HELLER CHARGE **PANS** CD



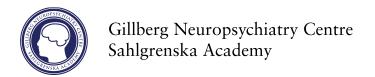
From MBD to ESSENCE Is ESSENCE really of the essence? A personal review

- · Christopher Gillberg, MD, PhD, professor or associated at
- Gillberg Neuropsychiatry Centre at the Sahlgrenska Academy, University
 of Gothenburg, and Queen Silvia Hospital and Kochi Prefecture and Kochi University
 Medical School (Sweden and Japan) GO TO www.gu.se/gnc
- Universites of Glasgow and Edinburgh, and Royal Hospital for Children (Scotland)
- University of Stellenbosch and Uni of Cape Town (South Africa)
- Institute of Child Health, University College London (England)
- Institut Pasteur, Paris (France)

Stenungsbaden, January 2025

The last 100 years in "child neuropsychiatry": Before 1993

- Lauretta Bender
- Hans Asperger
- Lorna Wing
- Anna-Lisa Annell
- 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
- Maria Råstam
- Björn Kadesjö
- DIAGNOSIS AND TREATMENT OF AUTISM 1989 GOTHENBURG SWEDEN



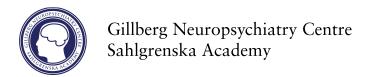
- All case-records of first-time visitors to an outpatient child and adolescent psychiatric centre from 1992 to 1996 were reviewed, and re-diagnosis was performed according to DSM-III-R.
- Fewer than 50% were seen by a psychiatrist. Neuropsychiatric diagnosis rose markedly from (0% in 1977) 24% in 1992 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



- Long-term positive effects of amphetamine treatment in children with ADHD (only ever long-term RCT with placebo)
- 7-15-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



- 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 DMCN



- 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 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)

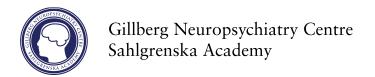
- STRIDER UNDER HJÄRNÅLDERN. Om ADHD, biologism, sociologism. Vanna Beckman. Enskededalen: Pavus utbildning, 2007.
- Vanna Beckman wrote a book about what she called one of the worst slander/smearing campaigns in Swedish history. The campaign was started in 1999 by "school health doctor" Leif Elinder and sociologist Eva Kärfve (who had written a book about witch hunts/trials). In the year 2000 Kärfve published her book about "Brain Ghosts – on DAMP and the Threat to Public Health" which portrayed Christopher Gillberg as an evil monster whose only remit was to drug young children into coma and oblivion. These people still "run" Wiki-pages about CG



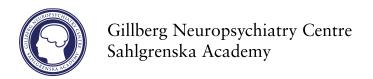
2000-2007 (2008) "The Gillberg Affair"

- Hela processen, och särskilt domarna i Kammarrätten i Göteborg, torde representera "den mest intressanta juridiska härdsmältan 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

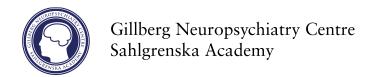




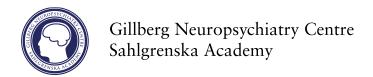
- The AQ arrives on the scene and the number of self-diagnosed cases of autism goes upincluding through the roof
- Neuropsychiatric disorders (but not classic autism) extremely common in di George (22q11 del) syndrome
- Autism much overrepresented in Down syndome previously said to be not "present" in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



- Strong link between glutamate receptor gene variation/mutation and autism documented in the PARIS study (Gillberg & Leboyer)
 - Jamain et al 2002 Mol Psychiatry

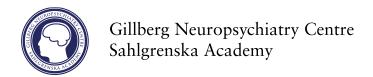


- Mutations of X-linked neuroligin genes in autism documented in Gothenburg family
- Long-term outcome of anorexia nervosa not as gloomy as previously believed, however link between ASD in anorexia and poor prognosis
 - Jamain et al 2003 Nature Genetics, Råstam et al 2003 ECAP



- 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

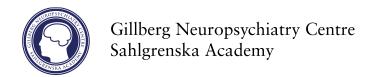
- Working memory training moderately effective in ADHD
- Development and validation of the A-TAC
- One third to one half of all individuals with classic autism develop epilepsy before age 40
 - Klingberg et al 2005 JACAP, Hansson et al 2005 Br J Psychiatry Danielsson et al 2005 Epilepsia



- 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

- High rate of melatonin synthesis abnormalities in autism
 - Melke et al 2008 Mol Psychiatry

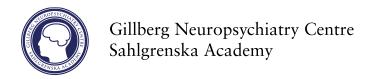
- Moderately positive effects of Omega 3/6 in the treatment of ADHD (RCT with placebo)
- ESSENCE launched at the Royal College of Psychiatrists meeting in Liverpool
 - Johnson et al 2009 JAD, Gillberg 2009



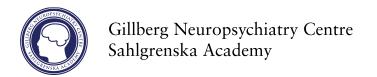
- Girls with social and/or attention deficits have extremly high rates of diagnostic level autism and ADHD this study set in motion a whole "movement" re "female autism"
- Low vitamin D levels in mothers from Somalia who have children with autism (vs non-autism)
- ESSENCE-paper published (fifth attempt "successful")
- GNC started by joing 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?

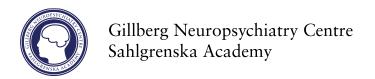
- ESSENCE Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations (Gillberg 1981/2009/2010/2021)
- Pre-school predictors of adult academic failure, being bullied and bullying, social exclusion, substance use, psychiatric disorder, eating disorders, pain syndromes, empathy problems, 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 Phenotypes, Rare Disorders/Health Conditions, including FAS and VAS) 2-3%)
 - ("NEUROLOGICAL SYNDROMES" (Epilepsy syndromes and other neurological disorders (HC, CP, neurometabolic): LKS, CSWS, FS+, FS? 0.8%)



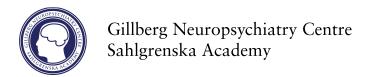
- High-intensity ABA no better than low-intensity ABA in autism- naturalistic independent study of 208 preschool children
- GNC inaugurated by HMD Queen Silvia and SUZANNE REUTER
 - Fernell et al 2011 Res Dev Disabil



- Medication for ADHD and criminality decreases risk of criminality by 32% in men and 41% in women, Lichtenstein´s group has since pubblished 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 moderatly to very positive results at 6- and 12- months follow-up
- First-ever prevalence study of autism in preschoolers showing 0.8% using M-CHAT (CHAT originally developed by CG in collaboration with S Baron-Cohen BJPsychiatry 1992)
- 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 2022, BMJ Open

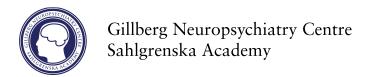


- Extremely high rate of ADHD in obesity already found in 2008 again stressed
- Very high rates of undiagnosed ADHD in adult psychiatry
- Different types of neurodevelopmental symptoms have a shared genetic etiology
- High rates of RAD in deprived areas, and high rates of associated ESSENCE in RAD
- 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



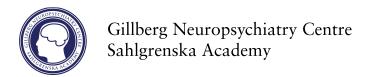


- Individuals with autism "feel/recognize" pain without being able to communicate this, challenges the notion of pain insensitivity in autism
- Individuals born to mothers with intellectual disability have poor psychosocial outcomes
 - Hadjikkhani et al 2014 Transl Psychiatry, Lindblad et al 2014 JID



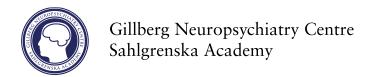


- Low vitamin D at birth in children who later develop autism (much lower than in their non-autism siblings)
- Extreme demand avoidance in one of every six children with autism in the Faroe Islands
- Autism phenotype showing no increase over time whereas registered autism breaks out like an avalanche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



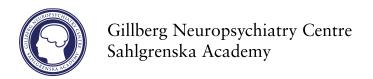


- First ever prospective study of 20 year outcome of Asperger syndrome much better (and much more variable) than in classic autism but still restricted for many
- Can early diagnosis of autism/Asperger syndrome prevent later development of psychosis/schizophrenia?
- First validation of the ESSENCE-Q (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



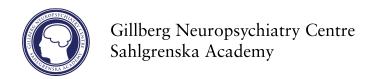


- Serial killing and autism low rate in autism but autism common in serial killers
- Maltreatment associated with high rate of ESSENCE but background is shared genes (i.e. could be that genes "lead" to ESSENCE in parent plus ESSENCE in child and this leads to maltreatment?
- Cholesterol metabolism and 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

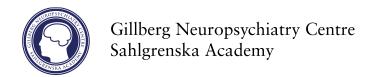




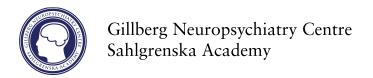
- General anaesthesia associated with increased rates of ESSENCE in children who already had some kind of brain problem before the anaesthesia
- Bumetanide for autism increases eye contact and decreases amygdala activation
- Fewer and fewer symptoms required for clinical diagnosis of autism?
- FIRST INTERNATIONAL ESSENCE CONFERENCE ATTRACTS 1500 ATTENDANTS
 - Castellheim et al 2018 JCPP, Hadjikhani et al 2018 Scientific Reports, Arvidsson et al 1028 JCPP



- 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



- 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?
- HLA-polymorphism separates regressive and non-regressive autism
 - Dobrescu et al 2020 BJPsych, Wentz et al ECAP, Sarovic et al 2020 J Methods Psychatr Res, Tamouza et al 2020 Autism Res



- Very high prevalence of autism in immigrant population
- Very high rates of ESSENCE in CP
- Very high rates of ESSENCE in dyslexia
- Very high rates of ESSENCE in adult psychiatry
- RCT of PR-ESSENCE shows very good outcome after intervention (effect size 1.48)
- ESSENCE clinics started in Sweden
- Development of ESSENCE-Q and ESSENCE-D
- Publication of The ESSENCE of Autism and Other Neurodevelopmental Conditions
- DAMP at age 6 years predicts poor outcome at age 30 years
- Three-part systematic review of Gender Dysphoria
 - Linnsand et al 2021 JADD, Påhlman et al 2021 DMCN, Brimo et al 2021 Dyslexia, Eberhard et al 2022 Psychiatr Res, Nyrenius et al 2022 JADD, Johnson et al 2021 ECAP, Landberg et al 2022, Landgren et al 2022 BMJ Open, Thompson et al 2022 PLOS GPH



Dissertations from the "Gillberg Centre" group in the past 30 years

Hellgren L 1994

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 A 2014

Höglund-Carlsson L 2015

Kocovska E 2016

Barnevik-Olsson M 2016

Helles A 2016

Karjalainen L 2017

Hatakenaka Y 2018

Carlsson E 2019

Nilsson G 2020

Påhlman M 2020

Dinkler L 2020

Cavonius D 2022

Sarovic D 2022

Mårland C 2022*

Landgren V 2022

Nyrenius J 2023

Yasumitsu-Lovell K 2023

Marinopoulou M 2023

Häger L 2023

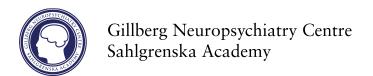
Linnsand P 2023

Schachinger-Lorentzson U 2024

Thorsson M 2024

Eberhard D 2025

Wallin L 2025





Dissertations from the Göteborg group over the past 30 years

Adolescent psychosis 1994

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

Autism Vitamin D

Eating dis ESSENCE 2017

ESSENCE screen 2018

Language and Autism 2019

Febrile seizures-ep 2020

CP-autism-ADHD-ID 2020

Eating dis ESSENCE 2020

Internet support in ESSENCE 2021

Autism biology 2022

A-TAC 2022

Family guidance 2022

ESSENCE outcome 2022

Autism adults 2023

Pre- and perinatal 2023

ESSENCE cognition 2023

Executive function 2023

Immigrant ESSENCE 2023

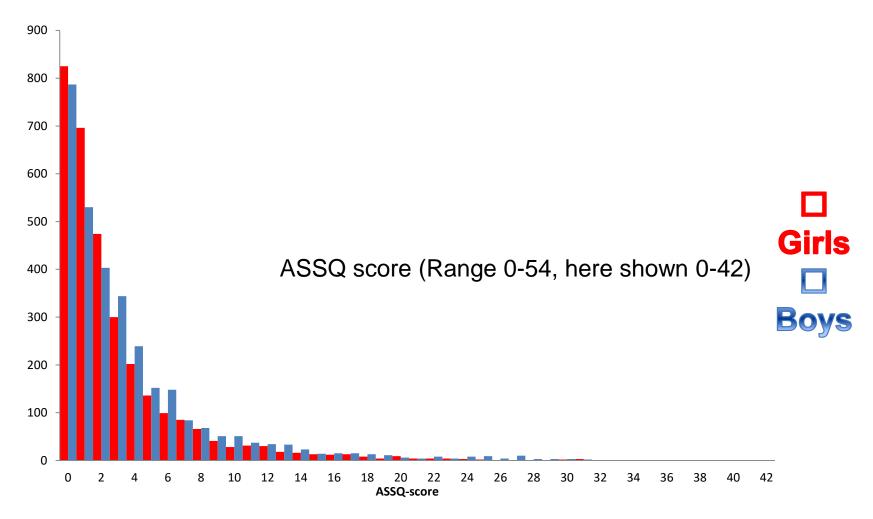
Language screen 2023

Social, motor ESSENCE 2024

Adult psychiatry ASD/ADHD 2025

Multimorbidity in 22q11del 2025

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



UNIVERSITY OF GOTHENBURG

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 2021

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
- Families with ESSENCE are just that: whole families with ESSENCE!

"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, including tic disorders, DCD, and DLD) 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 and need lifetime/family perspectives from the start
- DSM-6 or DSM-5-TR or an altogether new "bible"; ICD-11 NO GOOD?