Autism and Comorbid Disorders

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Definition

“The Pervasive Developmental Disorders (PDD) are a group of neurodevelopmental / neuropsychiatric disorders characterized by specific delays and deviance in social, communicative and cognitive development with an early onset, typically in the first years of life. Although commonly associated with mental retardation, these disorders differ from other developmental disorders in that their developmental and behavioural features are distinctive and do not simply reflect developmental level”

(Rutter, 1978)

Concerns about the current situation

- The massive increase in reported prevalence over the last decade
- DSM and "cook-book" diagnosis
- Service provision and diagnostic requirements
- Is “the spectrum” a valid construct?
- Unconventional ideas regarding aetiology
- Unproven and unorthodox treatments
Autistic disorder

Leo Kanner 1894-1981
Kanner's syndrome, classical autism
Kanner, L. Autistic disturbances of affective contact. Nervous Child 1943; 2:217

Kanner, 1943

11 children studied

- "extreme autistic aloneness"
- abnormal speech with echolalia
- pronominal reversal
- literalness of speech
- inability to use language for communication
- monotonous repetitive behaviours
- "anxiously obsessive desire for the maintenance of sameness"

Kanner, 1943

- Sex ratio of 4 : 1 – male : female
- Enlarged head circumference in 5 of the 11 children
- The distinction from schizophrenia - although in later years he was less sure. He did however consider autism to be a psychotic condition. This view was still held by Rutter as late as 1973. (Rutter M. Foreword. In: Kanner L. Childhood Psychosis: Initial Studies. VH Winston and Sons, Washington DC)
- It's "constitutional" basis
Kanner, 1943
Quotations

- “The children have come into the world with an innate inability to form the usual, biologically provided affective contact with people”
- A “profound aloneness dominates all their behaviour”
- The children “looked upon as feebleminded,” also bear “strikingly intelligent physiognomies and, when alone, may even assume an expression of beatitude”
- Language was not used for the purposes of communication but “was deflected in a considerable measure to a self-sufficient, semantically or conversationally valueless or grossly distorted memory exercise”

Kanner, 1943

- the parents: “Highly intelligent, preoccupied with abstractions of a scientific, literacy or artistic nature and limited in genuine interest in people”
- “there are very few really warm-hearted fathers and mothers”
- “There is resemblance between their make-up and that of their children, except their aloofness has not reached the gross proportions of that of their children”
- He was not parent blaming in stating this, he failed to notice “a sample bias” – in his initial study there was preferential referral: 4 of the first 11 children had fathers who were themselves psychiatrists.

Kanner, 1943

Unfortunately:

“...Kanner’s use of the term autism has proven to be somewhat unfortunate, because of its association with the term used by Bleuler to describe the withdrawal into an active fantasy adopted by schizophrenics. Actually the concept of autism describes the very absence of any creative fantasy life which characterizes the withdrawal of such children.”

Eugen Bleuler

1911
- First use of the word “autism” in his work on Dementia Praecox (Kraepelin 1905)
- The three “A’s” of schizophrenia:
  - altered association
  - altered affectivity
  - ambivalence and autism

Eugen Bleuler

Autism: the “undirected fantasy thinking”
- “the most severe schizophrenics live in a world of their own”.
  Bleuler E. The Theory of Schizophrenic Negativism 1912
- “autistic schizophrenics” have “turned away from reality; they have retired into a dream life, or at least the essential part of their dissociated ego lives in a world of subjective ideas and wishes, so that to them reality can bring only interruptions”
  Bleuler, Eugen. Dementia Praecox or The Group of Schizophrenias. (1911)

Autism and Schizophrenia

Israel “Issy” Kolvin (1929 – 2002)

There was long standing confusion between “infantile autism”, childhood psychosis and schizophrenia. The seminal work of Kolvin and his group (part of the “Newcastle Group”) in the early 1970s separated schizophrenia from autism. It was thought, prior to Kolvin that many adult schizophrenics had childhood histories of autism and a high proportion of childhood autists became schizophrenic.
Asperger’s syndrome

Hans Asperger 1906-1980

Asperger, H. Die “Autistichan Psychopathen” im kindersalter
Archive fur Psychiatrie und Nervenkrankheiten 1944; 117: 76-136.

Asperger’s syndrome

- Impaired social interaction
- Restricted range of interests and activities
- Early language skills preserved but communication skills impaired (pragmatics)
- Conversational ability hampered for example by intense interests in certain topics (trains, weather, electricity, space, dinosaurs and factual lists)
- Can speak incessantly – “little professors” – using unusual words and phrases
- Numerous faux pas
- Motor delays are common
- Usually of normal intellect but frequently have learning disabilities
- Closely related is Nonverbal Learning Disability (NLD, NVLD)

History / Classification / DSM III – 1980

Autism (as we know the concept today) did not become a “diagnostic entity” until 1980 when “operational criteria” for “infantile autism” were established. “Infantile autism” was considered one of a group of conditions brought together under a new term “Pervasive Developmental Disorder” – meaning the developmental disability pervaded all spheres of the child’s life.

- onset before 30 months of age
- lack of responsiveness to other human beings
- gross impairment in communication and language
- bizarre responses to the environment

History / Classification / DSM-IIIR – 1980

The revised version of DSM (DSM-IIIR - 1987) changed the term “infantile autism” to “autistic disorder” and created 16 categories in the criteria for diagnosis.

A seeming advance, but the diagnosis became:

- overly inclusive
- false positives
- differed widely from ICD-10 (and the rest of the world!)


History / Classification / DSM-IV (1994)

Brought the ICD and DSM classifications and diagnostic categories closer into line – however the DSM criteria are still more inclusive than ICD.

This is very similar to the trans-Atlantic differences in prevalence of schizophrenia during the 1950s – 1960s.


Definitional issues remain a major part of the substantial problems in establishing accurate epidemiology, understanding the natural history of autism, comparing studies, replicating research findings and speculating on prognosis …….. and understanding the comorbidities

The DSM-IV Pervasive Developmental Disorders

Autistic Disorder

Rett’s Disorder

Childhood Disintegrative Disorder (CDD)

Asperger’s Disorder (AD)

Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS)
Clarity?

Not in the least!
The late 1980s and 1990s exploded with a host of “new diagnoses”

- High functioning autism
- Sensory Integration Disorder
- Regulatory Disorder of Infancy
- Non-verbal Learning Disability
- Right Hemisphere Syndrome in Children
- Hyperlexic Syndromes
- Visual Spatial Motor Disorder
- DAMP (deficits in attention, motor control, memory and perception)
- Multiplex Developmental Disorder
- Pragmatic Language Disorder
- Etc, etc

“Autistic symptoms”

Have been described in:

- Numerous genetic disorders / syndromes
- Brain injury / frontal lobe syndromes
- A host of neurological disorders
- Gilles de la Tourette's Syndrome
- Obsessive Compulsive Disorder
- Social Anxiety Disorder
- Disorders of Written Expression
- Developmental Coordination Disorder
- Adult diagnosed personality disorders
- Etc
Not only was there an explosion in “diagnoses” but also in theories of causation

- numerous genetic conditions with “autistic like” symptoms (congenital rubella, tuberous sclerosis, phenylketonuria, fragile X and many others)
- heavy metals toxicity: lead, mercury
- abnormalities in trace elements
- environmental pollution
- infection: candida albicans etc
- pre-natal viral brain infection
- pre-natal alcohol exposure
- immunizations (MMR)
- hypoglycaemia and malabsorption
- electromagnetic radiation
- ultrasound in pregnancy
- a seizure variant
- “starving brains” – nutritional causes
- allergies to all and everything
- a variant of attachment disorder
- psychodynamic causes
- psychodynamic causes
- GI causes: gluten
- prenatal and perinatal injury / hypoxia etc

Further reported causative theories of autism:

- Opioid Excess Theories
  - Opioid like substances
  - Enkephalinergic Antagonists
  - Dose and duration
- Opioids and immunosuppression
- Gluten/Celiac Theories and Relation to Celiac Disease
  - Opioid receptors
  - Urinary UAG
- Fatty Acids
- Gamma Interferon Theory
- Free Sulphate Theory
  - Other Sulfation Problems in Autism

- Cholecystokinin and Autism
- Oxytocin and Vasopressin in Autism
- Autism and Amino Acids
  - Methylation Theory of Autism
- Stress and Immunity
- Autoimmune Theory
  - Antibodies to Myelin Basic Proteins Found in Autistic Children
- Viral Infection Theory
- Vaccinations and Autism
  - SEF and brain damage
  - MMR vaccine and autism
  - Research on MMR, Autism Connection Concluded
  - Elevated Robert Robert and MMR Vaccines
  - Vaccination During Pregnancy and Risk for Autism
  - Vaccination and the risk for autism
• Action of Secretin Theories
  • Secretin and cAMP
  • Exocrine and enteric

• Intestinal Permeability Theories
  • The Concept of Increased Intestinal Permeability
  • Environmental Alterations Affect Children with Autism
  • Binstock’s Sensor Insular Cortex Hypothesis for Epic-Binos Linkage

• Prenatal Aspartame Exposure

• Vitamin A Deficiency and Autism

• Orphanin Protein: Orphanin FQ/nociceptin (OFQ/N)

• Smoke and Air Pollution May Be Related to Learning and Behavioral Problems

The occupational hazard of academics attempting to understand autism

“Ha! Webster’s blown his cerebral cortex”

SEPARATING FACT FROM FICTION IN THE ETIOLOGY AND TREATMENT OF AUTISM

A Scientific Review of the Evidence
James D. Herbert, Ian R. Sharp, and Brandon A. Gaudiano
Sci Rev Ment Health Pract, 2002

An excellent review article about the reasons why autism is such a fertile ground for pseudoscience and unorthodox treatments
Diagnosis

- Classic autism on history and examination easily identified.
- Most children are not diagnosed until age 4 to 5 years.
- Typically 2 to 3 years after parents first seek professional help.
- Most children are seen by at least three professionals prior to diagnosis.
- As one moves “up the spectrum” and with increasing age the more important a detailed developmental history and solid phenomenological mental state examination becomes (especially with “atypical autism”).

Relationship between age of recognition of first disturbances and severity in young children with autism

Baghdal A, Picot MC, Pascal C, Poy R, Amoussou C

193 children, from 21 months to 7 years from 49 French Child Psychiatry Clinics
158 (82.4%) infantile autism, 28 (14.6%) atypical autism
81.3% boys, 18.7% girls
39% additional medical condition (genetic / neurological disorders present at birth)

Age of recognition of first disturbances: findings

- 37.6% of parents noticed developmental abnormalities the first birthday
- 20.6% reported problems between 12 and 18 months
- 19.4% difficulties noted between 18 and 24 months
- 18.8% between 24 and 36 months
- 3.6% after 36 months
Severity of developmental delay, deficits in social adaptation and autistic symptoms linked to the age of initial recognition

Children recognized before 18 months had more severe symptoms than children who were recognized after 18 months and lower social, communication and daily living skills levels

A strong association between early recognition and neurological diseases and hearing impairment

No associations with sex, birth order, socioeconomic class

The presence of social adaptation deficits and medical disease were most closely related to early recognition.

Age of recognition of first disturbances: findings

Conclusions:

- Age of first recognition is not necessarily the same time symptoms begin
- Early recognition is more related to the degree of developmental delay and neurological symptoms than to the severity of autism
- The best predictor of early recognition is delayed daily living skills and the presence of neurological problems and auditory difficulties.

Prevalence

The Genetics of Autism
(PEDIATRICS Vol. 113 No. 5 May 2004, pp. 472–486)

"Autism is a complex, behaviorally defined, static disorder of the immature brain that is of great concern to the practicing pediatrician because of an astonishing 556% reported increase in pediatric prevalence between 1991 and 1997, to a prevalence higher than that of spina bifida, cancer, or Down's syndrome. This jump is probably attributable to heightened awareness and changing diagnostic criteria rather than to new environmental influences. Autism is not a disease but a syndrome with multiple nongenetic and genetic causes."
Prevalence

- Prevalence rates have increased over the last decade
- A true increase
- Related to shifting diagnostic criteria and categories
- Due to international differences (DSM vs ICD-10)
- A “fashionable” diagnosis
- Better education of teachers, psychologists and physicians

Analysis of prevalence trends of autism spectrum disorder in Minnesota.
Gaines JL, Fritz MS, Nue KK, Stevens P, Nueschaff CS, Skipio EG.

- School district sampling.
- Between the years 1991-92 and 2001-02, the rates of diagnosis of autism in children in the Minnesota school system increased from 3 in 10,000 children to 44 in 10,000 children.
- Most of the increase could not be accounted for by “diagnostic substitution,” that is, instead of having a diagnosis of mental retardation, a child would be given a diagnosis of autism with a secondary diagnosis of mental retardation.
- There was, however, a leveling off at the end of the study period, with no more rate increases found.

The Changing Prevalence of Autism in California
Croen, LA., Grether, JK., Hoogstrate, J., Selvin, S.

To examine the degree to which improvements in detection and changes in diagnosis contribute to the observed increase in autism prevalence.

Population-based study of eight successive California births cohorts - children born 1987 – 1994 with autism were identified from the statewide agency responsible for coordinating services for individuals with developmental disabilities.

A total of 6036 children with full syndrome autism were identified from 4,590,333 California births, a prevalence of 11.8 per 10,000.

During the study period, prevalence increased from 5.8 to 14.9 per 10,000.
An absolute change of 9.1 per 10,000.
Increase was not related to maternal age, race/ethnicity, education, gender.

During the same period, the prevalence of mental retardation without autism decreased from 28.8 to 19.5 per 10,000
An absolute change of 9.3 per 10,000.

This data suggests that improvements in detection and changes in diagnosis account for the observed increase in autism.
This table shows the estimated number of Canadian children with PDD, by province, based on 2001 Census data and a prevalence rate of 60/10,000. Current numbers would be higher, about 48,000 Canadian children.

<table>
<thead>
<tr>
<th>Province</th>
<th>Population</th>
<th>Children with PPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newfoundland &amp; Labrador</td>
<td>128,220</td>
<td>769</td>
</tr>
<tr>
<td>Prince Edward Island</td>
<td>36,875</td>
<td>221</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>226,775</td>
<td>1,361</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>180,770</td>
<td>1,085</td>
</tr>
<tr>
<td>Quebec</td>
<td>1,753,650</td>
<td>10,522</td>
</tr>
<tr>
<td>Ontario</td>
<td>3,002,165</td>
<td>18,013</td>
</tr>
<tr>
<td>Manitoba</td>
<td>314,140</td>
<td>1,885</td>
</tr>
<tr>
<td>Saskatchewan</td>
<td>285,540</td>
<td>1,713</td>
</tr>
<tr>
<td>Alberta</td>
<td>840,550</td>
<td>5,043</td>
</tr>
<tr>
<td>British Columbia</td>
<td>1,000,000</td>
<td>5,000</td>
</tr>
<tr>
<td>Total for Canada</td>
<td>7,778,865</td>
<td>46,673</td>
</tr>
</tbody>
</table>

One in 165 children now estimated to have pervasive developmental disorder, three times greater than previously thought.

Prevalence: comorbid disorders
Sample population: 152,732 children under the age of 16, 187 children
DSM IV autistic disorder. AS, Rett syndrome, CDD excluded.

- 19% more than one disorder
- 12.3% known or suspected genetic condition
- 18.2% seizure disorder
- 13.4% impaired ability to walk
- 8.6% hearing impairment (1.6% severe hearing loss)
- 7.5% associated neurological disorder
- 4.3% cerebellar palsy
- 3.7% blind
- 3.2% hydrocephalic
- 1.1% fetal alcohol syndrome

Associations with Medical Disorders

- Fombonne (2003): reported on 15 studies
  rates from 0 – 16.7%
  mean 6%

- Gillberg and Coleman (1996): about 25%

- Rutter et al (1994): I think more accurate at 10%

In general the proportion of cases attributable to *specific* medical conditions is low and identifying clear causal relationships is complex.

Speculations of such associations were usually based on case reports.

For example: it was “established” clinical impression that there was a strong relationship between autism and congenital rubella – this “idea” had to be revised because it became apparent that cases became “less autistic” with the passage of time.
Associations with Medical Disorders

Data does not suggest more than chance associations between autism and:

- Down’s syndrome
- Congenital rubella
- Cerebral palsy
- Phenylketonuria
- Neurofibromatosis

However:

- 4% of autistic children have fragile X syndrome (Dykens and Volkmar 1997)
- Rates of autism are increased in tuberous sclerosis (Smalley et al 1992)
- Infants with sensory handicaps may present with “autistic like” symptoms because of unusual movements and / or language difficulties, but usually the criteria for DSM Autistic disorder are not met.

Epilepsy

- In various studies rates from 5 – 38.3%
- Mental retardation in autism is predictive for the development of seizures
- Rates are highest in adolescents and adults – up to 1/3 may have seizures

(However in 1 study (Rutter et al 1994) 39% of children under age 3 years had seizures. A UK study using narrow diagnostic criteria – i.e. severe classical cases)
Recommended testing

- Theories abound about causes for autism, very few have good supporting evidence - use accredited laboratories
- Significant language, learning problems in addition to ASD: karyotyping, Fragile X
- If regression and developmental delay, testing for Rett Syndrome (MECP2 gene)
- Pica: lead levels (no need for routine screening for lead toxicity of all children suspected of having an ASD)
- Inadequate diet due to “pickiness”: iron deficiency anemia
- Creatinine phosphokinase (CPK): boys, developmental, language, and walking delay
- If in the second year, a child shows regression or an unusual pattern of behaviour, consideration should be given to looking for a seizure disorder. EEG studies should then be done. EEGs need not be done routinely on all children with ASDs.
- Only in the presence of suspicion that a child has Tuberous Sclerosis, or in some cases, an unusual finding on EEG, should tests such as CT scanning or MRIs be done

There is no evidence to support testing:
- urinary peptides
- vitamin/mineral profiles
- intestinal antibodies
- hair analysis

American Academy of Child and Adolescent Psychiatry (1999)
American Neurological Society (2000)

Cognitive Function

Fombonne (2003):  
40% severe retardation  
30% mild to moderate retardation  
30% normal intellect  

Includes all “subtypes”: classical, Asperger’s syndrome and PDD-NOS

Classical autism:  
75% severe to profound mental retardation
Associations with Psychiatric Disorders

- Numerous reports of associations with “behavioural disorders”
- Are such associations greater than would be expected by chance alone?
- Are such symptoms and behavioural manifestations part of the primary autistic condition or the manifestation of other comorbid conditions? (Tsai 1996)

Associations with Psychiatric Disorders

Associations include:

- Oppositional behaviour
- Anxiety
- Depression
- Hyperactivity
- Poor attention
- Tics
- Obsessive and compulsive behaviour

Volkmar et al: Practice Parameters for the Assessment and Treatment of Children, Adolescents and Adults with Autism and Other pervasive Developmental Disorders. J. AM. ACAD. CHILD ADOLESC PSYCHIATRY. 38.12 Supplement, December 1999

Associations with Psychiatric Disorders

- Diagnosis of these disorders is particularly difficult in individuals who are largely or entirely mute or function in the severely or profoundly mentally retarded range
- Diagnosis of these associated problems in higher functioning individuals (e.g. the gifted, Asperger’s disorder, high functioning autism etc) may result in functional diagnoses of Generalized anxiety disorder
  - Social anxiety disorder
  - Obsessive compulsive disorder
  - Schizoid, schizotypal, avoidant or other personality disorders
- In some cases these may be assumed to be primary diagnoses standing alone and mask exploration of underlying autistic spectrum disorders. This can be particular problem in adult psychiatry
Associations with Psychiatric Disorders

Obsessive compulsive problems probably occur with equal frequency across the spectrum but manifest differently as a property of severity and degree of cognitive delay, for example:

A severely autistic person with severe to profound IQ delay may sit and arrange blocks or spin wheels in a purposeless manner

A higher functioning person may demonstrate sophisticated rituals or want to count in binary or insist on relating all numbers to degrees Kelvin

Deficits in Attention, Motor Control and Perception (DAMP)

- DAMP may be defined as a combination of motor coordination and perception dysfunctions and pervasive attention deficit, in any child of normal or low-normal intelligence, who does not meet the criteria for cerebral palsy.

DAMP

- 1% - 2% of seven year olds present with severe DAMP
- 3 to 6% of seven year olds with mild disorder

- Co-morbidities are extensive
  - Depression: approximately 30%, peaks at age ten
  - Oppositional / behavioural disorder: 50% of ten year olds
  - 50% of children with severe DAMP demonstrate autistic symptoms and traits. It is frequently impossible to distinguish severe DAMP and Asperger’s syndrome.

- Emerging personality distortion in the teenage years – up to 60%.

- High incidence of forensic difficulties and emerging criminal behaviors.

- Approximately 80% of this population have dyslexia and dysgraphia.
Triad of social, communication, and behavioral delay and SMR

Kanner's syndrome (classical autism)

Asperger's syndrome

DAMP

(extreme handicap) (milder handicap)

Kanner's Syndrome (High functioning autism)

("classical" autism + SMR) (MMR or average intellect)

Asperger's Syndrome + SMR

50% of severe DAMP

Deficits in attention, motor control and perception

DAMP (ADHD)(D)

Mild ADHD 7%

Asperger's Syndrome 9%

Hypothalamic Syndrome

Developmental Coordination Disorder / Chcury child syndrome

Severe DAMP (ADHD)(D)

1.2%

Gilberg, 1983 and Gilberg and Gilberg, 1986a

Kanner's Syndrome ("classical" autism + SMR)

High functioning autism (SNMR or average intellect)

Asperger's Syndrome

"Atypical Autism"

50% of severe DAMP
The feral child

- Reared by wolves or other wild animals.
- Mute, walk on all fours, insensitive to cold and eat only raw food.
- Numerous cases described in the 18th and 19th centuries, especially in India.
- Ireland (1875) described them as “idiots” who had been abandoned by impoverished parents and that idea that cruel animals would spare the “innocents” was an “agreeable myth”
- Tredgold felt these children had “isolation dementia”

(Tredgold AF. A Textbook of Mental Deficiency (Amenia). Balliere, Tubblin and Cox, London 1947.)
Jean Itard and “wild boy of Aveyron”

Itard: 1775-1838

- Originally a banker he had to leave “this comfortable position” to join the army. Not wanting to be in the army, he presented himself as a physician and was thus employed as an assistant physician to a military hospital in Soliers.

- Known for “Itard's catheter” – Eustachian catheter.

- Itard-Cholewa symptom: Numbness of the tympanic membrane in otosclerosis.

- But best known for the “enfant sauvage” Victor

Jean Itard and “wild boy of Aveyron”

Victor

- Found naked in the woods in 1798, aged about 11 or 12 yrs
- There was failed earlier capture when he was about 6 yrs old
- Insensitive to noise and pleasing smells
- Made only guttural sounds
- Did not imitate
- Attended only to objects he wanted
- Rocked to and fro
- Appeared profoundly melancholy but responded with outbursts of laughter in sunlight
- Ate acorns, potatoes and raw chestnuts

Jean Itard and “wild boy of Aveyron”

- Itard devised a careful behavioural program.
- Within 9 months Victor could match letters of the alphabet.
- Within 5 years he could distinguish emotions, became genuinely affectionate, loved helping people and used object imaginatively – but his spoken language never progressed beyond meaningless monosyllables.
- Itard later devoted his life to the education of deaf and mute children.
A modern “feral child”

Genie

- Until her discovery at the age of 13, she lived in a state of severe sensory and social deprivation, strapped to a potty-chair in her home in Temple City, Los Angeles, California.
- When she reached 18, Genie was returned to the care of her mother, where she stayed only a few months.
- She then lived in six different foster homes and now lives sheltered accommodation in Southern California.
- She is severely delayed, has little useful speech and displays many “autistic” symptoms.

(psychosocial dwarfism, international adoptions, famine, genocide)

Dr. Bruce Perry

- Senior Fellow, Child Trauma Academy, Houston, Texas.
- Extensive research and publications on the neurodevelopmental impact of child maltreatment.
- His paper The Neuroarcheology of Childhood Maltreatment The Neurodevelopmental Costs of Adverse Childhood Events is essential reading.