



TICS
CSWS WING PANS IDD
ADD AUTISM ATTENTION ESES
HYDROCEPHALUS ENCEPHALITIS 22Q11DEL
TOURETTE EPILEPSY TUBEROUS SCLEROSIS MAPP CHARGE
ESSENCE VITAMIN D KANNER OCDEDA
ADHD EXECUTIVE FAS ODD NVLD FRAGILE X
SOCIAL MOEBIUS COHERENCE NEVILLE SUBSTANCE USE
BIEDERMAN FASD LANDAU-KLEFFNER ADHD SLI CSWS
FEBRILE SEIZURES DCD MIND TICS DUCHENNE MBD
VERBAL LD ASPERGER COLEMAN COMMUNICATION
DAMP OCD VALPROIC PERCEPTION
CP PREMATURITY PANDAS BORDERLINE TOURETTE
EPILEPSY CRIMINALITY FEBRILE SEIZURES BARKLEY ADD
PREMUTATION MIND DCD RAD HELLER
MEMORY CP
IDD
CHARGE
PANS
CD



From child neuropsychiatry 1996 through ESSENCE 2009 to DSM-6? Is ESSENCE really of the essence? A personal review

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- University of Stellenbosch (South Africa)
- Institute of Child Health, University College London (England)
- Institut Pasteur, Paris (France)

Gothenburg, March 2021



The last quarter of a century in "child neuropsychiatry": Before 1996

- Laretta Bender
- Lorna Wing
- Anna-Lisa Anell
- Martin Bax
- The Hagbergs
- Michael Rutter
- Max Frisk
- Olle Hansson
- The Gillbergs (theses in 1981 and 1987)
- Brian Neville
- Michael Bohman
- Peder Rasmussen
- Anne-Liis von Knorring
- Berit Lagerheim
- Elisabeth Fernell
- Björn Kadesjö
- **DIAGNOSIS AND TREATMENT OF AUTISM 1989 GOTHENBURG SWEDEN**



The last quarter of a century in "child neuropsychiatry":1996

- All case-records of first-time visitors to an outpatient child and adolescent psychiatric centre from 1992 to 1996 were reviewed, and re-diagnosis was performed according to DSM-III-R.
- **Fewer than 50% were seen by a psychiatrist. neuropsychiatric diagnosis rose markedly from (0% in 1977) 24% in 1992 to 45% in 1996.**
- **AUTISM 1996 Svenska Mässan Gothenburg Sweden**
 - Kopp & Gillberg 1996, 1999, Läkartidningen, Gillberg 2010 Res Dev Disabil, revised Gillberg 2021 JKP, see also Gillberg & Höök 1977 Socialmedicinsk Tidskrift



The last quarter of a century in "child neuropsychiatry":1997

- **Long-term positive effects of amphetamine treatment in children with ADHD** (only ever long-term RCT with placebo)
- 7- to 15-year-olds in Göteborg, Sweden, were screened for **selective mutism**. The rate of **typical selective mutism** was **0.2%**. **Subclinical** cases occurred in **0.9% of children**.
- **School refusal** prevalence and outcome findings were reported from Göteborg. **More than 1%** had school refusal (ages 7-12 years) in the 1970s and outcome after age 30 years was poorer than in other child psychiatric cases.
- Do these two groups correspond to those that we now refer to as **hikkikomori**, **"hemma-sittare"**?
 - Gillberg et al 1997 Arch Gen Psychiatry, Kopp & Gillberg 1997 JCPP, Flakierska-Praquin et al 1997 Br J Psychiatry



The last quarter of a century in "child neuropsychiatry":1998

- **50 cases of PANDAS described for the first time by Susan Swedo**
- **6.1% of 7-year-old children in Karlstad had the combination of ADHD and DCD (=DAMP);** similar rates had been reported in Göteborg 16 years earlier, later used as "evidence" of fraudulent research
- Ganglioside-levels were found to be increased in the CSF of children with autistic disorder both in Göteborg and Oslo, indicating **increased synaptic activity in autism**
- **Retinopathy of prematurity (ROP) was found to be strongly linked to autism (56% vs 14% other forms of congenital blindness)**
 - Swedo et al 1998 JCAP, Kadesjö & Gillberg 1998 DMCN, Nordin et al 1998 DMCN, Ek et al 1998



The last quarter of a century in "child neuropsychiatry":1999

- **Gillberg & Wing reviewed autism prevalence studies finding 1%** probably had the disorder, findings that probably apply today, in the face of reported enormous increases in the rate of "the disorder" worldwide
- **Ehlers, Wing and Gillberg "officially" published the ASSQ which had been validated for the first time by Ehlers and Gillberg in 1993, ASSQ now the most widely used autism screening instrument in the world for children**
 - Gillberg & Wing 1999 Acta Psychiatr Scand, Ehlers et al 1999 JCPP

The last quarter of a century in "child neuropsychiatry": 2000

- **The first-ever review of comorbidity in autism**
- **First-ever population-based study of Tourette syndrome prevalence**
- **Natural outcome study of ADHD+DCD showing poor outcome from 7-21 years of age**
- **Gillberg and Coleman publish Third Edition of Biology of the Autistic Syndromes**
- Gillberg & Billstedt 2000 Acta Psychiatr Scand, Kadesjö & Gillberg 2000 JAACAP, Rasmussen & Gillberg 2000 JAACAP, Gillberg & Coleman, Cambridge University Press 2000

Leif Elinder, Eva Kärfve & the Scientologists appear on the stage



The last quarter of a century in "child neuropsychiatry": 2000-2007 (2008)

- **STRIDER UNDER HJÄRNÅLDERN. Om ADHD, biologism, sociologism. Vanna Beckman. Enskededalen: Pavus utbildning, 2007.**
- Vanna Beckman skrev en bok om en av de värsta förtalskampanjer som genomförts i Sverige under de senaste 100 åren. Den inleddes under slutet av 1990-talet av barnläkaren Leif Elinder och lundasociologen Eva Kärfve. År 2000 gav Eva Kärfve ut sitt *magnum opus* i kampanjen, boken *Hjärnspöken – DAMP och hotet mot folkhälsan*, i vilken svensk damp- och adhd-forskning sågades i allmänhet, och göteborgsprofessorn Christopher Gillberg i synnerhet påstods droga ned barnen samt stå för en ondskefull människosyn



2000-2007 (2008) “The Gillberg Affair”

- Hela processen, och särskilt domarna i Kammarrätten i Göteborg, torde representera ”den mest intressanta juridiska härdsmltan i Sverige på många år”. Christopher Gillberg sammanfattade det kafkaliknande skeendet sålunda (citerat ur Beckmans bok, s. 171): ”Det kan enligt min mening inte vara rimligt att jag, först, av staten (genom Göteborgs universitets etiska kommitté), åläggs att avge stränga sekretesslöften (personligen och med egen namnteckning) för att få genomföra medicinsk forskning, därefter, av staten (genom Göteborgs universitets rektor), åläggs att bryta dessa hundratals sekretesslöften under hot om anmälan till Statens Ansvarsnämnd, sedan, av staten (i form av Justitieombudsmannen och åklagare), åtalas, och, till sist, av staten (tingsrätt och hovrätt), döms som brottsling för att jag inte brutit de sekretesslöften, som jag haft statens uppdrag att avge. Någonting är uppenbart fel i denna kedja, men det är svårt att se hur felet kan vara mitt.”
- **Elias Eriksson & Kristoffer Hellstrand**, *GU-Journalen*, *SvD*, *GP*, interna skrivelser GU
- **Elisabeth Fernell & Eva Nordin et al** nationell konferens till stöd för gruppen 2006
- **Gornall, Jonathan**, ”Hyperactivity in children: the Gillberg affair”, *British Medical Journal* 335, 2007, s. 370–373
- **Mats Johnson**, ”Professor Gillberg och hans medarbetare måste få upprättelse”, *Läkartidningen*, 2006
- **Elisabeth Rynning**, ”Integritetsskyddet i forskningen – en känslig historia”, *Förvaltningsrättslig Tidskrift*, 2005, s. 459–486





The last quarter of a century in "child neuropsychiatry": 2001

- **The AQ arrives on the scene and the number of self-diagnosed cases of autism goes up**
- **Neuropsychiatric disorders (but not classic autism) extremely common in di George (22q11 del) syndrome**
- **Autism much overrepresented in Down syndrome – previously said to be not "present" in DS**
 - Baron-Cohen et al 2001 JADD, Niklasson et al 2001 Genetics in Medicine, Rasmussen et al 2001 DMCN



The last quarter of a century in "child neuropsychiatry": 2002

- **Strong link between glutamate receptor gene variation/mutation and autism documented in the PARIS study (Gillberg & Leboyer)**

- Jamain et al 2002 Mol Psychiatry



The last quarter of a century in "child neuropsychiatry": 2003

- **Mutations of X-linked neuroligin genes in autism documented in Gothenburg family**
- **Long-term outcome of anorexia nervosa not as gloomy as previously believed, however link between ASD in anorexia and poor prognosis**

- Jamain et al 2003 Nature Genetics, Råstam et al 2003 ECAP



The last quarter of a century in "child neuropsychiatry": 2004

- Evidence of interhemispheric transfer problems in autism
- **Development of the FTF (5-15) questionnaire (currently the most widely used screener for "ESSENCE" problems in the Nordic countries)**
 - Nydén, Carlsson, Carlsson, Gillberg 2004 DMCN, Kadesjö et al 2004, ECAP



The last quarter of a century in "child neuropsychiatry": 2005

- **Working memory training moderately effective in ADHD**
 - **Development and validation of the A-TAC**
 - **One third to one half of all individuals with classic autism develop epilepsy before age 40**
- Klingberg et al 2005 JACAP, Hansson et al 2005 Br J Psychiatry Danielsson et al 2005 Epilepsia



The last quarter of a century in "child neuropsychiatry": 2007

- **Posserud, Lundervold and Gillberg show the extremely high rates of autistic features in the general population of 7-9-year-old Bergen children (only 16% having no indication whatsoever of autistic features) – Wing always maintained that "there is a touch of autism in everybody"**
 - Posserud et al 2006 JCPP



The last quarter of a century in "child neuropsychiatry": 2008

- **High rate of melatonin synthesis abnormalities in autism**

- Melke et al 2008 Mol Psychiatry



The last quarter of a century in "child neuropsychiatry": 2009

- **Moderately positive effects of Omega 3/6 in the treatment of ADHD (RCT with placebo)**
- **ESSENCE launched at the Royal College of Psychiatrists meeting in Liverpool**
 - Johnson et al 2009 JAD, Gillberg 2009



The last quarter of a century in "child neuropsychiatry": 2010

- **Girls with social and/or attention deficits have extremely high rates of diagnostic level autism and ADHD – this study set in motion a whole "movement" re "female autism"**
- Low vitamin D levels in mothers from Somalia who have children with autism (vs non-autism)
- ESSENCE-paper published (fifth attempt "successful")
- GNC started by joining efforts from GU, SU and STENA
 - Kopp, Kelly and Gillberg 2010 JAD, Fernell et al 2010 Acta Paediatrica, Gillberg 2010 Res Dev Disabil



MBD, DAMP, ADD, ADHD, ASD, TS, DCD, IDD, LD, PANS, RAD, BPS, CP, EP, and their many associated neurodevelopmental/psychiatric/physical problems – what is the essence?

- **ESSENCE - Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations** (Gillberg 1981/2009/2010/2021)
- **Pre-school predictors of adult **academic failure**, being bullied and bullying, social exclusion, substance use, psychiatric disorder, eating disorders, pain syndromes, empathy problems, antisocial lifestyle, poor ADL skills, and early death**
 - **ADHD with or without ODD (Oppositional Defiant Disorder) 5-7%**
 - **SLI/LD (Language Disorder including precursors of Dyslexia) 4-6%**
 - **DCD (Developmental Coordination Disorder) 5%**
 - **IDD (Intellectual Disability/Intellectual Developmental Disorder) 2%**
 - **ASD (Autism Spectrum Disorder) 1.2% - with or without EDD/PDD**
 - **ARFID (Avoidant Restrictive Food Intake Disorder) 1%??**
 - **TD/TS/OCD (Tic Disorders/Tourette Syndrome/OCD) 1%**
 - **RAD (Reactive Attachment Disorder)? 0.5-1.5%**
 - **PANS (Pediatric Acute-onset Neuropsychiatric Syndrome)? 0.1%?**
 - **(BIF (Borderline Intellectual Functioning) 12%)**
 - **(BPS (Behavioural Phenotype Syndromes, including FAS and VAS) 2.5%)**
 - **(“NEUROLOGICAL SYNDROMES” (Epilepsy syndromes and other neurological disorders (HC, CP, neurometabolic): LKS, CSWS, FS+, FS? 0.8%)**



The last quarter of a century in "child neuropsychiatry": 2011

- **High-intensity ABA no better than low-intensity ABA in autism- naturalistic independent study of 208 preschool children**
- **GNC inaugurated by HMD Queen Silvia and SUZANNE REUTER**
 - Fernell et al 2011 Res Dev Disabil



The last quarter of a century in "child neuropsychiatry": 2012

- **Medication for ADHD and criminality decreases risk of criminality by 32% in men and 41% in women, Lichtenstein's group has since published results indicating positive results as regards accidents and possibly suicide attempts**
- **Open-label** study of modified CPS/PR-ESSENCE showing positive results for ADHD+ODD, later RCT showing moderately to very positive results at 6- and 12- months follow-up
- **First-ever prevalence study of autism in preschoolers showing 0.8%**
- **No evidence for "evidence-based" triple-P in pre-schoolers**
- **Is ASD common in the background of schizophrenia?**
- **And Mary Coleman and Christopher Gillberg published the fourth Edition of THE AUTISMS**
 - Lichtenstein et al 2012 N Engl J Med, Johnson et al 2012 Acta Paediatr, Nygren et al 2012 JADD, Wilson et al 2012 BMC Medicine, Unenge-Hallerbäck et al 2012 Psychiatry Res, Lugnegård et al 2012 Schizophrenia Res, Coleman and Gillberg 2012 Oxford University Press, Johnson et al 2021, submitted



The last quarter of a century in "child neuropsychiatry": 2013

- **Extremely high rate of ADHD in obesity already found in 2008 again stressed**
- **Very high rates of undiagnosed ADHD in adult psychiatry**
- **Different types of neurodevelopmental symptoms have a shared genetic etiology**
- **High rates of RAD in deprived areas, and high rates of associated ESSENCE in RAD**
- **High rates of ADHD in MCI in 65-80 year-olds?**
- **And this is the year when the GD-boom starts (with the intro of DSM-5 GD??)**
 - Fernell et al 2013 Acta Paediatr, Nylander et al 2013 Nord J Psychiatry, Pettersson et al 2013 JCPP, Minnis et al 2013 BJPsych, Guldberg-Kjär 2013, Steensma et al 2013 Horm Behav



The last quarter of a century in "child neuropsychiatry": 2014

- Individuals with autism "feel/recognize" pain without being able to communicate this, challenges the notion of pain insensitivity in autism
- **Individuals born to mothers with intellectual disability have poor psychosocial outcomes**
 - Hadjikhani et al 2014 Transl Psychiatry, Lindblad et al 2014 JID



The last quarter of a century in "child neuropsychiatry": 2015

- **Low vitamin D at birth in children who later develop autism (much lower than in their non-autism siblings)**
- **Extreme demand avoidance in one of every six children with autism in the Faroe Islands**
- **Autism phenotype showing no increase over time whereas registered autism breaks out like an avalanche**
 - Fernell, Bejerot, Humble et al 2015 Mol Psychiatry, Gillberg et al 2015, Lundström et al 2015 BMJ



The last quarter of a century in "child neuropsychiatry": 2016

- First ever prospective study of 20 year outcome of Asperger syndrome – much better (and much more variable) than in classic autism but still restricted for many
- Can early diagnosis of autism/Asperger syndrome prevent later development of psychosis/schizophrenia?
- **First validation of the ESSENCE-Q (in Japan)**
- **ESSENCE extremely common in febrile seizures**
 - Gillberg IC, Helles et al 2016 JADD, Marinopoulou et al 2016 JADD, Hatakenaka et al 2016 Neuropsychiatr Dis Treat, Nilsson et al 2016 Neuropediatrics



The last quarter of a century in "child neuropsychiatry": 2017

- Serial killing and autism – low rate in autism but autism common in serial killers
- **Maltreatment associated with high rate of ESSENCE but background is shared genes (i.e. could be that genes "lead" to ESSENCE in parent plus ESSENCE in child and this leads to maltreatment?)**
- Cholesterol metabolism and autism (testosteron high, vitamin D low, cholesterol low) linked?
- **"Look me in the eyes" and people with autism overactivate their amygdalae – should we refrain from trying to teach people with autism to "have eye contact", or intervene extremely early?**
- **Omega 3/6 improves reading in mainstream school children**
 - Allely 2017 J Psychol, Dinkler et al 2017 KCPP, Gillberg et al 2017 Autism Res, Hadjikhani et al 2017 Scientific Reports, Johnson et al 2017 JCPP



The last quarter of a century in "child neuropsychiatry": 2018

- General anaesthesia associated with increased rates of ESSENCE in children who already had some kind of brain problem before the anaesthesia
- **Bumetanide for autism increases eye contact and decreases amygdala activation**
- **FIRST INTERNATIONAL ESSENCE CONFERENCE ATTRACTS 1500 ATTENDANTS**
 - Castellheim et al 2018 JCPP, Hadjikhani et al 2018 Scientific Reports



The last quarter of a century in "child neuropsychiatry": 2019

- **Women with childhood diagnosis of ADHD and/or autism have very high rates of pain syndromes later in life**
- **Children with regressive autism more impaired at follow-up than those who never showed regression**
- **Children with PANS "really exist" and have very high rates of familial autoimmunity**
 - Asztely et al 2019 J Pain Res, Thompson et al 2019 JADD, Johnson et al 2019 Lancet



The last quarter of a century in "child neuropsychiatry": 2020

- **30-year follow-up of anorexia nervosa – longest in history – still poor outcome associated with comorbid ASD**
- **Increased levels of serum neurofilament 30 years after anorexia nervosa onset**
- **Autism classifiable by MRI?**
 - Dobrescu et al 2020 BJPsych, Wentz et al ECAP, Sarovic et al 2020 J Methods Psychiatr Res



The last quarter of a century in "child neuropsychiatry": 2021

- **Very high prevalence of autism in immigrant population**
- **Very high rates of ESSENCE in CP**
- **ESSENCE clinics started in Sweden**
- **Development of ESSENCE-Q and ESSENCE-D**
 - Linnsand et al 2021 JADD, Pålman et al 2021 DMC, Landberg et al 2021



Dissertations from the Göteborg group in the past 25 years

- **Nordin V 1997**
- **Ehlers S 1997**
- **Åkefeldt A 1998**
- **Ivarsson T 1998**
- **Landgren M 1999**
- **Ervik S 1999***
- **Bilenberg N 1999***
- **Wentz E 2000**
- **Nydén A 2000**
- **Kadesjö B 2000**
- **Kortegaard L 2001***
- **Kadesjö C 2002***
- **Pedersen D 2004***
- **Lindström K 2006***
- **Niklasson L 2007**
- **Miniscalco C 2007***
- **Johansson M 2007**
- **Cederlund M 2007**
- **Billstedt E 2007**
- **Posserud MB 2008**
- **Danielsson S 2009**
- **Hofvander B 2009***
- **Ullebö AK 2010**
- **Kopp S 2010**
- **Nylander L 2011**
- **Lundgren T 2012**
- **Nygren G 2012**
- **Unenge Hallerbäck 2012**
- **Hagberg B 2013**
- **Westman-A G 2013**
- **Eriksson M 2013**
- **Lindblad I 2013**
- **Johnson M 2014**
- **Lundholm-Hedvall Å 2014**
- **Höglund-Carlsson L 2015**
- **Barnevik-Olsson M 2016**
- **Helles A 2016**
- **Karjalainen L 2017**
- **Hatakenaka Y 2018**
- **Nilsson G 2020**
- **Påhlman M 2020**
- **Dinkler L 2020**



Dissertations from the Göteborg group in the past 25 years

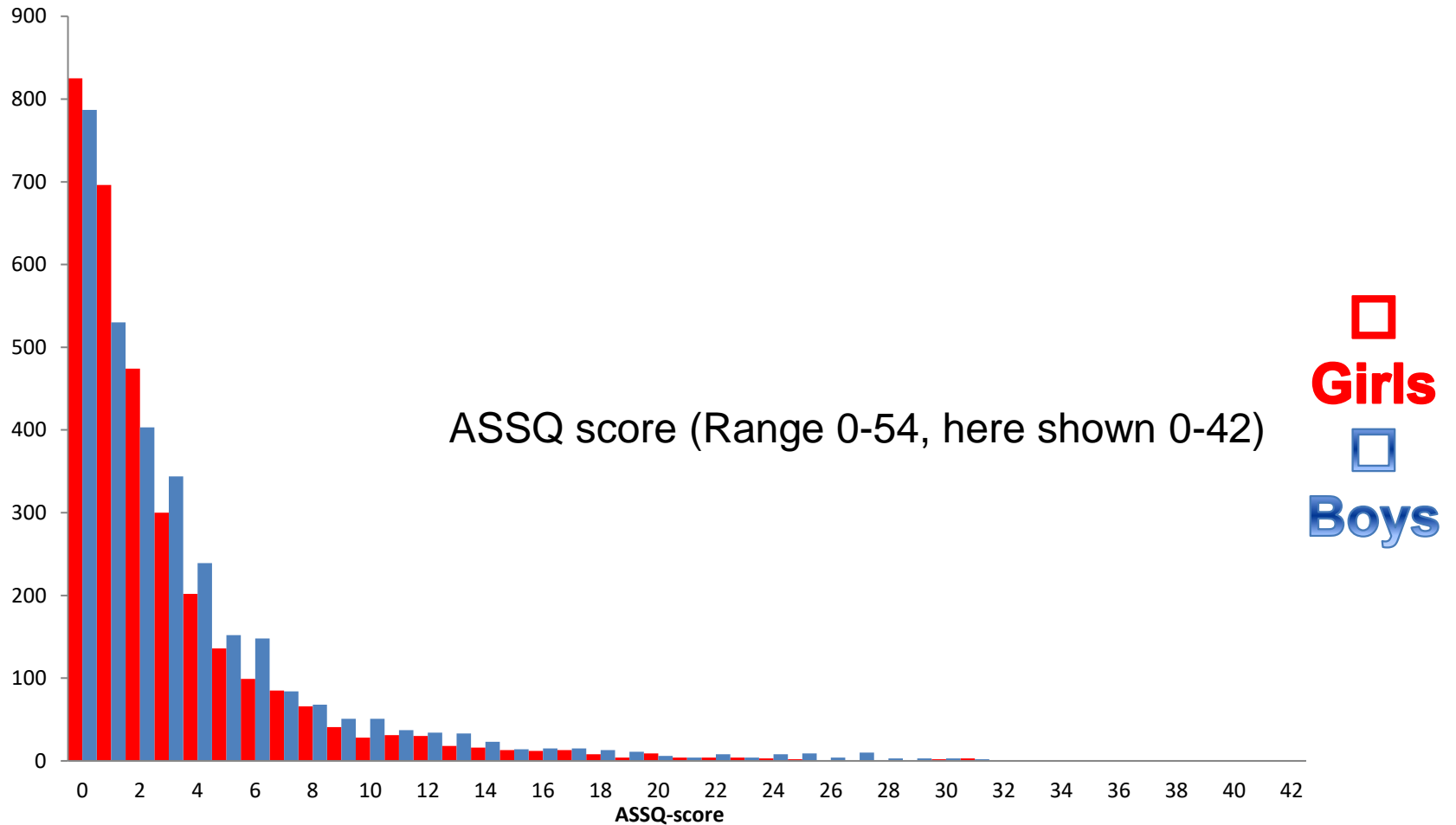
- Autism 1997
- Asperger 1997
- Prader-Willi 1998
- Depression 1998
- ADHD+DCD 1999
- Asperger 1999
- CBCL 1999
- Anorexia nervosa 2000
- Autism 2000
- ADHD comorbidity 2000
- Eating disorders 2001
- ADHD 2002
- Psychiatr disorder 2004
- Outcome neonatal 2006
- 22q11del syndrome 2007
- Language outcome 2007
- Autism in BPS 2007
- Asperger outcome 2007
- Autism outcome 2007
- Autism traits/autism 2008
- Autism-epilepsy 2009
- Autism/ADHD adults 2009
- ADHD 2010
- Girls autism/ADHD 2010
- ADHD/autism adults 2011
- Autism/schizophrenia 2012
- Autism early screen 2012
- Autism/schizophrenia 2012
- ESSENCE neuropsych 2013
- Autism young 2013
- Autism genetics 2013
- ID 2013
- ADHD non-stimulant 2014
- Autism young 2014
- Autism young 2015
- Autism young 2016
- Asperger outcome 2016
- Eating dis ESSENCE 2017
- ESSENCE screen 2018
- Febrile seizures-ep 2020
- CP-autism-ADHD-ID 2020
- Eating dis ESSENCE 2020



How many people are affected by ESSENCE?

- **At least 10% of children under 18 years** of age are or have been affected by “neuropsychiatric/neurodevelopmental disorders” (**ESSENCE**) (12% of boys, 8% of girls) - including ADHD, ASD, TS, CD, DCD, IDD – half this group “discovered” by age 6 years; **many more than half this group will have persistent problems in adult life**
- **Overlap/” Comorbidity”/Co-existence is the rule**; almost never “one problem only”
- When looking back: **vast majority had symptoms <5 years**
- **Girls usually are not recognized until adolescence/adult age (and usually as non-ESSENCE)**
- **Half or (many?) more of all “chronic” adult psychiatric patients have had ESSENCE?**
 - Gillberg 1981, 1983, Nylander et al 2009, Gillberg 2010, Gillberg 2013, Gillberg 2014, Gillberg 2021

PARENT REPORTS ON AUTISM SYMPTOMS (ASSQ) N= 6200+ CHILDREN AGED 7-9 YEARS DATA FROM BCS





Autism

- L van Beethoven
- A Bruckner
- B Bartok
- E Satie
- HC Andersen
- A Conan Doyle
- A Robbe-Grillet
- I Kant
- L Wittgenstein
- G Morandi
- A Einstein
- W Kandinskij
- P Klee
- E Hopper
- G Garbo
- D Springfield
- A Warhol
- S Kubrick
- S Jobs
- S Boyle
- G Thunberg
- **“ALL THE LONELY PEOPLE – WHERE DO THEY ALL COME FROM”**
 - Gillberg 1992, Baron-Cohen 2003, Fitzgerald 2005, Wing 2011, Gillberg 2020



Treatments and interventions

- Diagnosis (including in-depth assessment plus medical-genetic) and information are most important interventions
- Psychoeducation and special education for all
- Motor task training for DCD
- Medications for ADHD
- Structured concrete and predictable education for autism
- Bumetanide for autism?
- Immunotherapies for PANS?
- Personalized medicine
- All children presenting with major and impairing ESSENCE symptoms need to be followed up – ESSENCE clinics of the essence!
- **Education of whole societies, school children first and foremost**



“Take home message”

- **ADHD and ASD are but two of a group of ESSENCE that overlap genetically, symptomatically and as regards brain dysfunction/variation**
- ASD and ADHD (and other ESSENCE) are genetically based in many cases, but environment and immune factors play an important role (to be studied: how important)
- Immunology important but how?
- Most ESSENCE persist into adult life
- ADHD common+still underdiagnosed (c. 5%), ASD relatively common+overdiagnosed (c. 1%), DCD common+missed (5%), LD common (5%), ID common+missed (2%)
- ADHD one of the most “treatable” of all disorders, accidents, criminality, obesity can be prevented if diagnosis and treatment instituted before adult age
- Other psychiatric disorders/problems/academic failure emerge or become “diagnosable” over time – these are the diagnoses that adult psychiatrists will make
- **Autism *in itself* has different outcome, not necessarily poor, current focus on autism only in early screening and intervention programmes probably a big mistake**
- **IDD has “poor” outcome, ADHD probably has worse outcome than ASD “in itself”, IDD/ADHD/LD often the “real reasons” for poor outcome, DCD often associated with anxiety/depression often missed**
- **Girls missed** or misdiagnosed
- Early diagnosis makes a difference, therefore **ESSENCE centres** of the essence
- ESSENCE are lifetime disorders that need a **lifetime perspective from the start**
- **DSM-6 or DSM-5.1 or an altogether new “bible”?**