Autism Spectrum Disorder (ASD) Update

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Acknowledgements: Professor E Susser
Introducing myself

An epidemiologist working actively in the field of psychiatric epidemiology.

Epidemiologists study distribution of diseases in given populations and risk factors for these diseases.

Best ways to intervene once we better understand causality.

Engage with epidemiology of psychiatric disorders including trauma, ASD, addiction, schizophrenia and HIV/AIDS and mental health.
University of the Witwatersrand
Ever since Shelley first randomized her siblings, she knew she wanted to be a clinical epiduckologist.
Structure of today’s Autism Spectrum Disorder update…

1. Definitions related to Autism Spectrum Disorder (ASD)
2. History of ASD
3. The epidemiology of ASD
4. Theory of mind hypothesis of ASD
5. Latest insights into the Autistic Brain
6. Current Interventions
Kim Peek, Inspiration for ‘Rain Man,’ Dies at 58

By MIKE WEBER

In 1988, the film “Rain Man,” about an autistic savant played by Dustin Hoffman, shed a humane light on the travails of autism while revealing the extraordinary powers of memory that a small number of otherwise mentally disabled people possess, ostensibly as a side effect of their disability.

The film won four Oscars, including best picture, best actor and, for Barry Morrow and Ronald Bass, best original screenplay. But it never would have been made if Mr. Morrow had not had a chance meeting with Kim Peek, who inspired him to write the film.

Mr. Peek was not autistic — not all savants are autistic and not all autistic are savants — but he was born with severe hand abnormalities that impaired his physical coordination and made ordinary reasoning difficult. He could not dress himself or brush his teeth without help. He found metaphoric language incomprehensible and concept formation baffling.

But with an extraordinary skill that allowed him to read facing pages of a book at once — one with each eye — he read as many as a dozen volumes a day. Even more remarkable, he could remember what he had read.
What is Autism Spectrum Disorder?

- Autism Spectrum Disorder (ASD) refers to a group of complex disorders of brain development.
- Varying degrees, of difficulties in social interaction, verbal and nonverbal communication and repetitive behaviours.
- Term Asperger’s syndrome refers to a high functioning condition on the autism spectrum.
Diagnosis of Autism Spectrum Disorder

- Onset of ASD symptoms typically occurs by age 3.
- Symptoms may only manifest by school age.
- Research has suggested that symptoms can emerge between the ages of 6 and 18 months.
- Approximately 4 males are affected for every female.
- Sex ratio decreases with increasing severity of symptoms.
- Sex disparity consistent across all studies.
Diagnosis of Autism Spectrum Disorder

• Common ASD associated impairments include intellectual disability, attention deficits, sensory sensitivities, gastrointestinal problems, immune deficits, anxiety and depression, sleep disturbances and seizures.

• Fragile X syndrome, Tuberous Sclerosis Complex, Timothy Syndrome and Savant syndrome are common in individuals with ASD.
Comorbidity in autism spectrum disorder: A literature review

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ARTICLE INFO

Article history:
Received 10 September 2013
Accepted 10 September 2013

Keywords:
Comorbidity
Autism spectrum disorder
Attention deficit/hyperactivity disorder (AD/HD)
Epilepsy
Sleep problems
Gastrointestinal symptoms

ABSTRACT

Comorbidity is defined as the co-occurrence of two or more disorders in the same person (Matson & Nebel-Schwalm, 2007). The current study provides a review of the literature on comorbidity, in relation to comorbid psychiatric and medical disorders in babies and infants, children, adults and across the lifespan. We also examine comorbid conditions such as attention deficit/hyperactivity disorder (AD/HD), epilepsy, gastrointestinal symptoms, sleep problems, feeding problems and toileting problems in individuals with autism spectrum disorder.

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<td>Baby and Infant Scale for Children with Autism Traits (RISCUT) (Part II) (Matson, Bregel, &amp; Wilkins, 2007)</td>
<td>Infants with Autism Disorder had higher anxiety and avoidant behavior scores than those with PDD-NOS and atypically developing children</td>
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<td>Kurlanski, Matson, Bova, and Rieske (2012)</td>
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<td>RISCUT (Part II)</td>
<td>Children with Autism Disorder had more feeding and sleeping difficulties than children with PDD-NOS or atypically developing children.</td>
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Diagnosis of Autism Spectrum Disorder

• A clinical diagnosis of ASD requires expertise to detect impairment.

• Changes in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) eliminates sub-types in favour of an all inclusive Social and Communication Deficit criteria.

• NIMH RDOC encourages deconstruction of diagnostic categories and a focus on neurobiological features.

• Tools available for screening for ASD.
DSM V Criteria for ASD

Currently, or by history, must meet criteria A, B, C, and D

A. Persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays, and manifest by all 3 of the following:
   1. Deficits in social-emotional reciprocity
   2. Deficits in nonverbal communicative behaviors used for social interaction
   3. Deficits in developing and maintaining relationships

B. Restricted, repetitive patterns of behavior, interests, or activities as manifested by at least two of the following:
   1. Stereotyped or repetitive speech, motor movements, or use of objects
   2. Excessive adherence to routines, ritualized patterns of verbal or nonverbal behavior, or excessive resistance to change
   3. Highly restricted, fixated interests that are abnormal in intensity or focus
   4. Hyper-or hypo-reactivity to sensory input or unusual interest in sensory aspects of environment;

C. Symptoms must be present in early childhood (but may not become fully manifest until social demands exceed limited capacities)

D. Symptoms together limit and impair everyday functioning.
Victor the wild boy of Averyon
History of Autism Spectrum Disorder

In 1943 a child psychiatrist, Leo Kanner in the USA noticed that 11 of his patients inhabited private worlds, enjoyed rituals, were panicked by change and were often unable to speak.

A year later, a psychiatrist in Vienna, Hans Asperger saw four young patients who were disconnected from their families and others.

Aspergers’ patients spoke fluently, had ability in mathematics and science and he named them ‘little professors’

(Silberman, 2015)
Dr Leo Kanner
Dr Hans Asperger
THE CURIOUS INCIDENT
OF THE DOG IN THE NIGHT-TIME

A NEW PLAY BY SIMON STEPHENS

BASED ON THE NOVEL BY MARK HADDON
Professor Uta Frith
Professor Simon Baron-Cohen
Is Asperger syndrome/high-functioning autism necessarily a disability?

SIMON BARON–COHEN

University of Cambridge
Early Steps in the field…

Frith’s work on theory of mind in autism proposes the idea that people with autism have specific difficulties understanding other people’s beliefs and desires.

Collaborative work with Simon Baron-Cohen who was her PhD student.

Individuals with autism have ‘weak central coherence’, and are better than typical individuals at processing details but worse at integrating information from many different sources.

A neuro-cognitive approach to developmental disorders. Underlying cognitive causes of these disorders and to link them to behavioural symptoms as well as to brain systems.
The epidemiology of ASD

Epidemiology of Autism Spectrum Disorders

Alison Presmanes Hill, Katharine Zuckerman and Eric Fombonne
The Changing Epidemiology of Autism Spectrum Disorders

Kristen Lyall,¹ Lisa Croen,² Julie Daniels,³ M. Daniele Fallin,⁴,⁵ Christine Ladd-Acosta,⁴,⁶ Brian K. Lee,⁷,⁸ Bo Y. Park,⁴,⁵ Nathaniel W. Snyder,¹ Diana Schendel,⁹,¹⁰,¹¹ Heather Volk,⁴,⁵ Gayle C. Windham,¹² and Craig Newschaffer¹
The epidemiology of ASD

• In the USA in 2012, the Center for Disease Control estimated that 1.5% of children aged 8 had ASD.

• Finding based on active surveillance and review of health and education records.

• Community awareness, effective screening tools and possibly new DSM criteria may account for higher prevalence of ASD than previously thought.

• Tremendous societal costs including comorbid conditions.
Suicidal ideation and suicide plans or attempts in adults with Asperger’s syndrome attending a specialist diagnostic clinic: a clinical cohort study

Sarah Cassidy, Paul Bradley, Janine Robinson, Carrie Allison, Meghan McHugh, Simon Baron-Cohen

Summary
Background Asperger’s syndrome in adulthood is frequently associated with depression, but few studies have explored the lifetime experience of self-reported suicidal ideation and suicide plans or attempts in this clinical group. We aimed to assess this prevalence in a clinical cohort of patients in the UK.

Method In a clinical cohort study, we undertook a retrospective analysis of clinical survey data from adults newly diagnosed with Asperger’s syndrome at a specialist diagnostic clinic between Jan 23, 2004, and July 8, 2013, in England. Patients completed a self-report questionnaire before clinical assessment, recording lifetime experience of depression, suicidal ideation, and suicide plans or attempts, along with self-reported measures of autistic traits and empathy. We compared the rate of suicidal ideation in the sample with published rates of suicidal ideation in the general population and other clinical groups. We also assessed associations between depression, autistic traits, empathy, and likelihood of suicidal ideation and suicide plans or attempts.

Findings 374 adults (256 men and 118 women) were diagnosed with Asperger’s syndrome in the study period. 243 (66%) of 367 respondents self-reported suicidal ideation, 127 (35%) of 365 respondents self-reported plans or attempts at suicide, and 116 (31%) of 368 respondents self-reported depression. Adults with Asperger’s syndrome were significantly more likely to report lifetime experience of suicidal ideation than were individuals from a general UK population sample (odds ratio 9·6 [95% CI 7·6–11·9], p<0·0001), people with one, two, or more medical illnesses (p<0·0001), or people with psychotic illness (p=0·019). Compared with people diagnosed with Asperger’s syndrome without depression, people with Asperger’s syndrome and depression were more likely to report suicidal ideation (p<0·0001) and suicide plans or attempts (p<0·0001).

Interpretation Our findings lend support to anecdotal reports of increased rates of suicidal ideation in adults with Asperger’s syndrome, and depression as an important potential risk factor for suicidality in adults with this condition. Because adults with Asperger’s syndrome often have many risk factors for secondary depression (eg, social isolation or exclusion, and unemployment), our findings emphasise the need for appropriate service planning and support to reduce risk in this clinical group.
The epidemiology of ASD

- Centre for Disease Control (CDC) in the USA funds large surveys to detect prevalence of ASD in the USA across different groups.
- What is required is ascertainment of cases through effective screening and universal definitions.
- Large sample size and definition of samples.
- Danger of under-estimating prevalence of ASD.
- Strong registry allows for the possibility of detecting incidence of ASD.

(Fombonne, 2003)
Professor Daniel Geschwind
Genetics of Autism Spectrum Disorders

Daniel H. Geschwind
Program in Neurogenetics, UCLA Department of Neurology, Center for Autism Research and Treatment, Semel Institute, and Departments of Psychiatry and Human Genetics, David Geffen School of Medicine at UCLA, 695 Charles E Young Drive South, Los Angeles, CA 90095-1761
Genetics a quick recap...
Genetics a quick recap…

• DNA, or deoxyribonucleic acid, is the hereditary material in humans, present in all cells.

• Most DNA is located in the cell nucleus (where it is called nuclear DNA), but a small amount of DNA can also be found in the mitochondria.

• The information in DNA is stored as a code made up of four chemical bases: adenine (A), guanine (G), cytosine (C), and thymine (T).

• The order, or sequence, of these bases determines the information available for building and maintaining an organism, similar to the way in which letters of the alphabet appear in a certain order to form words and sentences.
Genetics a quick recap...

- Gene, a segment of DNA gives instructions to the cell on how to make a certain protein.
- Chromosomes, a structure of many genes are made from strands of DNA.
- DNA is wrapped together to form chromosomes.
- Each cell has 46 chromosomes.
- Each gene adds a specific protein to the recipe.
- Proteins build, regulate and maintain your body. For instance, they build bones, enable muscles to move, control digestion, and keep your heart beating.
What exactly is a human genome?

• A genome is an organism’s complete set of DNA, including all of its genes.

• Each genome contains all of the information needed to build and maintain that organism.

• In humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus.
How can the message go wrong?

• A DNA mutation/variant in one of a person’s genes e.g. a sequence change.
• This change in sequence can change the way that the gene works, for example by changing the protein that is made.
• A person can be born with a different number of chromosomes i.e. 1 extra or 1 missing.
• A small part of a chromosome can be missing.
Genetics of Autism Spectrum Disorder

• Since the 1980s there has been interest in the genetic aetiology of ASD.
• Genetic aetiology supported by twin studies with heritability estimates in Europe and the USA ranging from 50% to 90%.
• Estimates of recurrence risk among siblings of autistic children range from 3% to 18%.
• Reported genes among common variants include those implicated in oxytocin and serotonin transport.

(Tick et al, 2016)
Insights into Autism Spectrum Disorder Genomic Architecture and Biology from 71 Risk Loci

Why is the locus important?

‘The discovery of the first autism locus at genome-wide significance means that basically we found a region of the genome that is part of the chromosomes that we inherit that is highly likely to have within it a gene that predisposes to autism. This is the first step in the process of identifying the gene, so therefore it is very important. It is as if you are looking for a needle in a haystack but you’re in a field of a thousand haystacks. Here, we’ve found the haystack, and now we have to find that needle within the haystack, and we are moving in fairly rapidly now because genetic technology allows us to do this very rapidly. This particular region is on chromosome 17q, that is the long arm of chromosome 17’
Exome analysis in ASD

• We have spoken about the 3 billion nucleotides or “letters” of DNA.
• Only a small percentage — 1.5 percent — of those letters are actually translated into proteins, the functional players in the body.
• The “exome” consists of all the genome’s exons, which are the coding portions of genes.
• The term exon was derived from “EXpressed regiON,” since these are the regions that get translated, or expressed as proteins.
Exome analysis in ASD

- The exome (the protein-coding region of the human genome) represents less than 2% of the genetic code, but contains ~85% of known disease-related variants.
- Some cases of autism reflect rare, inherited point mutations that existing study designs, often involving families with one or two affected individuals, are not designed to capture.
- Partial loss of functioning in particular genes.

(Yu et al, 2013)
Further complexities in genetic aetiology

• Difficulties with studying genetics of ASD as it is very heterogeneous.

• Measurable components of the disorder, called endophenotypes e.g. language and social behaviour.

• We can measure in the unaffected relatives.

• May be seen in a less critical form.

• E.g. Child with ASD who is not speaking, his siblings may have some form of mild language delay,
  • We can use that information and measure that to have more power to identify genes.
Let’s define gene environment interactions…
Gene environment interactions

An environmental risk factor, a “high-risk genotype,” and a disease of interest.

Examples of environmental risk factors include: exposure, either physical (e.g., radiation, temperature), chemical (e.g., polycyclic aromatic hydrocarbons), or biological (e.g., a virus); a behaviour pattern (e.g., late age at first pregnancy); or lack of folate.

High-risk genotype is broadly defined.

(Ottman, 2010)
Interplay among genes and environment

Mutagens – affect a structural change in the DNA.

Gene-gene interactions- environmental exposure could trigger the expression of a gene that in turn modifies other genes.

Transcription Factors- proteins that help turn specific genes "on" or "off" by binding to nearby DNA.

Epigenetics-changes in gene expression.
Environmental Factors in ASD

• An intriguing area of ASD aetiology…
• Hampered by myths.
• Among the first was that of refrigerator mothers.
• Brain child of Bruno Bettelheim, a child psychologist.
• Children with ASD were the product of mothers who were cold, distant and rejecting, thus depriving babies of the chance to "bond properly".
During the 1950s and 1960s, the medical establishment, thanks to Bruno Bettelheim, blamed autism on the child's mother for failing to bond with her child. These mothers were called a "refrigerator mother." Thousands of autistic children received gloomy therapies based on this theory. Many children were taken away from their parents. Their mothers endured a difficult period of blame, guilt and self-doubt.

"the precipitating factor in infantile autism is the parent's wish that his child should not exist."
Dr Andrew Wakefield
Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Bereiowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associated by the parents, with measles, mumps, and rubella.

Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and vomiting and, in some cases, food intolerance. We describe the clinical findings, and gastrointestinal features, of these children.

Patients and methods

12 children, continuing, referred to the department of paediatric gastroenterology as a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms (nausea, abdominal pain, bloating and food intolerance), were investigated. All children were admitted to the ward for a week, accompanied by their parents.

Clinical investigations

We took histories, including details of immunisations and exposure to infection diseases, and assessed the children. In 11 cases, the history was obtained by the senior clinician (JW-S). Neonatal and psychiatric assessments were done by consultant staff (PH, MB) with HMS-4 criteria. Developmental assessments included a review of prospective developmental records.
‘In 1998, Andrew Wakefield and 12 of his colleagues published a case series in the Lancet, which suggested that the measles, mumps, and rubella (MMR) vaccine may predispose to behavioral regression and pervasive developmental disorder in children. Despite the small sample size (n=12), the uncontrolled design, and the speculative nature of the conclusions, the paper received wide publicity, and MMR vaccination rates began to drop because parents were concerned about the risk of autism after vaccination. Almost immediately afterward, epidemiological studies were conducted and published, refuting the posited link between MMR vaccination and autism. The logic that the MMR vaccine may trigger autism was also questioned because a temporal link between the two is almost predestined: both events, by design (MMR vaccine) or definition (autism), occur in early childhood.’
TRUMP’S DANGEROUS SUPPORT FOR CONSPIRACIES ABOUT AUTISM AND VACCINES
Aetiology of ASD

• Increase in prevalence of ASD has led to interest in environmental risk factors.
• Autism Birth Cohort (ABC) aimed to explore prenatal or postnatal infection, obstetric risk factors, and dietary and/or environmental exposure to potential toxins during pregnancy and postnatal life.
• ABC resources include a serial collection of detailed questionnaires and biological samples for genetic, transcriptomic, proteomic, microbiologic and toxicologic analyses.
Environmental risk factors for ASD

The International Collaboration for Autism Registry Epidemiology (iCARE): Multinational Registry-Based Investigations of Autism Risk Factors and Trends

Diana E. Schendel · Micheline Bresnahan · Kim W. Carter · Richard W. Francis · Mika Gissler · Therese K. Grønborg · Raz Gross · Nina Gunnes · Mady Hornig · Christina M. Hultman · Amanda Langridge · Marlene B. Lauritsen · Helen Leonard · Erik T. Parner · Abraham Reichenberg · Sven Sandin · Andre Sourander · Camilla Stoltenberg · Auli Suominen · Pål Surén · Ezra Susser
Parental Obesity and Risk of Autism Spectrum Disorder

WHAT'S KNOWN ON THIS SUBJECT: Maternal prepregnancy obesity is associated with an increased risk of neurodevelopmental disorders in children, but previous studies have not taken paternal obesity into account. This has precluded differentiation between the effects of intrauterine exposures and potential genetic associations.

WHAT THIS STUDY ADDS: Robust associations were demonstrated between paternal obesity and the risk of autistic disorder and Asperger disorder in children. This study is the first to implicate paternal obesity as a risk factor for autism, and replication is warranted.

AUTHORS: Pål Surén, MD, MPH, a,b Nina Gunnes, PhD, a,c Christine Roth, MD, MSc, a,b Michaeline Bresnahan, PhD, d,e Mady Hornig, MD, f Deborah Hirtz, MD, f Kari Kveim Lie, MD, g W. Ian Lipkin, MD, h Per Magnus, MD, PhD, i Ted Reichborn-Kjennerud, MD, PhD, j Synne Schjølberg, MSc, k Ezra Susser, MD, DrPH, l,n Anne-Siri Øyen, PhD, m,n George Davey Smith, MD, PhD, n and Camilla Stoltenberg, MD, PhD. p,q

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Association Between Maternal Use of Folic Acid Supplements and Risk of Autism Spectrum Disorders in Children

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Importance  Prenatal folic acid supplements reduce the risk of neural tube defects in children, but it has not been determined whether they protect against other neurodevelopmental disorders.

Objective  To examine the association between maternal use of prenatal folic acid supplements and subsequent risk of autism spectrum disorders (ASDs) (autistic disorder, Asperger syndrome, pervasive developmental disorder—not otherwise specified [PDD-NOS]) in children.

Design, Setting, and Patients  The study sample of 85,176 children was derived from the population-based, prospective Norwegian Mother and Child Cohort Study (MoBa). The children were born in 2002-2008; by the end of follow-up on March 31, 2012, the age range was 3.3 through 10.2 years (mean, 6.4 years). The exposure of primary interest was use of folic acid from 4 weeks before to 8 weeks after the start of pregnancy, defined as the first day of the last menstrual period before conception. Relative risks of ASDs were estimated by odds ratios (ORs) with 95% CIs in a logistic regression analysis. Analyses were adjusted for maternal education level, year of birth, and parity.

Main Outcome Measure  Specialist-confirmed diagnosis of ASDs.

Results  At the end of follow-up, 270 children in the study sample had been diagnosed with ASDs: 114 with autistic disorder, 56 with Asperger syndrome, and 100 with PDD-NOS. In children whose mothers took folic acid, 0.10% (64/61,012) had
Theory of mind hypothesis in ASD

Let us revisit the theory of mind hypothesis in ASD...

Intention is to link the Theory of Mind Hypothesis to Insights into the Autistic Brain
Theory of Mind and Autism: A Review

SIMON BARON-COHEN

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Theory of mind hypothesis in ASD

• Theory of mind is the ability to infer the full range of mental states (e.g. beliefs, desires, imagination) of oneself AND others.

• Deficit in theory of mind is a core cognitive feature in ASD.

• Example 4 year old children can distinguish between appearance and reality.

• Difficult for children with ASD.
Some Tests of Theory of Mind in People with Autism

1. The mental-physical distinction (Baron-Cohen, 1989a)
2. Understanding of the functions of the mind (Baron-Cohen, 1989a)
3. The appearance-reality distinction (Baron-Cohen, 1989a)
4. First-order false belief tasks (Baron-Cohen et al., 1985, 1986; Leekam & Perner, 1991; Perner et al., 1989; Reed & Peterson, 1990; Swettenham, 1996; Swettenham et al., 1996)
5. “Seeing leads to knowing” tests (Baron-Cohen & Goodhart, 1994; Leslie & Frith, 1988)
6. Tests of recognizing mental state words (like “think,” “know,” and “imagine”) in a wordlist (Baron-Cohen et al., 1994)
7. Tests of production of the same range of mental state words in their spontaneous speech (Baron-Cohen et al., 1986; Tager-Flusberg, 1992)
8. Tests of the production of spontaneous pretend play (Baron-Cohen, 1987; Lewis & Boucher, 1988; Ungerer & Sigman, 1981; Wing et al., 1977)
9. Tests of understanding more complex causes of emotion (such as beliefs) (Baron-Cohen, 1991; Baron-Cohen et al., 1993)
10. Tests of recognizing the eye-region of the face as indicating when a person is thinking and what a person might want (Baron-Cohen et al., 1995; Baron-Cohen & Cross, 1992)
11. Tests of being able to monitor their own intentions (Phillips et al., 1998)
12. Tests of deception (Baron-Cohen, 1992; Sodian & Frith, 1992; Yirmiya et al., 1996)
13. Tests of understanding metaphor, sarcasm, and irony
14. Tests of pragmatics in their speech (Baron-Cohen, 1988; Tager-Flusberg, 1993)
15. Tests of recognition of violations of pragmatic rules (Surian et al., 1996)
17. Correlation with real-life social skills, as measured by a modified version of the Vineland Adaptive Behaviour Scale (Frith et al., 1994)
18. Second-order false belief tests (Baron-Cohen, 1989b; Bowler, 1992; Happe, 1993; Ozonoff et al., 1991)
19. Understanding stories in which characters are motivated by complex mental states, such as bluff and double bluff (Happe, 1994)
20. Decoding complex mental states from the expression in the eye-region of the face (Baron-Cohen & Hammer, 1997; Baron-Cohen et al., 1997b,c, 1997)
The Autistic Brain
HELPING DIFFERENT KINDS OF MINDS SUCCEED

TEMPLE GRANDIN
and RICHARD PANEK
Parts of the Brain
Affected by Autism

Cerebral Cortex:
A thin layer of gray matter on the surface of the cerebral hemispheres. Two thirds of this area is deep in the tissues and folds. This area of the brain is responsible for higher mental functions, general movement, perception and behavior reactions.

Amygdala:
This is responsible for all emotional responses including aggressive behavior.

Basal Ganglia:
This is gray masses deep within the cerebral hemisphere that connects the cerebrum and the cerebellum. It helps regulate automatic movement.

Hippocampus:
This makes it possible to remember new information and recent events.

Corpus Callosum:
This consists of closely packed bundles of fibers that connect the right and left hemispheres of the brain and allows them to communicate with one another.

Brain Stem:
The Brain Stem is located in front of the cerebellum and serves as a relay station, passing messages between various parts of the body and the cerebral cortex. It controls the primitive functions of the body essential to survival including breathing and heart rate.

Cerebellum:
This is located at the back of the brain. It fine tunes motor activity, regulates balance, body movements, coordination and the muscles used for speaking.
Basic structure of a neuron
A diagram of a synapse
A diagram of a neurotransmitter
Interaction between neuron and synapse
Reduced GABAergic Action in the Autistic Brain

Highlights
- Behavioral marker of inhibitory/excitatory neurotransmission is perturbed in autism
- Marker predicts higher-order autistic symptom severity
- Inhibitory and excitatory neurotransmitters measured in the brain predict behavior
- Action of the inhibitory neurotransmitter, GABA, is reduced the autistic brain

Authors
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In Brief
An imbalance in inhibitory/excitatory neurotransmission is proposed to affect the autistic brain, but empirical evidence in humans is lacking. Robertson et al. report a link between a robust autistic perceptual symptom and reduced action of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA), in the brains of autistic individuals.
Developing Human Brain
Loss of mTOR-Dependent Macroautophagy Causes Autistic-like Synaptic Pruning Deficits

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http://dx.doi.org/10.1016/j.neuron.2014.07.040
Baron-Cohen’s theory of empathy

Drawing on his work on theory of mind in ASD, Baron Cohen posed a theory of empathy in 2011.

Suggests an empathy spectrum

An empathy neuro-circuitry

Theory of human cruelty

ASD under-activity in frontal operculum, amygdala and anterior insula.
SIMON BARON-COHEN
ZERO DEGREES OF EMPATHY
A NEW UNDERSTANDING OF CRUELTY AND KINDNESS

"Fascinating ... dazzling ... a full-scale assault on what we think it is to be human"
SUNDAY TELEGRAPH
THE SCIENCE OF EVIL

KEY
AI - anterior insula
Amyg - amygdala
cACC - caudal anterior cingulate cortex
dMPFC/vMPFC - dorsal/ventral medial prefrontal cortex
FO - frontal operculum
IFG - inferior frontal gyrus
IPL - inferior parietal lobule
IPS - inferior parietal sulcus
MCC - middle cingulate cortex
OFC - orbitofrontal cortex
pSTS - posterior superior temporal sulcus
RTPJ - right temporal-parietal junction
SMC - somatosensory cortex

Figure 4: Regions in Empathy Circuit (produced by Mike Lombardo, with thanks)
Interventions ASD
Interventions ASD

Dr. Catherine Lord
Founding Director, Center for Autism, NY-Presbyterian Hospital
Interventions ASD

A longitudinal study of two cohorts of children referred for possible diagnosis of autism at age two.

The sample is now in late adolescence.

We are looking at changes in diagnostic features and academic achievement as well as family well-being.
Interventions ASD

• Evidence-based treatment of core deficits of autism
• 5 different multi-site randomized controlled trials
• Parent-implemented treatment of communication deficits in toddlers with autism
• Group treatment of social skills in verbal school age children with autism
• A pilot project creating a communication treatment specifically developed for low income families of toddlers and preschool children with autism.
Interventions ASD

This project seeks to confirm reduced oxytocin levels in an independent sample of people with Asperger Syndrome.

Treatment trials of intravenous oxytocin in autism report benefits for emotion recognition.

A nasal spray since this acts directly on the brain.
Mapping ASD Research on the African continent
Professor Petrus de Vries
Professor Charles Newton

Profile

Charles Newton: changing perceptions of neurodisability in Africa

Born in the Great Rift Valley in Kenya, Charles Newton has always had “Africa in the system”, he says. And throughout a career that has criss-crossed the globe, he has done more than most to shine a light on two aspects of morbidity often overlooked on a continent where the focus has understandably been on mortality: neurodevelopmental disorders and neurodisability. “Now that mortality in African children is decreasing, I think all the issues around neurodisability and quality of life for people with neurodisabilities need to be addressed”, Newton told The Lancet. “I think that’s one of the biggest challenges for Africa over the next couple of decades”, he insists. From his base at the Kenya Medical Research Institute-Wellcome Trust Research Programme, in Kilifi on the Kenyan coast, Newton is helping to meet that challenge head on.

Newton, who is also Cheryl and Reese Scott Professor
Dr Rosa Hoekstra
Dr Angelina Kakooza
Adaptation of the “ten questions” to screen for autism and other neurodevelopmental disorders in Uganda

Angelina Kakooza-Mwesige¹, Keron Ssebyala¹, Charles Karamagi¹, Sarah Kiguli¹, Karen Smith², Meredith C Anderson², Lisa A Croen³, Edwin Trevathan⁴, Robin Hansen⁵, Daniel Smith² and Judith K Grether²
So much needs to be done in Africa!
Essa Adam (July 1993-May 2016)
In conclusion…

‘Suzie taught me 4 important things in life. First, that you can be happy with absolutely nothing materially. She radiated happiness and in that sense I know she had a good quality of life.

Second, that no matter what life throws at you, you can keep your sense of humour and laugh your way through it. Every visit with her I came away happier than I arrived, and buoyed up. She had that special quality.

Third, you can have a deep relationship without words, even without concepts, just by being with another person, holding hands, and connecting.

And finally, social policies can try to divide a parent from their child, or a brother and sister from each other, but they won’t succeed. The love is too strong.

Suzie taught us more than we taught her, and our lives were richer for having shared the journey with her.’

(Simon Baron-Cohen)