.001).

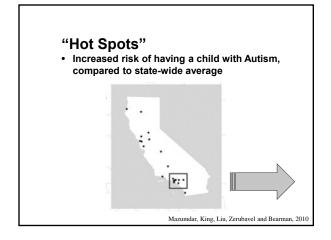
*SES: Socioeconomic status (income, education)

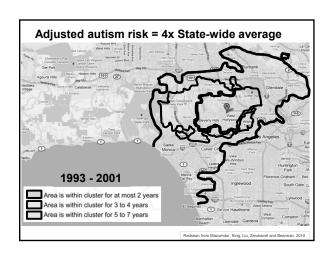
The spatial structure of autism in California, 1993–2001

Health & Place

Volume 16, Issue 3, May 2010, Pages 539-546 Soumya Mazumdar, Marissa King, Ka-Yuet Liu, Noam Zerubavel and Peter Bearman

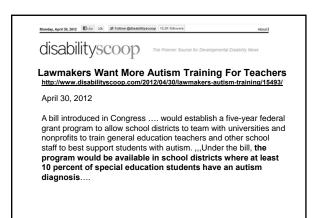
Institute for Social and Economic Research and Policy Columbia University, New York, NY, USA





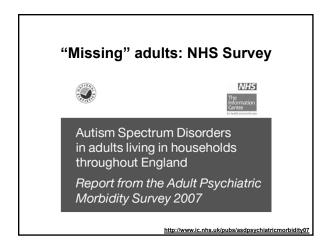
Following the money

- \$ earmarked for children with ASD
- Pressure to classify children with borderline symptoms as ASD in order to access to services
 - Improved recognition of children with mild ASD, or
 - Artificial ♠ in number of children with autism diagnosis?



Where have all the adults gone?

"Since 1% of adults don't have ASD, doesn't that prove we're in an epidemic?"

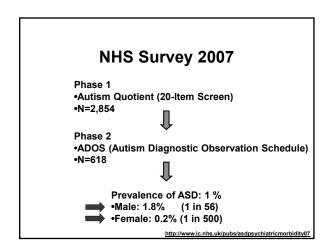


NHS Survey 2007

**National sample of survey of adults living in the community

*Excludes persons in residential care

*Therefore, under-counts adults with severe disability



NHS Survey 2007 Prevalence of ASD (ADOS 10+), by age All adults 2007 Age group 16-44 45-74 75+ % % % ASD (ADOS score of 10+)^a 1.1 0.9 0.8 Prevalence x Age: Not statistically significant

http://www.ic.nhs.uk/pubs/asdpsychiatricmorbidity0

"Missing adults"

Reality:

 The prevalence of ASD among today's senior citizens is roughly the same as among today's children.



Outline

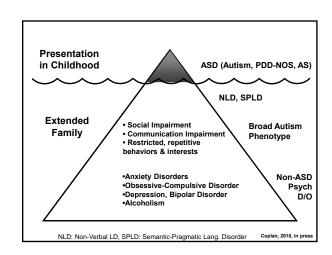
Etiology, Epidemiology, and Quackery [10:45-12:00]

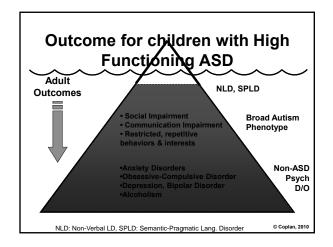
- The autism "explosion"
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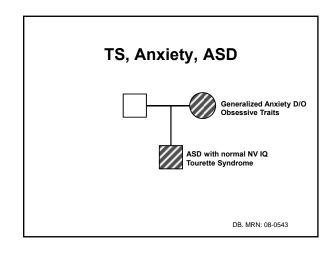
LUNCH

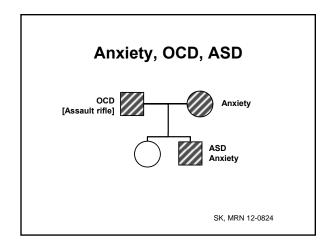


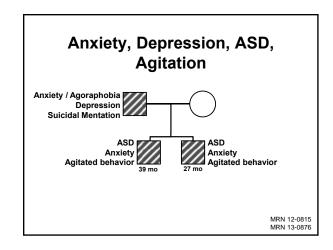
 Just because someone outgrows childhood criteria for ASD does not mean that they are cured

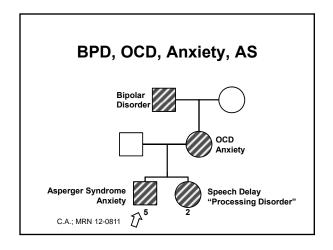












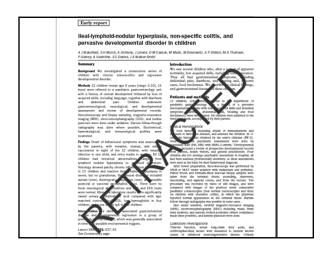
Causes of ASD

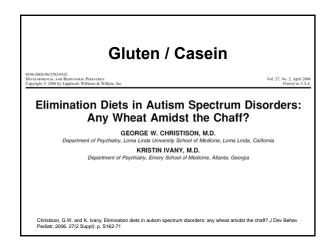
• Prenatal

- Genetic: Nearly all cases of ASD with a known etiology
- Teratogenic (rare; rubella, valproate)
- Associations: Parental Age; Infertility, ?ART

• Perinatal:

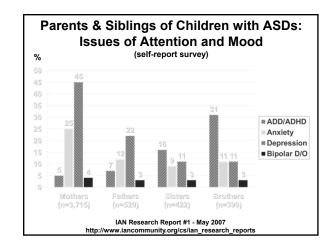
- Associations: (extreme prematurity), but no proven causes
- Postnatal:
 - Some associations, but no proven causes
 - No proof: Diet, immunizations





Testing: No proven benefit

- · Stool for yeast, parasites, metals
- Urine porphyrins
- Red Blood Cell elements
- · Hair analysis
- Allergy or Food Sensitivity (Gluten)

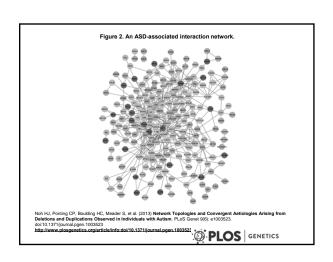


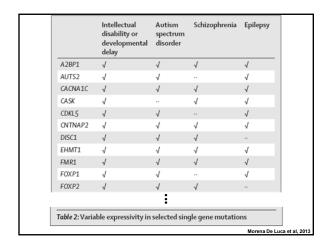
Network Topologies and Convergent Aetiologies Arising from Deletions and Duplications Observed in Individuals with Autism

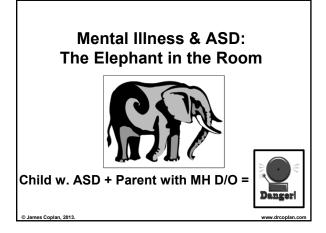
Hyun Ji Noh, Chris P. Ponting, Hannah C. Boulding, Stephen Meader, Joseph D. Buxbaum, Dalila Pinto, Christian R. Marshall, Anath C. LionelStephen W. Scherer, Caleb Webber PLOS Genetics, June 6 2013

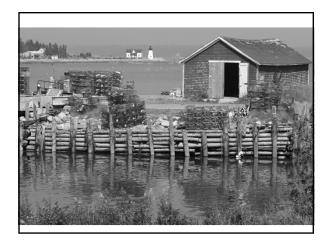
http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1003523

- 192 genes form an interconnected cluster
- Patients with copy number variations within this cluster possess on average, 3 CNV's
- Many of these genes are implicated in psychiatric disorders in humans (anxiety, e.g.), and/or behavioral abnormalities in animal models (abnormal nurturing behavior, e.g.)









Quackery - 1

"The promotion, for profit, of a medical remedy known to be false or unproven" (FDA)



http://www.quackwatch.org/01QuackeryRelatedTopics/quackdef.html

Promotional Techniques

- · Create a demand
- Deliver the pitch
- Close the sale
- Modern advertising originated with 19th Century "patent medicines"
 - Safe & Effective!
 - Satisfaction guaranteed!

 $Creating\ Demand\ for\ Prescription\ Drugs: A\ Content\ Analysis\ of\ Television\ Direct-to-Consumer\ Advertising\ http://www.annfammed.org/content/5/1/6.full$

Quack Therapies: The Pitch

- · Simple yet mysterious
- · All-powerful, yet safe
- · Able to cure multiple conditions
- Supported by Testimonials
- Thrive as the underdog: persecuted by, or challenger to, standard medical practice

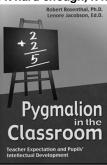
Show me the data

- Epidemiologic evidence & animal models to confirm causation
- Randomized Controlled Trials to demonstrate safety & efficacy
 - Parents need to demand, and then be willing to enroll their children, in RCTs

Expectation Bias - 1

 We see what we expect to see

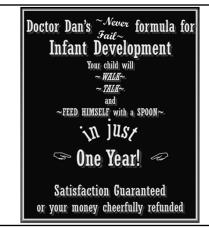
Expectation Bias – 2 (If you wish it hard enough, it is no dream)



Expectation Bias – 2

(If you wish it hard enough, it is no dream)

- Pygmalion Effect
- aka Rosenthal Effect; Teacher Expectation effect
- Randomly selected students were labeled "exceptionally bright"
- "Bright" students' scores rose on objective measures, compared to controls
- Moral: If you believe in a therapy strongly enough, your belief alone is enough to create objective change



Follow the money

- Who else is advocating a particular therapy, other than
 - parents who have already spent money it, and
 - vendors who make their livelihood providing it?

Implications

- Beware of any arguments that rest on the claim that we are in an epidemic
 - Allegations as to cause
 - Promises of cure



Summary

- Epidemiology:
 - Administrative Prevalence of ASD has risen
 - No proof that actual prevalence has changed
 - No info on Incidence
- Genetics
 - Accounts for most cases of known cause
 - Co-morbid mental health disorders
 - · In the affected child
 - In parents
- Quackery
 - Show me the data
 - Follow the money

