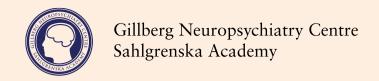




Asperger syndrome and ESSENCE

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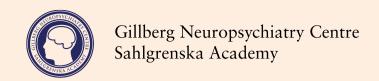
Asperger syndrome or Asperger's disorder – same "name" for different conditions?

Gillberg & Gillberg (1989) and Gillberg (1991)

- Based on Asperger's descriptions
- 6 domains affected
- 20 symptoms listed (as in ASDI (Gillberg 2001) brief interview)
- 9 required for diagnosis
- Speech-language-communication problems required
- Motor clumsiness required (at least in typical cases)
- Severe disorder in all cases

DSM-IV-TR and ICD-10

- Not at al in accordance with Asperger's descriptions
- 2 domains affected
- 8 symptoms listed
- 3 required for diagnosis
- No speech-language-communication problems required
- Normal development in first three years of life
- Mild/very mild disorder in most cases





Asperger syndrome or autism spectrum disorder?

DSM-V wants to make no distinction between autism and Asperger syndrome at the clinical diagnostic level

DSM-V may not even mention Asperger syndrome?

Hundreds of thousands of people (millions?) already have the clinical diagnosis of Asperger syndrome

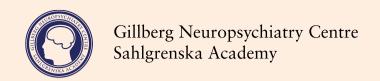




ESSENCE - Early Symptomatic Syndromes Eliciting Neuropsychiatric/Neurodevelopmental Clinical Examinations – predictors of empathy disorders and conscience disorders

Syndromes

- ASC (Autism Spectrum Conditions, including Disorders such as Asperger syndrome)
- ADHD (Attention-Deficit/Hyperactivity Disorder Spectrum)
- with or without ODD/CD (Oppositional Defiant Disorder /Conduct Disorder) - also termed DBD (Disruptive Behaviour Disorders)
- TS (Tic Spectrum Conditions including Tourette Syndrome)
- BD (Bipolar Spectrum Conditions including Disorder)
- SLI/LI ("Specific" Language Impairment), never specific?
- LD/MR (Learning Disability/Mental Retardation), NVLD (Non
 - -Verbal Learning Disability), Working Memory Disorder, and Slow Processing Disorder
- DCD (Developmental Coordination Disorder)
- BPS (Behavioural Phenotype Syndromes)
- Epilepsy Syndromes: Landau-Kleffner Syndrome, CSWS, FS+



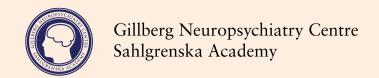


ESSENCE - where do we find the cases?

- Major symptoms from one or more (usually several) of the following domains before age 4 years are the markers of ESSENCE
 - General development (community pediatrics, GP)
 - Motor control/Perception-Sensory (OT, community pediatrics, GP)
 - Communication/Language (SLT, CAMHS, community pediatrics, neurology)
 - Activity/Impulsivity (CAMHS, psychology, community pediatrics)
 - Attention (CAMHS, neurology, psychology)
 - Social interaction/Reciprocity (CAMHS, autism centres)
 - Behaviour (CAMHS, community pediatrics, GP)
 - Mood swings (CAMHS, psychology)
 - Sleep (community pediatrics, GP)
 - Feeding (community pediatrics, dieticians, GP, CAMHS)

(plus CHILD HEALTH VISITING, WELL-BABY-CLINICS, PRE-SCHOOLS, SCHOOLS, NEW-BORN UNITS <u>AND</u> SOCIAL WORK)

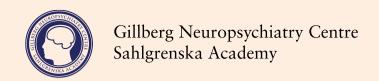
- Gillberg 2010





ESSENCE - signal symptom (language)

- Example: delayed language at 2.5 years
 - Screen takes no more than 5 minutes (deviance if comprehension difficulties, fewer than 25 communicative words, major dysarticulation)
 - About 2-6% of all children screen positive and have "confirmed" language delay at 2.5 years
 - -Screen positive and confirmed language delay at 2.5 years => 70% have "neuropsychiatric /neurodevelopmental" diagnosis (with clinical impairment) at age 7 years (ADHD, ASD, LD, DCD), virtually all have remaining speech-language problems
 - -i.e. all children with "SLI"/LI at 2.5 years need to be followed carefully and vast majority will need services
 - Miniscalco et al 2005, 2006, 2007, 2009





ESSENCE - another signal (autism)

- Example: suspected ASD under age 3 years
 - 28 Gothenburg children followed for several years from under age 3 years with suspected ASD: 75% met criteria for autistic disorder at age 6 years, and remainder had other neuropsychiatric diagnosis (other ASD, ADHD, LD)
 - Gillberg et al 1990
 - 208 Stockholm children with ASD diagnosis made by clinicians at age 0-4 years: 52% met criteria for autistic disorder at follow-up, 39% met criteria for other ASD, 9% had other neuropsychiatric diagnosis (ADHD, LD) - prevalence of ASD in this age group 0.6%
 - Of all Gothenburg children referred at 2 years of age with suspicion of ASD, 85-90% hadASD (and only 10% of these were already suspected of Asperger syndrome, 0.8% of all 2-year-olds
 - Fernell et al 2009, 2011, Nygren et al 2011
 - ASD diagnosis around age 2-4 years highly stable in 90% of cases, virtually no "over-diagnosis", many Asperger cases missed





Early symptoms (age 0-4 years) in ASD including Asperger syndrome

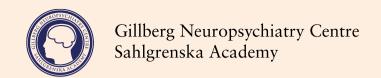
- Motor control problems first year of life (Moebius-like face, strange movements from back to front, compartmentalised motor development) 50-100%
- Perceptual abnormalities in 90-100%
- Language problems/pragmatic problems in 90-100%
- Behaviour problems in 90-100%
- No/little reaction to own name 50-100%
- No or limited <u>initiation</u> of joint attention (=> major social interaction problems) 80-100%
- Hyperactivity and impulsivity (often extreme) in 40-50%
- Hypoactivity in 10-25%
- Sleep problems in 40%
- Delayed general development in 20%
- Major mood swings in 10%
- One or several of the above could be presenting complaint
 - Coleman and Gillberg 2011





Early symptoms (age 0-4 years) in DBD (=ADHD and ODD)

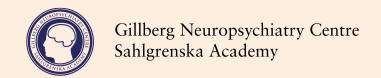
- Motor control problems first year of life 50-100%
- Perceptual-sensory abnormalities in 50-100%
- Language problems/pragmatic problems in 50%
- Behaviour problems in 50-100%
- Mood problems, including inability to control temper, in 50-100%
- Hyperactivity (sometimes, but rarely, extreme) in 30-50%
- Hypoactivity problems and inattention in 25%
- Major sleep problems in 40%
- Delayed general development in 15%
- Major mood swings in 5%
- One or several of the above could be presenting complaint
 - Gillberg 2010





Scope of problem: pre-school, school and adolescence

- At least 10% of children under 18 years of age are or have been affected by psychiatric disorders (12% of boys, 8% of girls) including ADHD, ASD, TS, CD, BD (and psychosis, eating disorder, depression, and anxiety disorders) half this group "discovered" by age 6 years
- Another 10% or more are affected by various kinds of psychosocial problems (including drug abuse), some of which may be triggered by or interacting with ESSENCE
- About 5% are affected by "dyslexia" (more than half of whom subsumed in previously mentioned groups)
- 1-2% are affected by LD (more than half in above groups)
- Overlap/"Comorbidity"/Co-existence is the rule; almost never "one problem only"
- When looking back: vast majority had symptoms <5 years





ASD/Asperger syndrome as an example of ESSENCE

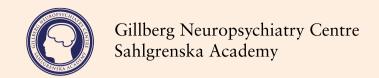
- At least one per cent of the general population of children and almost one per cent of the adult population (Gillberg et al 1991, Gillberg and Wing 1999, Wing and Potter 2002, Baird et al 2006, Gillberg et al 2007 a and b, Baron-Cohen et al 2009, Kovovska et al 2011, Brugha et al 2011)
- Half recognized in children under 6 years of age (Fernell et al 2010, Nygren et al 2011)
- Main presenting symptoms: motor -perceptual-sensory, attention, activity, no response to name, no initiation of joint attention, learning, sleep, social, and language





ASD co-existing disorders

- Epilepsy 20% (poor outcome if left undertreated)
- Other "medical disorders" 20%
- ID/MR 15-20% (poor outcome)
- ADHD 31-50% (negative outcome marker?)
- Tic disorders 40% (best positive outcome marker?)
- OCD 10%
- Depression 20%
- BPD 15%
- Catatonia 15%
- Anxiety (disorder) 20-41%
- No co-existing disorder 0%
- (Major sleep disorder 50%)
 - Gillberg and Coleman 2000, Billstedt et al 2005, Gjevik et al 2010, Mukkades et al 2010,
 Zappella 2010





ASD: background factors

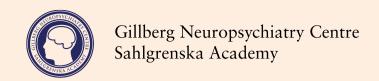
- ASD is a group of multifactorially determined conditions, and there are almost as many different causes as there are cases. Synapse and clock genes probably play a major role (and often affect synapse formation and function, e.g. neuroligin, neurexin, SHANK 3, melatonin genes), but environmental factors contribute to clinical presentation in many cases and can themselves cause ASD in some instances. The prefrontal, temporal, brainstem and cerebellar regions of the central nervous system are usually affected. These areas constitute a functional network, "the default network", which appears to be critically differently functioning in ASD. There is decreased inter- and intranetwork connectivity. The overlap with ADHD, DCD, TS, and LD is very considerable, both at the genetic and clinical level, no clear separation possible between autism "cases" and individuals with "autistic traits"
 - Iacoboni 2006, Buckner and Vincent 2007, Bourgeron 2007, Monk et al 2009, Gillberg 2010, Lundström et al 2011. Coleman and Gillberg 2011, Lundström et al 2011





ADHD as an example of ESSENCE

- ADHD occurs in 4-7% of all school age children according to studies performed in Sweden, Denmark, Norway, Finland, Iceland, Germany, Spain, Australia, Brazil, Canada and the US; probably half of these are recognized or can be recognized under age 6 years
- Severe variants are at a rate of at least 1.5-3% of the general population or a little under half of all cases meeting diagnostic criteria for the disorder; these are the ones most likely to be recognized in very young children and those that are likely to remain diagnosable in adulthood





ADHD: background factors

- ADHD is largely genetic; similar phenotype results after various types of environmentally caused brain dysfunction. Atypical brain development in children with ADHD; loss of prefrontal component of normal asymmetrical brain development. Growing evidence that dopamine -dependent reward systems deviant in ADHD. ASD and ADHD are related in some families. CNS connectivity genes involved in ASD are relevant for development of ADHD symptoms. There is considerable genetic overlap with ASD and DCD
 - Curatolo et al 2008, Strang-Karlsson et al 2008, Melke et al 2008, Mulligan et al 2009, Kopp et al 2009, Sharp et al 2009, Shaw et al 2009, Volkow et al 2009, Bourgeron et al 2010, Lichtenstein et al 2010, Lundström et al 2011

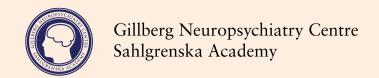




ADHD and underrated comorbidities

 Any significant comorbidity 	<u>y 85-100%</u>
 One comorbidity 	85-100%
 Two comorbidities 	65-70%
• Three comorbidities	35-50%

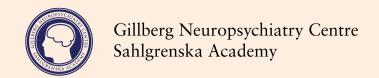
- Extreme clinical disability
- If 4-6% of general population of children have ADHD, then 2% at the very least - must be extremely impaired
 - Kadesjö and Gillberg 2001





ESSENCE and gender

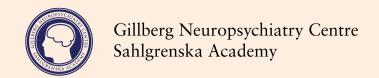
- More boys than girls in the clinical world (3:1)
- Girls are clearly missed (Kopp & Gillberg 2002, Kopp et al 2010, Kopp 2010)
- Girls may have a different phenotype goes for both ASD and ADHD too (Gillberg 1983, Kopp & Gillberg 2010)
- Males are overrepresented in almost all child neuropsychiatric disorders (Harris 1995)
- X chromosome important? Testosterone? Estrogen may have protective effect before menopause





ADHD, and ASD, Tourette syndrome and bipolar disorder

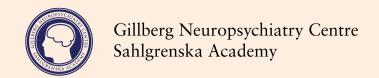
- Early onset extreme "ADHD" often signals ASD, but usually not the Asperger variant
- Early onset ADHD, mainly hyperactive-impulsive subtype and a family history of tics often indicates a later diagnosis of Tourette syndrome (or "Tourette syndrome with ADHD")
- Early onset ADHD with severe mood swings and a family history of bipolar disorder often equals early onset bipolar disorder (or "bipolar disorder with ADHD and ASD/Asperger syndrome)





Mental retardation/Intellectual disability /Intellectual developmental disorder

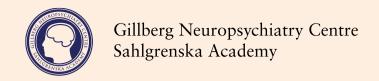
- Two per cent of the general population of children
- Half recognized in children under 6 years of age
- Main presenting symptoms: motor-perceptual, attention, activity, general learning, and language
- More than half of all with MR/ID have ASD, ADHD or both, very few with a clinical diagnosis of Asperger syndrome meet criteria for IDD (Intellectual developmental disorder)





Behavioural phenotypes

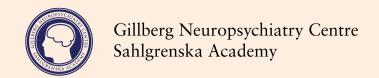
- 0.6-1.0% of general population of children
- All potentially recognizable before school age
- 80% have LD
- Specific genetic and other counselling needed
- Main presenting symptoms: "ASD/Asperger syndrome", "ADHD", general developmental delay, motor-perceptual-sensory problems, feeding difficulties/problems, physical stigmata, attention deficits, activity regulation problems, social, learning, and language difficulties





ASD: implications

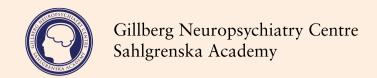
- ASD (including Asperger syndrome) is always a signal that comorbidities MUST BE SCREENED for
- ADHD in ASD (not least in Asperger syndrome) is often responsive to treatment, both pharmacotherapy and computerized training programmes/CBT
- Epilepsy MUST be treated as a top priority, but many hazards re: side-effects
- BD should often be treated with mood stabilizers
- Catatonia may need very intensive specialist interventions, including medication with SRIs and lorazepam
- DCD is often responsive to focused motor training (not least in Asperger syndrome)
- OCD rarely responsive to SRI, old tricyclics sometimes much better
- Sleep disorders often responsive to melatonin
- Violent behaviours/SIB can be responsive to low-dose atypical neuroleptics (aripiprazol, risperidone) but should <u>never</u> be used for long periods of time
- "Multiple comorbidities" with ASD can be responsive to Omega-3
- Psychoeducation and behaviour therapy first and foremost





ASD: further implications

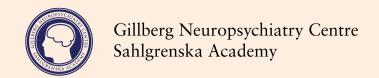
- Severe cases should all be recognized in preschool (majority under 3 years of age)
- Asperger syndrome will not usually be diagnosed until school age (risk that some of these will be missed under DSM-V), but some will have been diagnosed as autism or ADHD before that age
- ASD predicts ASD, not necessarily bad outcome
- The other ESSENCE problems may be more important for outcome than ASD "per se"
- Severe hyperactivity/"ADHD" often major presenting symptom
- Tics may be indicative of better prognosis
- LD, epilepsy, CP, genetic disorders, and ADHD all contribute to worse prognosis





ADHD: implications

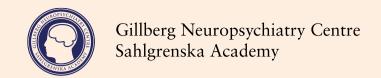
- ADHD is always a signal that comorbidities MUST BE SCREENED for
- Most of the comorbidities (except ODD and DCD) are probably unresponsive to stimulants
- Some of the comorbidities respond to physiotherapy (DCD), CBT (OCD, anxiety), psychoeducation (autism, academic failure), language therapies ("SLI") or non-stimulant medications (depression, tics, OCD, sleep disorders)





Tourette syndrome diagnosis and intervention

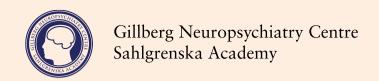
- Almost never handicapping in preschool age UNLESS there is comorbid ADHD or severe comorbid OCD
- Severe cases of Tourette syndrome comorbid with ADHD, OCD, and ASD in vast majority of cases; these ESSENCE "comorbidities" usually the cause of impairment
- Tics should not be treated with medication unless extreme





ESSENCE conclusions

- ASD (including Asperger syndrome), ADHD, TS, bipolar disorder, LD, SLI, DCD etc. overlap to a marked degree throughout life and are often not clearly separable under age 5 years
- All children presenting with major and impairing ESSENCE symptoms (developmental delay, language delay, motor control problems, perceptual-sensory problems, activity problems, inattention, social interaction, general behaviour, mood or sleep problems) need to be followed up and considered for "re-diagnosis", particularly around school entrance and in connection with major life changes
- Even though refined diagnosis is needed in all cases, at early stages ESSENCE may be the only "safe" label however, ESSENCE is not a "neurodevelopmental/neuropsychiatric diagnosis



ESSENCE conclusions

- Never proclaim: "He/she will grow out of it" no evidence whatsoever that this is likely to happen in more than a small minority of cases
- There are effective excellent interventions available for ADHD, OCD, Tourette syndrome, DCD, and depression
- There is clear evidence that early ASD diagnosis improves outcome
- It is not clear that extremely intensive ASD ABA -interventions are better than low-intensity ABA or TEACCH
- Parents and everybody else "dealing with" the child need top-class education about ESSENCE (not just about Asperger or other ASD)
- Society needs a changed attitude (equally true, but in different ways, across the world)