Attention-deficit/hyperactivity disorder and autism spectrum disorders in adult psychiatric patients

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For Magnus

Medicine's ground state is uncertainty. And wisdom – for both patients and doctors – is defined by how one copes with it.
Atul Gawande

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ABSTRACT

Background: Knowledge about attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) in adult psychiatry is scant. **Aims:** Estimate prevalence, psychiatric morbidity patterns and impact of ADHD/ASD diagnoses in general adult psychiatry services. **Material and methods**: Two adult psychiatric out-patient groups were screened and clinically examined for ADHD and ASD. A new screening instrument, the Autism Spectrum Disorders in Adults Screening Questionnaire (ASDASQ) was developed for ASD. The Wender Utah Rating Scale was used for retrospective screening of childhood ADHD symptoms. A new questionnaire was used in an attempt to measure the subjective impact of receiving an ADHD or ASD diagnosis in adulthood in a group of consecutively clinically evaluated adult patients and their significant others. A very large data-set of all registered psychiatric patients at one clinic over a 20-year-period was used to assess time trends in clinical diagnoses of ADHD and ASD and "comorbidities"/psychiatric service use. **Results:** Of screened adult psychiatric patients 1.4% had ASD and most of these were treated at a centre for chronic disorders. The rate of ASD in this centre was 3.2%. A quarter of the patients with ASD had previous diagnoses of schizophrenia. The ASDASQ showed good psychometric properties. The rate of ADHD in the screened group of general psychiatric out-patients was 21.9%. These patients had been variably diagnosed, often with affective disorder. Greater subjective impact of the diagnosis for patients with ADHD than ASD was suggested. Perceived positive post-diagnosis change was reported by patients and significant others, and as regards medication (ADHD), housing and habilitation service contact (ASD). The rate of ADHD diagnoses increased from 1990 to 2009, but only about 2.7% of the whole adult psychiatric patient group received this diagnosis. ASD diagnosis rates also went up but only to about 1.3% of all registered patients. **Discussion**: In adult psychiatry, many patients have ADHD or ASD, developmental disorders that underlie or are overshadowed by "psychiatric illness". Some patients seek help for problems related to the formerly unrecognized ADHD or ASD rather than for "psychiatric disorder". ADHD seems to be much more common than ASD, and in both disorders concomitant psychiatric illness is usually present. It is important not to rely only on self-assessment questionnaires for diagnosis. An essential part of diagnostic work-up is a detailed history taking and testing of cognitive and adaptive development/capacity, currently not standard in adult psychiatric practice. Measuring the subjective impact of ADHD or ASD diagnoses proved to be difficult. The rate of diagnosed ADHD/ASD in adult psychiatry went up over the past two decades but was, by 2010, far below the likely "real" rate. The underdiagnosis of ADHD/ASD in adult psychiatry remains a huge clinical problem.

Keywords: Attention-Deficit/Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD), adults, psychiatry, Autism Spectrum Disorder in Adults Screening Questionnaire (ASDASQ).
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SAMMANFATTNING PÅ SVENSKA

När jag i början av 1990-talet blev intresserad av autismspektrumtillstånd hade jag arbetat som specialistläkare i vuxenpsykiatrin i mer än 10 år, men aldrig där hört nämnas att autismspektrumtillstånd uppmärksammats hos någon vuxen patient. Detta syntes mig egendomligt, eftersom det dels var en allmän uppfattning att autismspektrumtillstånd är livslånga funktionsnedsättningar och dels hade visats att autismspektrumtillstånd inte bara kunde finnas också hos personer med normal begåvningsnivå utan att denna grupp – innefattande Aspergers syndrom – sannolikt är större än gruppen med utvecklingsstörning och autism. Snart blev jag varse att det fanns patienter som behandlades i vuxenpsykiatrin och vars symtombild och problematik varit förbryllande men som stämde väl med autismspektrumtillstånd. Ungefär samtidigt publicerades en artikel av Henning Beier i Läkartidningen med titeln ”Autism en angelägenhet också för vuxenpsykiatrin” – det fanns alltså fler som samtidigt börjat uppmärksamma detta, och som såg utvecklingsrelaterade funktionsnedsättningar som ett sätt att bättre förstå vissa vuxna patienters svårigheter och sårbarhet för psykisk ohälsa.

Genom att jag kom i kontakt med professor Christopher Gillberg (Göteborg) och hans medarbetare, och genom honom dr Lorna Wing (London), väcktes mitt intresse också för forskning inom området och även för andra utvecklingsrelaterade kognitiva funktionsnedsättningar, framförallt ADHD. Eftersom det vid den tiden inte fanns några studier av huruvida ADHD eller autismspektrumtillstånd kunde finnas hos vuxenpsykiatrins patienter beslöt jag att försöka ta reda på detta, ungefär samtidigt som ett av Sveriges första ”neuropsykiatriska diagnosteam” för vuxna startade sin verksamhet i Lund hösten 1998. Samtliga fyra studier är utförda inom vuxenpsykiatrin i Lund, en del av Psykiatri Skåne (tidigare Universitetssjukhuset i Lund).

Ett enkelt screeningformulär för beteenden tydande på autismspektrumtillstånd, avsett att fyllas i av vårdpersonal utformades, och användes för att screena alla aktuella öppenvårdspatienter i en sektorsklinik i Lund. Samtidigt gjordes en studie av formulärets psykometriska egenskaper som befanns vara goda. Formuläret har sedan använts i studier i flera länder där patienter/klienter har screenats. Efter screening och noggrann klinisk undersökning visades 1.4% av sektorsklinikens hela patientgrupp ha ett klart autismspektrumtillstånd. Majoriteten av denna grupp hade kontakt med en enhet för patienter med svåra och långvariga sjukdomstillstånd, företrädesvis psykoser. Vid denna enhet var andelen patienter med autismspektrumtillstånd ca 3.2%. De diagnoser dessa patienter fått i psykiatrin varierade, med övervikt för psykosdiagnoser, särskilt schizofreni. Autismspektrumtillstånd är således en

differentialdiagnos till schizofreni som är värd att överväga, och dessutom, vilket senare har visats av andra författare, en sårbarhetsfaktor för psykossjukdom.

Förekomsten av ADHD undersöktes bland patienter vid en allmänpsykiatrisk (innebärande att patienter med huvuddiagnos psykossjukdom eller missbruk/beroende inte deltog) öppenvårdsmottagning i Lund, där 406 patienter erbjöds delta i screening med ett formulär för retrospektiv skattning av barndomssymtom på ADHD. Endast 141 (34.7%) av tillfrågade patienter valde att delta i screeningen, men bortfallet skiljde sig inte signifikant från deltagarna ifråga om olika bakgrundsfaktorer. Efter noggrann klinisk undersökning visade sig 22% av de deltagande patienterna (31 av 141) uppfylla kriterierna för ADHD, tydande på att kanske åtminstone var femte allmänpsykiatrisk patient har ADHD som bakgrund till sin psykiska ohälsa. De sjukdomar dessa patienter behandlades för i psykiatrin var varierande. Ett observandum i denna studie var att två patienter som fått mycket höga poäng på screeningformuläret inte uppfyllde kriterierna för ADHD vid den kliniska bedömningen, och sannolikt inte heller hade haft ADHD utan andra problem i barndomen. Resultatet av denna studie kan tolkas som att ADHD bör ingå som ett diagnostiskt alternativ – som enda diagnos, eller som bakgrund till annan ohälsa – vid bedömning av vuxna som söker psykiatrisk hjälp. I diagnostiken bör man emellertid inte förlita sig på frågeformulär utan göra en allsidig och noggrann klinisk bedömning.

Eftersom en verksamhet för diagnostisering av ADHD, autismspektrumtillstånd och Tourettes syndrom hos vuxna hade startats i Lund och då liknande så kallade neuropsykiatriska diagnosteam var under uppbyggnad på allt fler håll, blev det av intresse att försöka undersöka huruvida det var betydelsefullt och ledde till någon förändring i patienternas liv att få en utvecklingsrelaterad funktionsnedsättning diagnostiserad i vuxen ålder. Det fanns också ett intresse av att ta reda på hur patienterna upplevt undersökningen och dessutom hur närstående, som oftast varit involverade i utredningen, uppfattat utredningen och dess eventuella konsekvenser. Vi ville också ta reda på om närstående upplevde patientens funktionsnedsättning som praktiskt och/eller känslomässigt betungande. Denna studie omfattade 225 av 231 patienter som utretts och som fått diagnos ADHD, autismspektrumstörning, Tourettes syndrom eller – efter utredning – ingen av dessa diagnoser. Den senare gruppen användes som jämförelsegrupp. Ett omfattande frågeformulär skickades till patienterna ett till drygt tre år efter utredningen, och i de fall där detta medgavs, till närstående.

Även i denna studie blev bortfallet omfattande, och slutsatsen av de svar som kom blev att merparten av de patienter som fått en ”ny” diagnos upplevt undersökningen som positiv men inte att livet förändrats i någon större omfattning. Patienterna med ADHD upplevde en större positiv förändring än övriga, och hade ofta fått ändrad farmakologisk behandling. Fler patienter med autismspektrumstörning hade fått eget boende respektive kontakt med habilitering vid uppföljningen än i de andra grupperna. Närstående uppfattade utredningen som positiv för patienterna, och angav i samtliga grupper en tyngre emotionell än praktisk börda. Studien har emellertid metodologiska tillkortakommanden, exempelvis stort bortfall och en liten och inte representativ kontrollgrupp, som gör resultaten svårtolkade. En slutsats av denna och den föregående studien är att metoden att utföra undersökningar via utskickade frågeformulär kan innebära svårigheter att minimera bortfallet.

Slutligen gjordes en genomgång av registerdata avseende de av klinikens (Verksamhetsområde Vuxenpsykiatri Lund-Eslöv-Landskrona) vuxna psykiatripatienter som någon gång under de senaste 20 åren fått någon av diagnoserna ADHD respektive ASD, här kallade indexdiagnoser. I studien redovisas vilka diagnoser dessa patienter haft utöver indexdiagnosen samt konsumtionsmönster av sluten och öppen psykiatrisk vård i den offentligt drivna vuxenpsykiatrin. Bland 56462 patienter som haft kontakt med psykiatrin under de 20 åren fanns 437 som fått diagnosen ADHD och 270 som fått någon diagnos inom autismspektrum (ASD). I båda grupperna fanns fler män än kvinnor. Antalet ställda ADHD-diagnoser hade ökat mycket kraftigt under de senaste åren, medan ökningen av ASD-diagnoser var mer måttlig. Antalet diagnoser i båda grupperna var dock betydligt lägre än förväntat utifrån de tidigare studierna. För varje år, särskilt under 2000-talet, har antalet personer med ADHD eller ASD som behandlats i psykiatrin ökat. I vardera gruppen hade ca 60% fått andra diagnoser. Bland patienter med ADHD var affektiv sjukdom vanligaste andra diagnos medan psykossjukdomar var vanligast i ASD-gruppen. Tillstånd relaterade till beroende/missbruk var betydligt vanligare bland patienter med ADHD än i ASD-gruppen. Den senare gruppen hade en högre konsumtion av sluten vård än patienterna med ADHD. I denna studie fanns endast ett litet antal, 14, patienter som fått båda diagnoserna ADHD och ASD.

Den slutsats som kan dras av de studier som ingår i avhandlingen är att det bland vuxna psykiatripatienter finns en, sannolikt betydande, andel som har så kallade ”developmental disorders”, eller utvecklingsrelaterade kognitiva funktionsnedsättningar, i dessa studier exemplifierat med ADHD respektive ASD. Dessa båda diagnoser ställs i ökande utsträckning inom vuxen-psykiatrin, men fortfarande inte i den omfattning som problematiken troligen finns hos patienterna, även patienter med andra diagnoser/sjukdomstillstånd.

Diagnoserna, och den utredning/bedömning av patientens utveckling och kognitiva funktion som ingår, verkar kunna bidra till att ge tillgång till förbättringar i vardagsliv och vårdkontakter för patienterna och uppfattas även positivt av anhöriga, även om de senares börda inte verkar minska nämnvärt. En bedömning av kognitiv funktion och en utvecklingsanamnes borde ingå i all psykiatrisk bedömning av komplicerade psykiatriska tillstånd hos vuxna. Metoder för bedömning av utvecklingsrelaterade funktionsnedsättningar finns inom barn- och ungdomspsykiatrin, och kan i stor utsträckning tillämpas även när patienten är vuxen. En hel del av vuxenpsykiatrins patienter har haft kontakt med barn- och ungdomspsykiatrin, och patientens övergång mellan dessa båda verksamhetsområden underlättas av kunskaps- och erfarenhetsutbyte mellan de professionella i respektive verksamhet. Inom barn- och ungdomspsykiatri finns tanken (uttryckt med förkortningen ESSENCE) att det hos barn kan finnas ett stort antal symtom som bör ge anledning till en grundlig bedömning av neurologisk och kognitiv utveckling och förmåga. Samma symtom kan finnas hos vuxna, och behöver utredas på likartat sätt.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Nylander L, Gillberg C. Screening for autism spectrum disorders in adult psychiatric out-patients: a preliminary report. Acta Psychiatr Scand 2001, 103:428-434.

II. Nylander L, Holmqvist M, Gustafson L, Gillberg C. ADHD in adult psychiatry. Minimum rates and clinical presentations in general psychiatry. Nord J Psychiatry 2009, 1:64-71.

III. Nylander L, Holmqvist M, Jönsson S, Gustafson L, Gillberg C. Is it possible to measure the impact of a developmental disorder diagnosis received in adulthood? An attempt at follow-up, and discussion of difficulties encountered in the process. Clinical Audit 201, 2: 1-10.

IV. Nylander L, Holmqvist M, Gustafson L, Gillberg C. Attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) in adult psychiatry. A 20 year register study. Manuscript (submitted).

CONTENT

ABBREVIATIONS

AAA	Adult Asperger Assessment
ADHD	Attention-Deficit/Hyperactivity Disorder
ADI-R	Autism Diagnostic Interview – Revised
ADOS-G	Autism Diagnostic Observation Schedule – Generic
APA	American Psychiatric Association
AQ	Autism Quotient
ASD	Autism Spectrum Disorder
ASDASQ	Autism Spectrum Disorder in Adults Screening Questionnaire
ASDI	Asperger Syndrome Diagnostic Interview
ASPD	Antisocial Personality Disorder
ASRS	ADHD Symptom Rating Scale
ASSQ	Autism Spectrum Screening Questionnaire
AUDIT	Alcohol Use Disorders Identification Test
BAP	Broad Autism Phenotype
CARS	Childhood Autism Rating Scale
CPT	Continuous Performance Test
CWT	Colour Word Test
DAMP	Deficits in Attention, Motor control and Perception
DCD	Developmental Coordination Disorder

DIP-Q	DSM-IV/ICD-10 Personality Questionnaire
DISCO	Diagnostic Interview for Social and COmmunication disorders
DSM-III	Diagnostic and Statistical Manual of Mental Disorders, Third Edition
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders. Third Edition - revised
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
ESSENCE	Early Symptomatic Syndromes Eliciting Neuro-developmental Clinical Examinations
FAS	Word Fluency Test
GAF	Global Assessment of Functioning
HKD	Hyperkinetic Disorder
ICD-10	International Classification of Diseases, 10th revision
IQ	Intelligence Quotient
MADRS	Montgomery Åsberg Depression Rating Scale
MBD	Minimal Brain Damage; Minimal Brain Dysfunction
MR	Mental Retardation
NIMH	National Institute of Mental Health
NOS	Not Otherwise Specified

OCD	Obsessive Compulsive Disorder
PDD	Pervasive Developmental Disorder
RAADS-R	Ritvo Autism and Asperger´s Diagnostic Scale-Revised
RCFT	Rey Complex Figure Test
SBU	Statens Beredning för Medicinsk Utvärdering
SCID-I	Structured Clinical Interview for DSM-IV Axis I Disorders
SCID-II	Structured Clinical Interview for DSM-IV Axis II Personality Disorders
SO	Significant Other
SPSS	Statistical Package for the Social Sciences
TMT	Trail Making Test
TOL	Tower Of London
TOVA	Test Of Variables of Attention
TS	Tourette's Syndrome
WAIS-R	Wechsler Adult Intelligence Scale-Revised
WCST	Wisconsin Card Sorting Test
WHO	World Health Organisation
WURS	Wender Utah Rating Scale
WURS-25	Wender Utah Rating Scale, 25 questions

1 INTRODUCTION

1.1 Disorders of cognitive development

The term "developmental disorder" is commonly used to signify a disorder of cognitive development, often with accompanying delay or aberrations in the development of motor and sensory functions, and thus implicitly a disorder of the development of the central nervous system. In child and adolescent psychiatry as well as in paediatrics, developmental disorders have attracted clinical and research interest for a long time. One of the most important remits of clinicians is to recognize signs of developmental disorders and to diagnose these properly, in order that the child and its family may be offered appropriate help and support. It is often assumed that early diagnosis and intervention are essential in order to halt further negative development (Howlin, Magiati & Charman, 2009; Sonuga-Barke & Halperin, 2010). It is well established that many developmental disorders carry with them susceptibility to psychiatric symptoms and syndromes (Faraone, Biederman, Spencer, Wilens, Seidman et al, 2000; Tantam, 2000; Sverd, 2003; Salum, Polanczyk, Miguel & Rohde, 2010; Skokauskas & Gallagher, 2010; Taurines, Schmitt, Renner, Conner, Warnke & Romanos, 2010; Stein, Blum & Barbaresi, 2011).

The best known of all developmental disorders is mental retardation (MR) (World Health Organisation (WHO), 1993; American Psychiatric Association (APA), 1994). There are numerous known causes of MR – e g chromosome abnormalities/genetic disorders, prenatal toxins and infections, or peri- or postnatal adverse events (Percy, 2007). Recently, epigenetic mechanisms have been suggested to play a part (Schaefer, Tarakhovsky & Greengard, 2011). MR is often associated with other developmental disorders, for example autism spectrum disorder (ASD) (Nordin & Gillberg 1996; Bryson, Bradley, Thompson & Wainwright, 2008; Matson & Shoemaker, 2009; Oeseburg, Dijkstra, Groothoff, Reijneveld & Jansen, 2011) or attention-deficit/hyperactivity disorder (ADHD) (Antshel, Phillips, Gordon, Barkley & Faraone, 2006; Lindblad, Gillberg & Fernell 2011). According to several studies, adults with MR are vulnerable to psychiatric disorders (Gustafsson & Sonnander, 2004; Morgan, Leonard & Jablensky, 2007; Morgan, Leonard, Bourke & Jablensky, 2008; Nettelbladt, Göth, Bogren & Mattisson, 2009). For the coming edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM), the DSM-5, the term "intellectual developmental disorder" has been suggested to replace "mental retardation" (DSM5.org, 2011a).

This thesis focuses on two developmental disorders with symptomatic onset in childhood and persistence into adulthood in the majority of cases, namely ADHD and ASD. In the last few years, in Sweden, it has become popular to lump ADHD and ASD (and sometimes also Tourette's syndrome, TS) together as comprising one category, referred to as "neuropsychiatric disorders" (a term which, when applied to adults, may imply other disorders, e. g. dementia). The label indicates that ADHD and ASD share some common features unique to them, which is not true. The common feature shared by ADHD and ASD but certainly not unique to these disorders is that they are developmental, meaning that they are present from early life and that they affect aspects of the child´s cognitive and adaptive development and, in turn, psychosocial and academic adjustment. These developmental disorders are usually diagnosable in early childhood or at least by school age. As the concepts of ADHD and ASD have evolved and diagnostic manuals and instruments have been revised, it has become clear that these developmental disorders often persist and cause impairment in adulthood. It has also become evident that a considerable number of adults have diagnosable but never diagnosed developmental disorders, contributing to vulnerability and difficulties in adjustment in adult life. Many of these adults become psychiatric patients, seeking treatment for different symptoms or problems that, up to recently, were not recognized as being affected by or indeed "caused by" developmental disorders (Shah, Holmes & Wing, 1982; Beier 1993). In a number of cases ADHD and ASD, respectively, coexist with MR, and several authors have found overlap also between the former two diagnoses (Gillberg 1983a; Ghaziuddin, Weidmer-Mikhail & Ghaziuddin, 1998; Kadesjö & Gillberg, 2001; Stahlberg, Soderstrom, Rastam & Gillberg, 2004; Anckarsäter, Stahlberg, Larson, Hakansson, Jutblad et al, 2006; Leyfer, Folstein, Bacalman, Davis, Dinh et al, 2006; Rydén & Bejerot 2008; Hofvander, Delorme, Chaste, Nydén, Wentz et al, 2009; Gargaro, Rinehart, Bradshaw, Tonge & Sheppard, 2011). Recently, it has been shown that ADHD (Guldberg-Kjär & Johansson, 2009) as well as ASD (James, Mukaetowa-Ladinska, Reichelt, Briel & Scully, 2006; van Niekerk, Groen, Vissers, van Driel-de Jong, Kan & Oude Voshaar, 2011) may underlie problems also in the elderly, and in the case of ADHD a connection with dementia has been found (Golimstok, Rojas, Romano, Zurru, Doctorovich & Cristiano, 2011).

Tourette's syndrome (TS) is, in current diagnostic manuals, defined by motor (including vocal motor) symptoms only (APA, 1994), while the so-called comorbidity with developmental (mainly ADHD and ASD) (Kadesjö & Gillberg, 2000) and psychiatric disorders (mainly OCD) (Bloch, Peterson, Scahill, Otka, Katsovich et al, 2006) is described as extensive. Conversely, TS and other tic disorders can be seen as examples of the prevalent but – at

least in adults – usually overlooked motor symptoms in psychiatric disorders (Rogers, 1992).

In child psychiatry, attention has been drawn to the concept of ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations) (Gillberg, 2010), implying that a number of symptoms or developmental abnormalities frequently co-exist in young children for whom psychiatric or medical advice is sought. The ”signal” symptoms referred to under the acronym are motor abnormality, general developmental delay, speech and language delay, social interaction/communication problems, behaviour problems, hyperactivity/impulsivity, hypoactivity, inattention, sleep problems and feeding difficulties, if causing major impairment in the first 4 years of life. One or, as is commonly the case, several of these symptoms is a signal that a broad, multidisciplinary evaluation should be offered and that the entire scope of the child's cognitive, physical and emotional function and well-being must be taken into consideration if his/her and the family's needs are to be adequately addressed. In some of these cases, a diagnosis of ASD or ADHD will be appropriate, while others will have their problems labeled as MR or learning disorder (including borderline cases and so-called non-verbal learning disability (Harnadek & Rourke 1994)), speech and language impairment, tic disorders/Tourette's syndrome, bipolar disorder with childhood onset, oppositional defiant disorder, a behavioural phenotype syndrome (such as tuberous sclerosis or fragile X syndrome) (O'Brien & Yule, 1995), epilepsy syndromes (including Landau Kleffner syndrome (Gillberg 1995a)) and others. The symptoms subsumed under the ESSENCE label can be regarded as signs of a mismatch between an individual with a vulnerable and/or dysfunctional nervous system, and demands made by the environment. A careful assessment of all the aspects of ESSENCE will lead to an understanding of the individual's strengths and weaknesses and of his/her interaction with the family and other environment. The assessment may thus lead to individually adapted service plans. The symptomatic overlap over diagnostic boundaries is considerable (Anckarsäter, Larson, Hansson, Carlström, Ståhlberg et al, 2008), and it is entirely possible that this may also change with age and further development. The most important issue is that children with symptoms referred to as ESSENCE and their families will not be well served by a care system where services are fragmented and delivered in a manner dependent on the overlapping and unstable categories referred to as “diagnoses”. Assessment and service teams with broad competence in developmental medicine and psychology, across diagnostic boundaries, would be more appropriate (Fernell & Gillberg, 2007).

1.1.1 Diagnostic procedure in adult psychiatry

Traditionally, diagnosis of psychiatric disorders in adults is based on a clinical interview with and observation of the patient, conducted by the psychiatrist. The psychiatrist is supposed to ask relevant questions to uncover symptoms/diagnostic criteria, which in many instances are feelings or other inner experiences that can exist unbeknownst to the environment unless the patient expresses them. In some cases, behavioural deviances are interpreted as signs of certain feelings or experiences, and the psychiatrist, while interviewing, also observes the patient. Most often in clinical practice, the diagnostic process is undertaken as an assignment with only two participants – patient and doctor – and the accuracy of diagnosis relies heavily on the psychiatrist's experience and clinical common sense (Gelder, Harrison & Cowen, 2006). In most instances, it is also essential that the patient has the capacity to express and communicate his/her inner processes. Much emphasis has been put upon the patient's current – and sometimes past - feelings, but, at least in recent years there has been little or no interest devoted to the patient's cognitive functions or to information regarding the adult patient's early development. This is surprising, given that cognitive functioning, also when within the normal IQ range, can vary enormously across individuals and be very uneven within one individual, and affect vulnerability to psychiatric disorder (Koenen, Moffitt, Roberts, Martin, Kubzansky et al, 2009) as well as symptom expression, communication and coping abilities. The importance of cognitive functioning for personality expression and disorders was clearly pointed out many years ago, for example by the Swedish psychiatrist Henrik Sjöbring (Sjöbring, 1973), and is expressed, even though rarely referred to, in the DSM-IV general criteria for personality disorder (APA, 1994). The patient's cognitive abilities can also be assumed to play a part in compliance with treatment (Medalia & Thysen, 2008; Waldrop-Valverde, Jones, Gould, Kumar & Ownby, 2010).

Assessing a person's cognitive abilities while conducting a clinical psychiatric interview can be a difficult task, especially if the patient has uneven skills or skills in the lower range of normality. Many adults with developmental cognitive problems have learnt effective ways to mask their deficits by being verbal and sociable, but their problems in coping with modern society's demands for abstract reasoning and theoretical knowledge are still pervasive and, for many, very embarrassing. On the other hand, some adults with very uneven skills and impairments in the area of social interaction may give a superficial impression of having lesser intellectual capacity than is actually the case, e.g. in some cases of ASD. In diagnostic interviews – whether they are performed with or without a manual such as the SCID-I (First, Gibbon, Spitzer & Williams, 1997) or SCID-II (First, Gibbon,

Spitzer, Williams & Benjamin, 1997) – in general, little or no time is devoted to taking a history of the patient's cognitive development. However, taking a detailed history of early cognitive development and school performance can often shed light on unexpected difficulties that have greatly influenced the patient's adjustment in adult life. In most instances, it is of great value if a collateral interview regarding the early development as well as current adjustment and needs can be performed, also when the patient is adult.

For the same reason, and, in addition, for its therapeutic value (Finn, 2007; Finn, 2009), it is very often appropriate to conduct a standardized psychological assessment of cognitive functioning, at least in cases where the diagnosis is not easy to make or where accurate treatment does not yield expected results. In child and adolescent psychiatry, in forensic psychiatry, and in many diagnostic centres, children, as well as adults, with complex difficulties are examined by a team of professionals working together. Why this way of working, in teams consisting of at least a psychiatrist and a psychologist in close collaboration, is not widely applied in adult psychiatry is difficult to understand since it is usually more effective, more reliable, safer and also well tolerated, indeed according to our experience usually highly appreciated, by patients and their accompanying family members. It is a way of taking the complexity of ESSENCE, as expressed in adult life, into account. It is sometimes argued that meticulous history taking, sometimes supplemented by collateral interviews and with involvement of a professional team, and neuropsychological assessments are too time-consuming to be used in general adult psychiatry. A common current trend is to hunt for shortcuts in diagnosis and assessment. Against this it can be argued that the problems of ESSENCE are pervasive, long-standing and impairing, that the impact on the adult patient's life is often major, and that it is reasonable that it will take time and competence to arrive at a full understanding of the individual's problems and needs. This understanding also needs to be shared with the patient and his/her family/significant others. In my experience, the assessment may well be looked upon as a therapeutic process, often very powerful, and the hours spent on careful assessment will probably save time and resources in the long run. Until we have safe and valid biological markers for psychiatric diagnoses – if we ever will – shortcuts to diagnoses, especially developmental disorder diagnoses, may do more harm than good.

1.2 Disorders of cognitive development in adult psychiatric patients

As ADHD and ASD have become increasingly well known by professionals in psychiatry, clinicians have observed that patients with ADHD or ASD

often have other psychiatric problems. A number of studies have shown that common psychiatric disorders such as affective (including bipolar) and anxiety disorders are prevalent among patients – children (Gillberg, 1983a; Biederman, Newcorn & Sprich, 1991) and adults - with ADHD (McGough, Smalley, McCracken, Yang, Del'Homme et al, 2005; Kessler, Adler, Barkley, Biederman, Conners et al, 2006; Sobanski, 2006; Sobanski, Brüggemann, Alm & Kern, 2007; Babcock & Ornstein, 2009; Halmöy, Halleland, Dramsdahl, Bergsholm, Fasmer & Haavik, 2010; Klassen, Katzman & Chokka, 2010; Gjervan, Torgersen, Nordahl & Rasmussen, 2011). As for ASD patients, affective and anxiety disorders have been shown to often affect children (Ghaziuddin, Weidmer-Mikhail & Ghaziuddin, 1998; Gillberg & Billstedt, 2000; Kim, Szatmari, Bryson, Streiner & Wilson, 2000; Leyfer, Folstein, Bacalman, Davis, Dinh et al, 2006; Joshi, Petty, Wozniak, Henin, Fried et al, 2010; Mattila, Hurtig, Haapsamo, Jussila, Kuusikko-Gauffin et al, 2010) as well as adults (Martin, Scahill, Klin & Volkmar, 1999; Ghaziuddin, Ghaziuddin & Greden, 2002; Hutton, Goode, Murphy, Le Couteur & Rutter, 2008; Hofvander, Delorme, Chaste, Nydén, Wentz et al, 2009; Bakken, Helverschou, Eilertsen, Heggelund, Myrbakk & Martinsen, 2010). Psychotic symptoms seem to be overrepresented among patients with ADHD (Dalsgaard, Mortensen, Frydenberg & Thomsen, 2002) as well as ASD (Stahlberg, Soderstrom, Rastam & Gillberg, 2004), especially PDD-NOS/atypical autism (Mouridsen, Rich & Isager, 2008; Rapoport, Chavez, Greenstein, Addington & Gogtay, 2009). Skokauskas and Gallagher (2010) provide a recent review of studies of psychoses, affective and anxiety disorders in individuals with ASD. Disorders in connection with alcohol and/or other psychoactive substance abuse have been shown to be very common in patients with ADHD (Biederman, Wilens, Mick, Faraone & Spencer,1998; Wilens, 2004; Kessler, Adler, Barkley, Biederman, Conners et al, 2006; Wilens, Martelon, Joshi, Bateman, Fried et al, 2011; Gjervan, Torgersen, Nordahl & Rasmussen, 2011), but may be comparatively uncommon in individuals with ASD (Joshi, Petty, Wozniak, Henin, Fried et al, 2010; Mattila, Hurtig, Haapsamo, Jussila, Kuusikko-Gauffin et al, 2010; Sizoo, van den Brink, Koeter, Gorissen van Eenige, van Wijngaarden-Cremers & van der Gaag, 2010).

A number of studies have also pointed to a significant overlap between ADHD and ASD (Gargaro, Rinehart, Bradshaw, Tonge & Sheppard, 2011), as well as between these and other developmental disorders (Gillberg & Billstedt, 2000; Xenitidis, Paliokosta, Pappas & Bramham, 2011). These findings could be taken as indicative of a vulnerability to disorders affecting the brain in individuals with a brain already made more sensitive by the neurodevelopmental disorder.

It has become evident that some of the patients treated by adult psychiatry – in some cases for many years (Beier, 1993; Scragg & Shah, 1994; Hare, Gould, Mills & Wing, 1999; Goodman & Thase, 2009) – have developmental disorders that were not diagnosed as such earlier in their lives. It is not uncommon for these patients to have been noticed for being "disturbed", "problematic" or "different" from their early years – that is, showing the symptoms labelled as ESSENCE –, but it is likewise common that the developmental disorder has not been clinically recognized and support has not been given. With the insight that many adults suffer from consequences of ADHD or ASD has come the organization of so-called "neuropsychiatric" teams within clinics for adult psychiatry. The remit of these units is usually to assess, diagnose and, if needed, treat patients with ADHD or ASD. The patients referred for assessment are to a great extent patients already in contact with psychiatric health care, but also adults with long-standing psychosocial problems and unattended needs who have never before come to the attention of psychiatry. Also, a number of prison inmates have been shown to have developmental disorders not earlier diagnosed, especially ADHD (Ginsberg, Hirvikoski & Lindefors, 2010)

1.3 ADHD: brief review of past and current concepts with a special focus on adults

1.3.1 Development of the concept of ADHD: Disease of attention – moral deficit – brain damage – brain dysfunction – behavioural dysfunction – cognitive dysfunction and symptoms

In 1798 a Scottish physician, Sir Alexander Crichton (1763-1856), described what appears to be a mental state corresponding to ADHD, in his book *An inquiry into the nature and origin of mental derangement: comprehending a concise system of the physiology and pathology of the human mind and a history of the passions and their effects*.

In the chapter "Attention", Crichton described "mental restlessness", a condition that is strikingly similar to ADHD as conceptualised in the DSM-IV and proposed DSM-5. He remarked on its frequency, early onset, and on the distractibility, inability to sustain attention, and fidgetiness so typical of "this disease of attention". He also believed it was inborn or caused by "accidental diseases" and that its clinical expression diminished with age. He

insisted that all teachers would be well aware of the problems caused by the disease, and that educational remediation would be needed (Crichton 1798; Palmer & Finger, 2001).

In 1902 the British pediatrician Sir George Still described hyperactive, often clumsy, children and characterized them as suffering from a deficit in "moral control" which was seen as different from mental retardation (Barkley, 2006). Some decades later, from the 1920's, the concept of minimal brain damage (MBD) gradually evolved after the effects of encephalitis lethargica became evident in some children who displayed a variety of symptoms of inattention, hyperactivity, learning difficulties, and motor control problems. However, as in many cases no structural brain damage could actually be shown, the acronym instead came to be used for minimal brain dysfunction in children (Barkley, 1998a). The first stimulant treatments of children with "behavior disorders", with positive results, are described from the 1930's (Bradley, 1937; Strohl, 2011). For several decades, no adults with MBD were described and the prognosis of MBD was generally believed to be that children "grew out" of these problems, even though some pioneers, e. g. Paul Wender, postulated that MBD often persisted into adult age, causing functional impairment. Wender supported this view by citing studies from the 1950's and 1960's, wherein children with symptoms resembling MBD had been followed for no less than 20 to 40 years (Wender, 1972).

As the DSM and ICD diagnostic manuals were developed, they were intended not to contain the etiologies of psychiatric disorders (which still are mostly unknown) but to be phenomenological descriptions. Thus the terminology changed to describe the observable symptoms, or diagnostic criteria, instead of the assumed and non-specific neurological background ("brain damage/dysfunction").

In the late 1970s, a Swedish group, for the first time, operationalized criteria for MBD, suggesting that the combination of inattention/hyperactivity (referred to as attention-deficit disorder, ADD; see below) on the one hand and motor control/perceptual problems (nowadays referred to as developmental coordination disorder or DCD (APA, 1994)) on the other would be the cornerstones of the diagnosis (Gillberg, Rasmussen, Carlström, Svenson & Waldenström, 1982). This concept was referred to as Deficits in Attention, Motor control and Perception (DAMP) (ibid) and later redefined as ADHD (see below) with DCD (Landgren, Kjellman & Gillberg, 1998; Kadesjö & Gillberg, 1998). These concepts antedated the terminologies used from 1980 and 1987 under APA´s Diagnostic and Statistical Manual of Mental Disorders (DSM).

In the DSM-III (APA, 1980) the diagnosis Attention-Deficit Disorder (ADD; with or without hyperactivity) was used. ADHD was the term adopted by the DSM-III-R (APA, 1987) and DSM-IV (APA, 1994), and will probably be retained in the DSM-5. The term ADHD is in much wider use than the overlapping but not completely corresponding ICD-10 diagnosis hyperkinetic disorder (HKD) (WHO, 1993**)**. With DSM-III, operational criteria in the form of 16 symptoms were introduced. These, via 14 symptoms in DSM-III-R, were to be followed by the 18 symptoms in DSM-IV that, together with criteria for age of onset, persistence and pervasiveness of symptoms, degree of impairment and exclusion criteria, are presently used for diagnosis in research and clinical work. DSM-IV allows for three subtypes of ADHD: Predominantly inattentive, predominantly hyper-active/impulsive and combined type. Consistently, the criteria have been divided into 9 symptoms of inattention and 9 symptoms of hyper-activity/impulsivity. In diagnostic praxis, cognitive functions with emphasis on sustained attention and impulse control are regularly examined, and the current, widely accepted concept of ADHD is that it is a disorder of development of executive functioning (Barkley, 1998a; Barkley, 2010). ADHD is well known in child and adolescent psychiatry and has been extensively studied in individuals before adulthood.

In 1976, Wood and collaborators examined 15 adults with current MBD-like complaints (Wood, Reimherr, Wender & Johnson, 1976) and in the same year a Canadian group published a preliminary report on 35 young adults who had been diagnosed with "severe hyperactivity" as children (Hechtman, Weiss, Finklestein, Werner & Benn, 1976).

From the 1980s, several follow-up studies have been performed, showing that a majority of children diagnosed with ADHD (or the even more MBD-like DAMP, see above) continue to have problems with attention, activity level control and impulsivity in young adulthood (Biederman, 2011). In many individuals, the symptomatology seems to change after adolescence, with less gross motor hyperactivity and more of mental hyperactivity and inner restlessness (Wilens, Biederman & Spencer, 2002; Mick, Faraone & Biederman, 2004). The extent of research into ADHD in adults has seen an almost explosive development from the 1970s and especially from 1990 (Conrad & Potter, 2000). Recently, it has been shown that ADHD can persist and cause maladjustment well into old age, defined as 60 years or older (Guldberg-Kjär & Johansson, 2009; Henry & Hill Jones, 2011).

For an extensive account of the history of the concept of ADHD from 1900, see Barkley (1998a).

1.3.2 ADHD in the brain

Many studies have been performed of brain anatomy, chemistry and functioning in children and adults with ADHD. Consistent findings have included smaller brains, thinner cortex and deviant progression of development of left-right brain discrepancies – especially affecting the frontal lobes – in patients with ADHD compared with matched control groups (Barkley, 1998b; Bradshaw, 2001). The research into neurochemistry has to a great extent focused on dopamine – not unexpectedly, given that the amphetamines and other central stimulants that have been shown to have significant ameliorating effects on the core ADHD symptoms are dopamine agonists. Interesting findings have been described by, for example, Volkow's group, who recently showed that patients with ADHD may have less available dopamine in the brain's reward system than matched controls (Volkow, Wang, Kollins, Wigal, Newcorn et al, 2009). As yet, however, there are no available biological markers for diagnosing ADHD in the clinic. The diagnosis, in adults as well as in children, rests on a carefully taken history and observation by experienced clinicians, as described below.

1.3.3 The causes of ADHD

As with most psychiatric disorders, the cause of ADHD is not known. According to a very consistent literature on twin studies in children, about 70-80% of the ADHD variance is accounted for by genetic factors (Faraone, Perlis, Doyle, Smoller, Goralnick et al, 2005).

It has been shown that children with ADHD often come from families with lower socio-economic status (Schlange, Stein, Taneli & Ulrich, 1975; Faraone & Biederman, 1994). It has also been concluded that ADHD symptoms contribute to academic and occupational under-achievement (Faraone, Biederman, Spencer, Wilens, Seidman et al, 2000; Rasmussen & Gillberg 2000; Kessler, Adler, Barkley, Biederman, Conners et al, 2006; Bernfort, Nordfeldt & Persson, 2008; Galéra, Melchior, Chastang, Bouvard & Fombonne, 2009), and, given the heredity mentioned below, ADHD symptoms in parents thus sometimes may account for the status of these families. It has been inferred, from a very large number of studies, that the greatest single risk factor is genetic (Faraone, Perlis, Doyle, Smoller, Goralnick et al, 2005). However, so far no single gene appears to have a very substantial impact, and it is currently considered more likely that the background is polygenetic with so called epigenetic mechanisms playing an important role (Elia, Laracy, Allen, Nissley-Tsiopinis & Borgmann-Winter, 2011). Environmental influence in utero or early life has been suggested, for example prenatal exposure to alcohol (Streissguth, Barr, Sampson &

Bookstein, 1994; Landgren, Svensson, Strömland & Andersson Grönlund, 2010) or nicotine (Milberger, Biederman, Faraone, Chen & Jones, 1996), or, with less certainty, food additives (Kanarek, 2011).

1.3.4 ADHD in adults: diagnosis and diagnostic procedures

Since the first follow-up studies showing persistence of ADHD into adulthood it has gradually become more common to diagnose and treat ADHD in adults. The diagnostic procedure recommended by most clinicians includes the examination of symptoms, or diagnostic criteria, experienced by the patient in his/her daily life, and an examination of cognitive function with focus on attention and impulse control. However, as has recently been shown by Barkley (2010; Barkley & Fischer, 2011), even in cases where the patient´s detailed history documents huge real-life executive function deficits, it may not be possible to demonstrate such problems at highly structured neuropsychological testing. Of great importance is the developmental history, since one important diagnostic criterion is that onset of symptoms should have been before age 7. A collateral interview, preferably with a parent and with focus on early development and on age of onset, is often performed. Since deficits in executive functioning, especially in sustained attention, are common symptoms or sequelae of many psychiatric and somatic disorders, the differential diagnosis can be difficult and the developmental history is often crucial.

1.3.5 Aids in the ADHD diagnostic process

Commonly used screening questionnaires are the WURS (Ward, Wender & Reimherr, 1993), containing 61 questions for retrospective assessment of childhood symptoms, and the Adult-ASRS (Adler, Spencer, Faraone, Kessler, Howes et al, 2006; Kessler, Adler, Gruber, Sarawate, Spencer & Van Brunt, 2007). The WURS is of particular value since it yields information about childhood symptoms of ADHD, without which a diagnosis of ADHD should not be made according to the DSM-IV. It is intended for completion by the patient, which may allow for some missed cases based on the difficulties in recall described in persons with ADHD (Miller, Newcorn & Halperin, 2010). For practical reasons, often the scores on only the 25 most valid questions of the WURS (WURS-25) are counted. False positives include cases of depression and of borderline personality disorder (Ward, Wender & Reimherr, 1993). The Adult-ASRS measures current symptoms based on DSM-IV diagnostic criteria reformulated to fit adults, and contains a scale for severity. Six of the questions can be used as a preliminary screening. The Adult-ASRS does not, however, address the important

question of age of onset. Several other questionnaires for assessment by patient, staff or family members/significant others of ADHD symptoms exist. Most of these are developed for the assessment of children, but can easily be adjusted to adults in clinical settings. The number of rating scales and questionnaires developed for adult patients is increasing (Rösler, Retz, Thome, Schneider, Stieglitz & Falkai, 2006); for a systematic review of 14 scales, see Taylor, Deb & Unwin (2011).

For the cognitive assessment it is often deemed important to use one of the current scales for cognitive level, most often the latest version of the Wechsler scales for adults (Wechsler, 2008). Although somewhat time-consuming, this gives a basis for further assessment and minimizes the risk that consequences of low general cognitive skills are mistaken for ADHD. The Wechsler scales contain tasks that challenge the patient's attentional and other executive skills, and thus can give an idea of problems suggestive of ADHD. In many cases, the patient is given a so-called CPT (Continuous Performance Test) (Barkley, 1998c) which is a computerized test of basic functioning of impulse control, attention, endurance and reaction time. Several variants of CPT exist, e.g. the Test Of Variables of Attention (TOVA) (Forbes, 1998; Lawrence, Greenberg, Carol, Kindschi, Clifford, & Corman, 2000). So-called test batteries for executive functions may be of less diagnostic value when examining adults for suspected ADHD (Barkley, 2010; Barkley & Fischer, 2011). When assessing an adult for ADHD, differential diagnostic considerations are very often clearly relevant (Kumar, Faden & Steer, 2011).

1.3.6 ADHD in adults: prevalence

In the last decade, some prevalence studies of ADHD in adults, also older adults, have been performed in different countries (Kooij, Buitelaar, van den Oord, Furer, Rijnders & Hodiamont, 2005; Kessler, Adler, Barkley, Biederman, Conners et al, 2006; Fayyad, de Graaf, Kessler, Alonso, Angermeyer et al, 2007; Guldberg-Kjär & Johansson, 2009). These studies show prevalence rates in the area from 1% meeting full DSM-IV criteria according to self-report only (Kooij, Buitelaar, van den Oord, Furer, Rijnders & Hodiamont, 2005) to 4.4% in a large sample and using more elaborate methodology (Kessler, Adler, Barkley, Biederman, Conners et al, 2006). The prevalence in school children is more extensively studied, and generally accepted to be in the range of 3 to 5 per cent of the population (APA, 1994). Half of the children with childhood onset symptoms (and a diagnosis) of ADHD have persistently diagnosable ADHD in young adult age, and the remainder have some persistent symptoms, often with associated psychiatric disorder of other types, such as depression, generalized anxiety disorder, and

substance use disorder (Wilens, Biederman & Spencer, 2002; Haavik, Halmöy, Lundervold & Fasmer, 2010), see below. Extrapolating these findings to the general population of adults, one would expect a rate of about 2-3% of all adults meeting diagnostic criteria for ADHD and another few per cent to have subclinical markers of the disorder (Faraone & Biederman, 2005). This corresponds well with the pooled prevalence 2.5% found by Simon and collaborators (2009) in a meta-analysis of six studies comprising 5307 individuals (mean ages 19 to 44), where the prevalence declined with age. The latter phenomenon has been shown by other authors, e. g. Faraone, Biederman and Mick (2006).

1.3.7 ADHD: psychiatric comorbidity in adults

Several studies have shown a high prevalence of psychiatric disorders in adults with ADHD (Dalsgaard, 2002; Kessler, Adler, Barkley, Biederman, Conners et al, 2006). Rates of criminal behaviour (Rasmussen & Gillberg, 2000; Dalsgaard, 2002) and of alcohol/substance abuse/dependence (Rasmussen & Gillberg, 2000; Dalsgaard, 2002; Kessler, Adler, Barkley, Biederman, Conners et al, 2006) are higher or much higher than in the general population. Conversely, when prisoners are assessed (Rasmussen, Almvik & Levander, 2001; Ginsberg, Hirvikoski & Lindefors, 2010), or patients treated for abuse/dependence disorders (Wilens, Spencer & Biederman, 1995; Wilens, 2007), high prevalence rates of ADHD have been shown in these populations. Other adjustment problems shown to be common in adults with ADHD are academic and/or occupational underachievement (Rasmussen & Gillberg, 2000; de Graaf, Kessler, Fayyad, ten Have, Alonso et al, 2008; Galéra, Melchior, Chastang, Bouvard & Fombonne, 2009) which can be assumed to impact negatively on quality of life for these individuals. One research group found that fatigue and chronic pain syndromes seem to be common in patients with ADHD (Young & Redmond, 2007).

The early descriptions of “clumsy children” have a current counterpart in the DSM-IV diagnosis of developmental coordination disorder (DCD) (APA, 1994). DCD entails problems with motor and sensory coordination that are not seldom encountered in patients with ADHD (Visser, 2003; Kopp, Beckung & Gillberg, 2010). Some researchers have found DCD to occur in children with ADHD with a frequency high enough to warrant the combination a syndrome status, namely DAMP (Kadesjö & Gillberg, 1998; Gillberg 2003). In adults, DCD, or motor clumsiness, in itself has been found to coincide with academic problems (Kirby, Sugden, Beveridge, Edwards & Edwards, 2008) and a history of having been bullied (Bejerot, Edgar & Humble, 2011).

The most common psychiatric disorders to affect adults with ADHD seem to be, apart from alcohol/substance abuse/dependence, affective disorders and anxiety disorders (McGough, Smalley, McCracken, Yang, Del'Homme et al, 2005; Kessler, Adler, Barkley, Biederman, Conners et al, 2006; Sobanski, 2006; Sobanski, Brüggemann, Alm & Kern, 2007; Babcock & Ornstein, 2009; Halmöy, Halleland, Dramsdahl, Bergsholm, Fasmer & Haavik, 2010; Klassen, Katzman & Chokka, 2010; Gjervan, Torgersen, Nordahl & Rasmussen, 2011). Commonly included in the anxiety disorders is obsessive compulsive disorder (OCD) (APA, 1994), which affects a number of ADHD patients. In adults with OCD and tic disorders, ADHD appears to be common (40%) (Coffey, Miguel, Biederman, Baer, Rauch et al, 1998), while in samples of OCD patients without tics it is less common. In the study by Coffey's group, 5% of adults with OCD without tics had ADHD, while Sheppard and collaborators (2010) found 11.8% with ADHD in a sample of 155 OCD-affected individuals (age range 4-82) without tic disorders. In recent years, concurrent with the notion of bipolar disorder as a spectrum disorder, interesting studies of bipolar disorder and ADHD have been done. These show that children and adults with ADHD are at elevated risk, compared to the general population, for bipolar disorder and that differential diagnosis sometimes may pose a problem (Klassen, Katzman & Chokka, 2010). A Swedish group has found that a history of ADHD affects the severity of the bipolar illness (Rydén, Thase, Stråht, Åberg-Wistedt, Bejerot & Landén, 2009). As to schizophrenia, Dalsgaard's studies of adult psychiatric outcome of children with ADHD revealed an increased risk for schizophrenia which has also been shown by other authors (Dalsgaard, 2002; Rubino, Frank, Croce Nanni, Pozzi, Lanza di Scalea & Siracusano, 2009; Peralta, de Jalón, Campos, Zandio, Sanchez-Torres & Cuesta, 2011). A classical study of Danish children at high risk for schizophrenia showed that the children most likely to get the illness were those with characteristics grossly overlapping with the symptoms of ADHD, namely shorter attention span and poorer control of affects and impulses, although the label ADHD was not used (Mednick, Parnas & Schulsinger, 1987). Another study, of adolescent onset psychosis, showed a high rate of premorbid DAMP in affected individuals (Hellgren, Gillberg & Enerskog, 1987). Interestingly, in the long time follow-up studies of children with MBD-like conditions referred to by Wender (1972) several of the probands fell ill with schizophrenia.

Personality disorders have been shown to be common in adults with ADHD, especially cluster B disorders. Anckarsäter and collaborators (2006) found antisocial personality disorder (ASPD) in 27.8% of adult patients with ADHD. In follow-up studies of children with ADHD ASPD was diagnosed in as many as 23% (van Dijk & Anckarsäter, 2011). The ASPD group has been

shown to be at a far greater risk for developing criminal behaviours and alcohol/substance abuse/dependence than ADHD patients without ASPD (Mannuzza, Klein, Bessler, Malloy & LaPadula, 1993; Herrero, Hechtman & Weiss, 1994). The overlap in symptoms between ADHD and emotionally unstable/borderline personality disorder has been noted by several authors (Wender, 1972; van Dijk & Anckarsäter, 2011). This overlap illustrates the diagnostic difficulties that arise when the same, or very closely resembling, symptoms/behaviours are diagnostic criteria for different disorders, as is often the case in psychiatry.

1.3.8 ADHD in adults: differential diagnostic considerations

Since deficits in executive functions such as those seen in ADHD are features of many chronic as well as acute psychiatric (Kumar, Faden & Steer, 2011) and neurological disorders, differential diagnostic considerations have to be made when these executive problems are seen in adults. One important differential diagnosis is, as mentioned above, mild or borderline intellectual disability. Other chronic disorders which also bring with them executive deficits are the autism spectrum disorders (ASD) (Russell, 1997; Hill, 2004). However, adult patients with ASD have attention deficits that are of a different quality – rather than not focusing on the relevant stimuli, people with ASD focus on irrelevant things (Klin, Jones, Schultz, Volkmar & Cohen, 2002) – than those seen in ADHD, and the ASD in itself seldom brings inner restlessness in adults without mental retardation. Lack of impulse control, or inhibition, is not typical of ASD (Hill, 2004; Gargaro, Rinehart, Bradshaw, Tonge & Sheppard, 2011).

In most psychiatric disorders that may affect adults, executive functions are impaired. This is well-known from research and clinical experience with schizophrenia (Weinberger & Gallhofer, 1997; Freedman & Brown, 2011). In depression and bipolar disorder, cognitive functions involving attention and executive functions have also been shown to be compromised (Goldberg & Chengappa, 2009; Maalouf, Brent, Clark, Tavitian, McHugh et al, 2011). Anxiety decreases the executive ability (Ferreri, Lapp & Peretti, 2011), as well as fatigue, influence of alcohol or narcotics and negative stress of all kinds, e.g. brought about by a somatic illness. The difference between ADHD and many other disorders where executive functions are compromised is the developmental history, where, in the case of ADHD, the chronicity of symptoms should be evident as well as their persistence also when the individual functions at his/her best.

1.3.9 ADHD in adults: prognosis, treatment and outcome

The long-term – meaning life-long – trajectory of ADHD has not yet been fully mapped out. Some earlier follow-up studies have shown that symptoms may lessen gradually over the years (Hill & Schoener, 1996), see also p 13. More recent prevalence studies indicate that, while a number of patients get syndromatic remission during their teens, functional impairment and in many cases several ADHD symptoms may persist for many years (Biederman, 2011). As already mentioned, screening by Swedish researchers in geropsychiatry (Guldberg-Kjär & Johansson, 2009) has recently shown that ADHD may persist well into retirement age.

A follow-up study in Gothenburg showed that children with unmedicated ADHD or DAMP as young adults more often than matched controls lived on welfare, tended to behave criminally and had psychiatric as well as alcohol/substance dependence disorders (Rasmussen & Gillberg, 2000). Similar results were obtained in a Danish follow-up study of a clinical group of children with ADHD (Dalsgaard, 2002), and many studies of the health and social circumstances of adults with ADHD have shown that this is a group with health problems as well as social adjustment difficulties (Faraone, Biederman, Spencer, Wilens, Seidman et al, 2000; Kessler, Adler, Barkley, Biederman, Conners et al, 2006; Stein, Blum & Barbaresi, 2011).

That adults to a great extent respond to the same pharmacological treatments as children with ADHD has been well substantiated (Spencer, Biederman, Wilens, Doyle, Surman et al, 2005; Bejerot, Rydén & Arlinde, 2010), but so far, the follow-up time in studies is short when the chronicity of the syndrome is taken into account. Long-term treatment outcome for adults with ADHD, by and large, is not known. Training of working memory and neurofeedback are methods that have become popular, while the evidence for efficacy of these methods is limited (SBU rapport, 2009). Different psychotherapeutic methods are being tried, individual as well as group methods, but so far there is no good evidence for any single method (McDermott, 2011). Many adults with ADHD are in need of treatment of concomitant mental health or alcohol/substance dependency problems and also of measures taken in non-medical settings, such as correctional treatment or support from social services. The outcome will thus depend on complex interactions between treatments.

1.4 ASD: brief review of past and current concepts with a special focus on adults

1.4.1 Development of the concept of ASD: Idiocy/imbecility – childhood schizophrenia – childhood psychosis – autism and Asperger's syndrome – the autism spectrum

Although there exist very early descriptions of adults who were noted for an unusual conduct reminiscent of today's concept of ASD (Frith, 1991; Houston & Frith, 2000), the behaviours of these individuals do not seem to have been labelled. However, persons with intellectual disabilities, among whom there certainly must have been a number with ASD, were labelled from at least the 18th century (Trent, 1994) and treated as different from those with psychiatric disorders from the 19th century (Harding, 1975).

Myths of so-called changelings and of feral children may well have been modelled after the strange ways of children with autism. The detailed account, given by his teacher Jean Itard, of the "wild boy" Victor gives a distinct impression that this boy may have had autism (Frith, 1991). Although there are some early descriptions of children with symptoms resembling autism (Ssucharewa & Wolff, 1996; Wolff, 2004), the American child psychiatrist Leo Kanner is recognized as the author of the first systematic description of children with what he called "autistic disturbances in affective contact" (Kanner, 1943) and low intellectual ability. The term "autism" had, however, been used in adult psychiatry since 1911, when Eugen Bleuler used the word to describe one of the symptoms of schizophrenia (Bleuler, 1911). Bleuler defines autism ("egocentric thinking" from the Greek "autos" for self) as "detaching oneself from outer reality along with a relative or absolute predominance of inner life". Interestingly and foregoing thoughts of a schizophrenia spectrum, he observed that "autistic thinking" can occur also in healthy individuals (Stotz-Ingenlath, 2000). For decades, infantile autism was considered a very rare condition, usually connected with intellectual disability and exclusively a concern for child psychiatry. The term autism for a childhood condition was not used in the diagnostic manuals when these were first introduced. The disorder was grouped with childhood schizophrenia, but, after being separated from schizophrenia by Kolvin et al (1971), the umbrella label was changed to childhood psychosis. In DSM-III (APA, 1980), the term "infantile autism" was used, followed by "childhood autism"/"autistic disorder" in ICD-10/DSM-IV. In the latter

manuals,"childhood autism" or "autistic disorder", respectively, were grouped together with some other diagnoses under the label "pervasive developmental disorders" (PDD) (WHO, 1993; APA, 1994).

Meanwhile, the British researchers Wing and Gould had been studying autistic symptoms in a large group of children with special needs. Their work resulted in the description of the so-called triad of basic autistic impairments, present in all children who fitted Kanner's description, which has since then been guiding diagnostic work (Wing & Gould 1979). Around the same time, Gillberg (1983a) showed that cases of children with "psychotic behaviour" (corresponding to the autism triad) were ten to twenty times more common in the general population than was "classic infantile autism", and that among institutionalised young people with MR, the rate of severe social impairment was 50% (Gillberg 1983b), supporting the notion of an "autistic continuum". Wing and Gould during their work, like Gillberg, observed that a larger group of children had functionally impairing traits of autism, always with the impairment in mutual social interaction, while not exactly meeting all criteria for autism proper. This observation gave rise to their idea that there exists an "autistic spectrum**",** wherein the symptom expression is variable depending on the individual's age as well as verbal and intellectual abilities (Wing, 1991; 1996; 1997). Further support for this thought was given by Asperger's description of children with "autistic psychopathy" (Asperger, 1944). Asperger's work as well as a suggestion to name autistic conditions in persons of average intellectual ability and with good verbal skills Asperger's syndrome was introduced to English-speaking medical professionals by Wing in 1981 (Wing, 1981). This article is also one of the first descriptions of adults with autistic conditions, and still unique in describing the same disorder in children and adolescents as well as in adults.

In DSM-IV and ICD-10 Asperger's disorder is listed among the pervasive developmental disorders, as are other ASDs such as atypical autism (ICD-10) and pervasive developmental disorder not otherwise specified (PDD-NOS; DSM-IV). The DSM-IV/ICD-10 diagnostic criteria for Asperger's disorder have been criticized, especially the criterion of normal development up to three years of age but also that no impairment in communication is required (Miller & Ozonoff, 1997; Leekam**,** Libby, Wing, Gould & Gillberg, 2000; Frith, 2004). Therefore, many clinicians and researchers have used the Gillberg criteria (Gillberg & Gillberg, 1989), observing that these more closely conform to Asperger's original descriptions. In adult psychiatry, schizophrenia as an exclusion criterion has sometimes posed a problem, but in the text revision DSM-IV-TR (APA, 2000) this has been changed.

For many years there were few descriptions and little research concerning adults with ASD. In earlier follow-up studies, children with autism – the great majority with autistic syndrome/infantile autism and intellectual disability - were followed for some years but rarely until adulthood (Lotter 1974**,** Gillberg 1983b**,** Gillberg & Steffenburg 1987**)**. Only in the last decade have follow-up studies into adulthood and middle age been performed, showing that autism spectrum disorders to a great extent are stable over time (Howlin, 2000; Howlin, Goode, Hutton & Rutter, 2004; Billstedt, 2007; Cederlund, 2007). As the concept of Asperger's syndrome has become increasingly well-known to professionals and to the public, a growing number of adults have been found to meet criteria for this disorder (Murphy, Beecham, Craig and Ecker, 2011).Still, with the exception of some case descriptions (James, Mukaetowa-Ladinska, Reichelt, Briel & Scully, 2006; van Niekerk, Groen, Vissers, van Driel-de Jong, Kan & Oude Voshaar, 2011), almost nothing is known about ASD in the ageing individual and the majority of studies on ASD concern children.

Nowadays, as regards adults, the autism spectrum is generally thought of as containing autistic syndrome, Asperger's syndrome and PDD-NOS. Childhood disintegrative disorder is not diagnosed in adults, and it is highly probable that individuals with this rare condition diagnosed in childhood meet criteria for autistic disorder as adults (Gillberg, 1995b). Rett's syndrome, a neurological disorder clearly misplaced in the ASD/PDD section in DSM-IV/ICD-10 is very rarely diagnosed in adults but new methods may change this (Percy, 2002).

1.4.2 ASD in the brain

Many efforts have been made during the years in order to find the brain basis of autism. Some of the more robust findings have been the larger brains of some children with autism, the anomalies in cellular organisation in certain areas at autopsy, signs of bilateral temporofrontal lesions and dysfunction, brainstem and cerebellar abnormalities (corresponding to the default network in the brain), and widespread poor connectivity (Coleman & Gillberg, 2011). Although much is known about brain abnormalities in autism, there has not been any consistent finding robust and specific enough to be used for clinical diagnosis. Today, many researchers seem to agree that autism probably does not imply pathology in one region or structure in an otherwise normally developed and well functioning brain, but a widespread condition affecting important social-communication networks in the brain (Müller, 2007; Ecker, Rocha-Rego, Johnston, Mourão-Miranda, Marquand et al, 2010)**.** Of recent interest are the mirror neuron systems described by Rizzolatti and collaborators (Rizzolatti & Fabbri-Destro, 2008). Other interesting new

efforts have been made by Ecker and collaborators who analyzed patterns of activity in several regions as well as cortical thickness, and have found that these methods can discriminate between ASD and "normality" with up to 90% accuracy (Ecker, Marquand, Mourão-Miranda, Johnston, Daly et al, 2010).

1.4.3 The causes of ASD

The unusual behaviours and uneven capacities of children with ASDs have given rise to much speculating and myth building regarding possible etiologies (Kristiansen, 1998). Today, among researchers in the field there is a consensus that genetic mechanisms influencing the development of the nervous system play a major role in most cases, and also that, as the ASDs are heterogenous, there may be many etiologies (Geschwind & Levitt, 2007; Abrahams & Geschwind, 2008). Environmental, e. g. obstetrical, factors may contribute, and become more important in cases where the genetical susceptibility is low (Dodds, Fell, Shea, Armson, Allen & Bryson, 2011).

1.4.4 ASD in adults: diagnosis and diagnostic procedures

As with ADHD, in recent years the need for diagnostic assessments of ASD in adults has become evident. In Sweden, ASD diagnoses are occasionally made in adult psychiatry and the examination commonly and preferably involves an assessment of cognitive ability, as many individuals with ASD have uneven, sometimes extremely uneven, cognitive profiles (Happé, 1994; Goldstein, Beers, Siegel & Minshew, 2001; Goldstein, Minshew, Allen & Seaton, 2002; Frith, 2004; Anckarsäter, Nilsson, Saury, Råstam & Gillberg, 2008). This unevenness, constituting an impairment in itself, makes an estimation of cognitive functioning without the use of a validated reliable scale very uncertain. Furthermore, in addition to the thorough clinical interview and observation of the patient, every effort must be made to obtain a developmental history also when the patient is middle-aged or older. For the difficult differential diagnosis, the developmental history, taken by an experienced clinician, is crucial.

Most patients with ASD have cognitive dysfunctions involving impairment of so-called central coherence (Happe & Frith, 2006), meaning a tendency to attend to details rather than observing the whole. Thus it may be helpful for the patient if the diagnostic procedure is planned as coherently as possible, avoiding fragmentation. Adults with ASD have described the diagnostic procedure, carried out according to these principles, as a positive experience with therapeutic values (Bejerot, 2004; Norrö, 2006).

1.4.5 Aids in the ASD diagnostic process

Several screening questionnaires and interview/observation aids for the diagnostic process have been constructed, in fact more for ASD than for ADHD (which is surprising given that ADHD is far more common, and, unlike ASD, can be treated effectively). Among the earliest is the Childhood Autism Rating Scale (CARS) (van Bourgondien, Marcus & Schopler, 1992; Nordin, Gillberg & Nydén, 1998), a semi-structured scale to be used when interviewing a parent and observing a patient. The scale allows for rating the ASD as mild, moderate or severe and can be used in clinical settings for adults, especially adults with mental retardation.

The ASSQ (Autism Spectrum Screening Questionnaire) (Ehlers, Gillberg & Wing, 1999) was created to screen for ASD in school children of normal intelligence. The scoring is meant to be done by teachers and/or parents. In clinics where adults are assessed, it can be used retrospectively.

Gillberg and co-workers have developed a semi-structured interview on the basis of their proposed criteria for Asperger's syndrome, the ASDI (Asperger Syndrome Diagnostic Interview) (Gillberg, Gillberg, Råstam & Wentz, 2001), in one version for parents and one for teen-agers. These can be used when assessing adults.

More extensive semi-structured "investigator-based" interviews to be used with parents (or other persons well-informed about the patient's early childhood and development) are the ADI-R (Autism Diagnostic Interview – Revised) (Lord, Rutter & Le Couteur, 1994) and the DISCO (Diagnostic Interview for Social and Communication disorders) (Leekam, Libby, Wing, Gould & Taylor, 2002). Both can be used with parents or other informants also if the patient is adult. The DISCO collects information not only about autistic symptoms but a wide range of developmental impairments. A secondary effect of parent interviews, also when the patient is adult, is the often very welcome opportunity for the parent to recount years of worries and unanswered questions.

ADOS-G (Autism Diagnostic Observation Schedule-Generic) (Lord, Risi, Lambrecht, Cook, Leventhal et al, 2000) is a standardized method of assessing autistic symptoms by behaviour observation. Module 4, developed for verbal adolescents, can be used with adults but has been shown to give false positive results with patients with schizophrenia (Bastiaansen, Meffert, Hein, Huizinga, Ketelaars et al, 2010).

The Autism Quotient (AQ) (Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001), a screening questionnaire to be filled in by adult patients, has been much used in adult psychiatry; however, its usefulness in differential diagnosis may be limited (Sizoo, van den Brink, Gorissen-van Eenige, Koeter, van Wijngaarden-Cremers & van der Gaag, 2009; Naito, Matsui, Maeda & Tanaka, 2010). The AAA (Adult Asperger Assessment) (Baron-Cohen, Wheelwright, Robinson & Woodbury-Smith, 2005) is combining AQ with other self-report questionnaires.

RAADS-R, the Ritvo Autism and Asperger´s Diagnostic Scale-Revised (Ritvo, Ritvo, Guthrie, Yuwiler, Ritvo & Weisbender, 2008; Andersen, Näswall, Manouilenko, Nylander, Edgar et al, 2011), is a self-report questionnaire with one important advantage, namely the inclusion of a developmental perspective in the form of retrospective rating of presence of symptoms before age sixteen. However, as always with self-reports, there are important caveats: the patient's capacity for recall and his/her wish to get, or not to get, a developmental disorder diagnosis.

Since, traditionally, "diagnostic instruments" are validated through the comparison with an experienced clinician's assessment, the latter must be considered as the ultimate "golden standard". There is no substitute for clinical experience (Wing, 2010).

1.4.6 ASD in adults: prevalence

The prevalence of ASD in adult non-clinical populations has not been much studied – only one such study, conducted in the United Kingdom by Brugha and collaborators (2011) exists to date. In this study, the prevalence of ASD in adults was found to be 0.98%. Since ASD in most cases seems to persist from childhood into adulthood (Billstedt, 2007; Cederlund, 2007), the prevalence in adults may be about the same as in children. From population studies of school-age children (Ehlers & Gillberg, 1993), it can be estimated to be between 0.6% and 0.9%. However, a recent study in Korea gives a considerably higher prevalence in children, 2.64% (Kim, Leventhal, Koh, Fombonne, Laska et al, 2011). There is some indication that symptoms may lessen over the years (Cederlund 2007; Seltzer, Krauss, Shattuck, Orsmond, Swe & Lord, 2003; Esbensen, Seltzer, Lam & Bodfish, 2009), according to clinical experience maybe even to the extent that diagnostic criteria no longer are met. It can be speculated that a number of individuals with normal intelligence and ASD eventually may learn how to cope with their difficulties and in some cases find work suited to their "islets of abilities".

In adult clinical or forensic populations some studies of ASD prevalence have been performed by British and Swedish groups, showing that individuals with ASD are more common in these settings than, presumably, in the population at large (Scragg & Shah, 1994; Hare, Gould, Mills & Wing, 1999; Söderström & Nilsson 2003; Anckarsäter, Nilsson, Saury, Råstam & Gillberg, 2008). This may be due to persons with ASD being vulnerable to psychiatric illness, and, in some cases, prone to criminal behaviour due to the impairment of social understanding. However, some researchers have found lower numbers, 0.2% and 0.6%, respectively, of adults with ASD in psychiatric settings in Italy and Taiwan, respectively (Raja & Azzoni, 2001; Chang, Juang, Wang, Huang, Chen & Hwang, 2003). Other groups have not found indications of higher rates of criminality in groups with ASD (Mouridsen, Rich, Isager & Nedergaard, 2008a; Hippler, Viding, Klicpera & Happé, 2010).

1.4.7 ASD: psychiatric comorbidity in adults

Several authors, working in different countries, have shown that adults with ASD – with or without intellectual disability – seem to be vulnerable to psychiatric disorder, or psychiatric symptoms (Ghaziuddin, Weidmer-Mikhail & Ghaziuddin, 1998; Mouridsen, Rich & Isager, 2008; Esbensen, Greenberg, Seltzer & Aman, 2009; Matson & Shoemaker, 2009; Hofvander, Delorme, Chaste, Nydén, Wentz et al, 2009; Helverschou, 2010; Bakken, Helverschou, Eilertsen, Heggelund, Myrbakk & Martinsen, 2010; Skokauskas & Gallagher, 2010). As in the population at large, the most common mental health problems are affective disorders and anxiety disorders, the latter including OCD (Skokauskas & Gallagher, 2010). Of adolescents with eating disorders, 10% to 12% have been found to meet criteria for ASD (Wentz, Lacey, Waller, Råstam, Turk & Gillberg, 2005). It is undisputable that individuals with ASD may be affected by psychoses, also schizophrenia (Petty, Ornitz, Michelman & Zimmerman, 1984; Howlin, 2000). A number of authors have found schizophrenia prevalences of 3 to 4 per cent (Mouridsen, Rich, Isager & Nedergaard, 2008b; Ståhlberg, Söderström, Råstam & Gillberg, 2004), while an Italian group investigating adult psychiatric patients found schizophrenia diagnoses in 16 of 22 patients with ASD (Raja & Azzoni, 2010). In a Danish follow-up study of patients with atypical autism, schizophrenia spectrum disorders had been diagnosed in more than one third of the probands (Mouridsen, Rich & Isager, 2008). An earlier study of young adults with ASD, 15 to 41 years of age, found schizophrenia in no more than 0.6%, consistent with the total population prevalence (Volkmar & Cohen, 1991). It can be argued that many of the patients in the latter study were younger than the median age of onset for schizophrenia (Gorwood, Leboyer, Jay, Payan & Feingold, 1995) and that

23% of all new cases of schizophrenia occur in patients older than 40 years (Harris & Jeste, 1988). An interesting finding is the high number of children diagnosed with PDD-NOS in a group that later, but still in their childhood, fell ill with schizophrenia (Rapoport, Chavez, Greenstein, Addington & Gogtay, 2009). Nylander, Lugnegård and Unenge Hallerbäck (2008) provide a review of literature and a discussion on the possible connection between autism and schizophrenia. In the light of current findings from genetic and brain imaging studies it has recently been suggested that there may be a possibility that autism and schizophrenia are related (King & Lord, 2011).

Adults with ASD and normal intelligence often meet criteria for personality disorders, especially obsessive-compulsive, paranoid, avoidant and schizotypal (Anckarsäter, Stahlberg, Larson, Hakansson, Jutblad et al, 2006; Bejerot, 2007; Barneveld, Pieterse, de Sonneville, van Rijn, Lahuis et al, 2011), but in my experience these additional diagnoses have little, if any, clinical value for the person with an ASD. The personality disorder diagnostic labels do not cover "new" problems, but are merely reflections of the fact that individuals with ASD often have the "symptoms" subsumed under "specific" personality disorder categories.

Several authors have found a high prevalence of attention deficits, sometimes labeled as attention deficit disorder (ADD) or ADHD, in children and adolescents with ASD (Ehlers & Gillberg, 1993; Ghaziuddin, Weidmer-Mikhail & Ghaziuddin, 1998; Leyfer, Folstein, Bacalman, Davis, Dinh et al, 2006; Mattila, Hurtig, Haapsamo, Jussila, Kuusikko-Gauffin et al, 2010; Gargaro, Rinehart, Bradshaw, Tonge & Sheppard, 2011; Barneveld, Pieterse, de Sonneville, van Rijn, Lahuis et al, 2011). ADHD in adults with ASD is less studied, but the literature points to a considerable overlap in the examined, mainly Swedish, populations (Stahlberg, Soderstrom, Rastam & Gillberg, 2004; Anckarsäter, Stahlberg, Larson, Hakansson, Jutblad et al, 2006; Rydén & Bejerot, 2008; Anckarsäter, Nilsson, Saury, Råstam & Gillberg, 2008; Hofvander, Delorme, Chaste, Nydén, Wentz et al, 2009**).**

Interestingly, and maybe in line with the concept of ESSENCE, in the four studies where the ASD group was split into subgroups, ADHD was more common in the PDD-NOS/atypical autism group, i. e. the group that is farthest from the description of "core autism". DSM-IV does not allow an ADHD diagnosis to be made in an individual with an ASD. This exclusion criterion has been suggested to be removed from the next edition of DSM.

1.4.8 ASD in adults: differential diagnostic considerations

Since some of the symptoms of ASD may be clinically impossible to discriminate from certain of the symptoms of schizophrenia (the so-called negative symptoms, and catatonic symptoms), persistent hallucinations or delusions are required for a schizophrenia diagnosis in a person with ASD (APA, 2000).

Certain personality disorders, eg obsessive-compulsive, phobic, schizotypal or schizoid, may have traits in common with and therefore be difficult to distinguish from ASD (Nagy & Szatmari, 1986; Wolff, 1995; Bejerot, 2007; Barneveld, Pieterse, de Sonneville, van Rijn, Lahuis et al, 2011). Social phobia can superficially resemble ASD, and some adults with ASD have an avoidant social behaviour (Bejerot & Mörtberg, 2009).

MR is associated with ASD in at least 20% of the cases (Nordin & Gillberg, 1996; Bryson, Bradley, Thompson & Wainwright, 2008), and MR is also an important differential diagnosis – in the clinic, mild or borderline MR can be mistaken for ASD.

In clinical settings, ADHD, or certain consequences thereof (social clumsiness, inattention to social signals), is sometimes mistaken for ASD.

An important differential diagnostic issue is to distinguish between ASD and so-called psychopathy (Cleckley, 1976) – both can be said to be disorders of empathy, but of different dimensions thereof (Rogers, Viding, Blair, Frith & Happé, 2006; Blair, 2008; Jones, Happé, Gilbert, Burnett & Viding, 2010; Baron-Cohen, 2011). Antisocial personality disorder, which is partly overlapping with the concept of psychopathy, was not found in any of 81 probands with ASD (without concomitant ADHD) when examined by Anckarsäter and collaborators (2006).

1.4.9 ASD in adults: prognosis, treatment and outcome

For many years, the prognosis of children with autism was described as gloomy in terms of amelioration of symptoms. Follow-up studies into adulthood of children with autism and MR still show that very few are able to live independently, work or engage in social activities or relationships outside their original families (Nordin & Gillberg, 1998; Howlin, Goode, Hutton & Rutter, 2004**;** Billstedt, 2007). Virtually none has children. As the concept of an autistic spectrum eventually has gained acceptance, follow-up

studies have been extended to include individuals with normal intelligence and with well developed language. Subsequently, the number of persons with ASD for whom a better prognosis has been shown has increased (Howlin, 2000; Cederlund, 2007) but still the outcome for most individuals is not on par with their level of intelligence (Cederlund, 2007). One study, by Farley and collaborators, showed more favourable outcomes in a population with long traditions of unusually extensive socially supportive networks (Farley**,** McMahon, Fombonne, Jenson, Miller er al, 2009). To become gainfully employed, adults with ASD may need special adaptations in work situations also when of normal intelligence; successful such programs have been launched (Mawhood & Howlin, 1999). Many have trouble coping with everyday life or getting adequate support (Balfe & Tantam, 2010; Griffith, Totsika, Nash & Hastings, 2011).

Treatment options have been numerous. For some decades, psychoanalytical views on the causes for autism prevailed, which resulted in treatment ideas such as holding (Howlin, 1998) or psychoanalytical therapy for parents (Kristiansen, 1998). From the 1980's the paradigm has shifted to a consensus that autism is a biological brain dysfunction and a number of biological treatments have been launched, pharmacological as well as others, alongside with therapies with a behavioural and/or pedagogical approach (Howlin, 2005). Almost all treatments which have been used for ASD have been intended for children. So far, there is no evidence for any treatment being essential for good outcome or for amelioration of autistic symptoms in adulthood (Föreningen Sveriges Habiliteringschefer, 2011). It has been shown that the symptoms, in particular the communication impairment, comprised in the autistic triad decrease over the years from diagnostic assessment in childhood into adult age (Seltzer, Krauss, Shattuck, Orsmond, Swe & Lord, 2003). The impact of treatment or services on this amelioration is not known. Many adults with autism receive psychopharmacological treatment, especially with antipsychotics, also in cases where no psychiatric disorder warranting treatment has been diagnosed (Åkerström, 2001). Esbensen and collaborators have recently shown this, and also that the number of medicines given to a patient with ASD tends to increase over time (Esbensen**,** Greenberg, Seltzer & Aman, 2009).

The research into ASD in adulthood – its expressions, trajectories, comorbidities and the outcome of service efforts in terms of quality of life – is still scarce. Even more scarce is the knowledge when it comes to ASD in the elderly, or the effect of autism on ageing and vice versa (James, Mukaetowa-Ladinska, Reichelt, Briel & Scully, 2006; Van Niekerk, Groen,

Vissers, van Driel-de Jong, Kan & Oude Voshaar, 2011; Geurts & Vissers, 2011).

1.5 Evolutionary aspects of ADHD and ASD

Research into the causes of ADHD and ASD has revealed a strong genetic influence and also a genetic overlap between these two disorders (Abrahams & Geschwind, 2008; Sharp, McQuillin & Gurling, 2009; Lichtenstein, Carlström, Råstam, Gillberg & Anckarsäter, 2010). If, as is sometimes suspected, the prevalence of these disorders had actually been rising in only the last decades, it would certainly be a very puzzling phenomenon since the evolution of man, as far as we know today, hitherto has been an extremely slow process (Darwin, 1859). It has thus been argued that environmental causes may have played a role in the very recent years.

As to ADHD, from clinical experience the fertility of persons with ADHD seems to be on par with that of the population in general. Thus, it is not surprising that the genes causing ADHD have survived and been spread. Contributing to this may have been the fact that some of the most striking ADHD symptoms in many cases decrease during adolescence (which, on the other hand, may have decreased the spreading of ADHD genes). It is not known whether persisting ADHD and ADHD with childhood but not adult impairment are genetically different. As evolution is driven by the ever-changing middle forms (Darwin, 1859), one may speculate that some of the traits of ADHD may be, at least to a degree or in circumstances when they are not impairing, evolutionary advantageous. For example being quick and impulsive, easily enthused and interested in new things without pondering too much about possible consequences may have been useful qualities in the competition for partners as well as in exploring new territories (Shelley-Tremblay & Rosén, 1996; Jensen, Mrazek, Knapp, Steinberg, Pfeffer et al, 1997).

As for classical autism, the fertility rates are supposed to be almost zero, the serious impairment in social interaction preventing mating. However, with the concept of so-called high-functioning autism and Asperger's syndrome, it has become evident that some persons, although according to clinical experience at a far lesser rate than the general population, with ASD have children. Research has also shown that parents and siblings of persons with ASD have a high frequency of traits that have been called autistic or "the broad autistic phenotype" (BAP) (Losh, Childress, Lam & Piven, 2008). The description of these traits – preference for solitude, slight language and communication difficulties, and obsessional traits – does not seem to suggest

any advantage in an evolutionary aspect, at least not in times up to very recently, when a person can communicate and "interact" socially through computers. Some of the cognitive traits of autism may, in a person of high intelligence, be of value for society, such as attention to details and facts, unconventional thinking and disinclination to be disturbed by (trivial) social signals. These traits still are not immediately advantageous in the competition for partners, but the possibilities for people with these traits – or with ASD – to find partners have increased in the latest decades, with new means of world-wide communications (D'Auria, 2010; Jordan, 2010).

2 AIMS

The aims of the study were to gain insight into the prevalence of ASD and ADHD in adult psychiatric patients, and into the potential benefit of recognition and diagnostic labeling of these disorders.

More specifically, the aims were to:

- develop a short screening questionnaire, to be used by staff, for ASD in adult psychiatric patients;
- use this questionnaire in order to examine the extent of previously undiagnosed and diagnosed ASD in a large group of psychiatric out-patients;
- examine the extent of previously undiagnosed and diagnosed ADHD in out-patients in general psychiatry, using the WURS-25 for screening;
- describe the impact of a diagnosis of ASD or ADHD when assigned in adulthood;
- describe the opinions about the diagnostic procedure held by patients and significant others;
- use register data to study changes in diagnostic practice regarding ASD and ADHD diagnoses in adult psychiatry during twenty years, and to describe diagnostic delay, concomitant diagnoses and service utilization in patients diagnosed with ASD or ADHD.

2.1 Ethical considerations

Each of the four studies was approved by the Regional Ethical Review Board, Faculty of Medicine, University of Lund. Informed consent was given by all the patients who were offered a clinical evaluation in Study I, all patients returning a screening questionnaire in Study II, and all patients returning a questionnaire in Study III. Study IV was conducted on de-identified register data, and thus informed consent was deemed unnecessary by the Regional Ethical Review Board.

3 SUBJECTS AND METHODS IN STUDIES I TO IV

3.1 Subjects

3.1.1 Study I – Screening for ASD in adult psychiatry

In Study I, the target population consisted of the total number of out-patients (n=1398) registered as being in treatment on a certain day (April 1st, 1996) in one "psychiatric sector" of Lund, Sweden (a geographic area where all patients were served by one service provider administration, with several units serving patients with different needs). Ninety-five per cent of these (n=1323) were screened for ASD by members of staff. For 75 patients, information was too scarce, or no current staff member felt able to complete the questionnaire. Since the clinic served adults only, the screened patients had an age range of 18 to 85 years with a mean of about 40 years. As most psychiatric patients are not subjected to neuropsychological assessment, the mental development range of these patients is not known in detail. However, from clinical observations it was surmised that intellectual levels in the study group varied from a few with severe mental retardation to superior ability, with most persons functioning in the normal (IQ 70-130) range. Of the screened patients 59.5% were women. The registered ICD-9 diagnoses of the patients varied. The largest diagnostic group was "neurosis and psychosomatic disorder" (19.1%) followed by "schizophrenia and paranoid psychosis" (16.5%) and "neurotic depression" (16.0%). The out-patients were served by two units, one for general psychiatry and one for patients with more complex needs. Most of the patients served by the latter unit (n=499) had psychotic illnesses, severe personality disorders or other chronic and severe disorders.

3.1.2 Study II – Screening for ADHD in adult psychiatry

In Study II, 406 consecutive out-patients treated for psychiatric disorders at a unit for general psychiatry in Lund, Sweden, were offered to participate in a screening for childhood ADHD symptoms. Another 145 patients visiting the unit during the same period had, for administrative reasons, not been asked to participate but this group did not differ significantly from the invited group regarding data registered in the clinic's central register (age, gender), and

showed a similar distribution of main diagnoses. Since we were interested in screening only those patients who were judged by professionals to have clinically relevant psychiatric disorders, patients making first visits had been excluded from the study. Eight patients actively refused participation, leaving 398 who were asked to take part in the screening by completing the WURS. Of this group, 66.3% were women. The 398 patients were treated for a variety of disorders, but only a very small number had diagnoses of psychotic disorders, due to the fact that patients with psychosis were treated at another, specialized, unit. There were no patients with alcohol or substance abuse/dependency as main diagnosis, since the latter group was not treated in psychiatry at the time of the study. Age range for the patients was 18 to 79 years with a mean just below 40 years. For a vast majority of the patients the intellectual level was not known in detail, but clinically estimated to be in the normal range of functioning (IQ 70-130).

3.1.3 Study III – Impact of ADHD/ASD diagnosis in adult age

In Study III, the target group consisted of all 225 available consecutive patients examined by an experienced adult psychiatrist (LN) and a clinical psychologist (MH), both with special expertise in ADHD/ASD, at the Neuropsychiatric Diagnostic Team for adults at the general psychiatric clinic of Lund University Hospital from the launch of the team in November 1998 until August 31st, 2002. During this period, 231 patients had been examined, but at the follow-up time, four of these had died and two had moved without leaving a forwarding address. The remit of the Neuropsychiatric Diagnostic Team was to, if applicable, diagnose ADHD or ASD (or TS) in adults. The age range of the study group was 18-60 years with a mean age of just over 30 years. Of those approached, 40% were women. A minority (13.8%) had mental retardation. Of the 225 patients, 83 were diagnosed with ADHD (including 3 with ADHD plus TS), 62 with ASD (including 2 with ASD plus TS) and 2 with TS only. The group of 78, for whom criteria for none of these disorders were met was heterogeneous, containing individuals with severe intellectual and/or psychiatric impairments as well as a few persons with only mild problems. The common factor was a suspicion of ADHD, ASD or TS. This group was included as comparison group. Diagnostic criteria used in the clinical work were those of DSM-IV, except for Asperger's syndrome, where the Gillberg and Gillberg criteria (Gillberg & Gillberg, 1989) were used. In study III an additional study group consisted of 60 significant others, mostly parents, of the patients with ADHD (n=29), ASD (n=20) or no new diagnosis (n=11).

3.1.4 Study IV – Register study of ADHD and ASD

The target group of study IV consisted of all 56462 patients from an administrative register held on patients in contact with the adult psychiatric clinic at the University Hospital in Lund, Sweden, over a period of 20 years (January 1st 1990 until December 31st 2009). The register was meticulously searched for patients who at any time during these two decades had been diagnosed with ADHD or ASD, or their ICD-9/ICD-8 equivalents (the latter converted to ICD-9 codes for the study). A smaller number of patients who were referred from other clinics in the area with the exclusive aims of being examined for ADHD or ASD (n=39, 22 diagnosed with ADHD and 17 with ASD) were excluded, since, after assessment, they had been referred back to their home clinic, and the Lund register did not contain any data on other diagnoses or psychiatric care for these patients. The patients finally included (n=707, 437 with ADHD and 270 with ASD) were identified by these diagnoses (below called index diagnoses). Of the 437 patients with ADHD, 38.2% and of the 270 with ASD 30.7% were women. Data on the 707 patients regarding birth year, gender, year of the index diagnosis, other diagnoses, and use of in-patient as well as out-patient psychiatric services for each year was collected in a separate research register where data were made unidentifiable. Data on each patient was controlled twice by the medical secretary responsible for the clinic's patient register, and also double-checked (de-identified data) by LN. The registers used contain data only on patients treated at the University Hospital Clinic in Lund. Data on patients treated in private practice was not available. Some patients treated in Lund came from places outside the clinic's catchment area, and a number of people living in the catchment area probably had been diagnosed and treated in other clinics. It has been estimated that the proportion of patients thus "exchanged" was around 10%.

3.2 Methods

3.2.1 Study I – Screening for ASD in adult psychiatry

In order to estimate the number of patients with hitherto undiagnosed ASD in a large group of psychiatric out-patients, a screening method was needed. Screening instruments available at the time, e.g. the Asperger Syndrome Screening Questionnaire (ASSQ), were aimed at parents and/or teachers and thus not relevant for this adult population. For several reasons, including varying degrees of insight and self-awareness in patients as well as an expected high degree of attrition, self-screening was not deemed feasible. In

the absence of an existing screening questionnaire, we developed one for use by members of psychiatric staff of varying professions. It would need to be reliable, short and easy to complete, based on observable behaviour rather than patients' inner experiences. The items had to be based on symptoms related to operationalized diagnostic criteria for ASD. The screening questionnaire thus developed was named the Autism Spectrum Disorder in Adults Screening Questionnaire (ASDASQ). The ASDASQ consists of nine questions relating to symptoms/impairment and are based on the Gillberg and Gillberg criteria for Asperger syndrome/ASD, and one item concerning previous contact with child and adolescent psychiatry. The latter item could be answered with "yes", "no" or "not known", while the other nine questions were of the "yes" (1) or "no" (0) variety. The range of possible scores was 0-9 (9 indicating maximal ASD loading).

The questionnaire, together with a list of patients registered as being in contact with the clinic's out-patient services on April 1, 1996, was distributed to staff members during the autumn of 1996. Staff were instructed orally and in writing to fill in the ASDASQ for every patient, resulting in 1323 (95% of all patients in the target group) being screened.

Inter-rater reliability for the ASDASQ was assessed within 0 to 13 months for 56 patients scoring 0 to 9 in the original screening, and who were each sufficiently well known by a second staff member. Test-retest stability was assessed after 11 to 13 months for 38 patients scoring 0 to 9 originally.

Cut-off for the screening was set at 5 points, excluding 1225 patients (92.6%) as being screen-negative. The psychiatric records of the 98 screen-positive patients were scrutinized. This resulted in the exclusion of a further 59 patients as not likely to have ASD. This was concluded from a convincing record of persistent hallucinosis and/or a clear description of previously good functioning with a distinct onset of illness. 31 patients scoring 6 to 9 and suspected of having ASD had either at this point been diagnosed with ASD elsewhere (n=7), or were invited to a clinical examination by the first author. The interview was in-depth, exhaustive and included checking of ICD-10 criteria for ASD, as well as the Gillberg and Gillberg criteria for Asperger's syndrome. During the interview, the patient was asked if a parent or other close relative might be interviewed. In the interviews of relatives the Asperger Syndrome Screening Questionnaire (ASSQ) and the Asperger Syndrome Diagnostic Interview (ASDI) were used; the former for retrospective assessment. ASD was diagnosed in cases meeting the Gillberg and Gillberg criteria for Asperger's syndrome or ICD-10 criteria for childhood autism or atypical autism. All diagnostic evaluations were made irrespective of earlier psychiatric diagnoses. Diagnoses (or "non-diagnoses")

of ASD for the interviewed patients were confirmed by two senior researchers (professor Christopher Gillberg; professor Maria Råstam) after oral case presentations.

Six of the patients scoring 6 to 9 and suspected of having ASD were not interviewed, owing to the patient's refusal, or being impossible to locate. Three were too ill to be interviewed. Eight patients scoring 5 and suspected of having ASD were not interviewed, due to lack of funding. Two of the 1225 patients scoring below 5 on the ASDASQ had been diagnosed with ASD as part of their clinical treatment. The procedure of Study I can be followed in Figure 1.

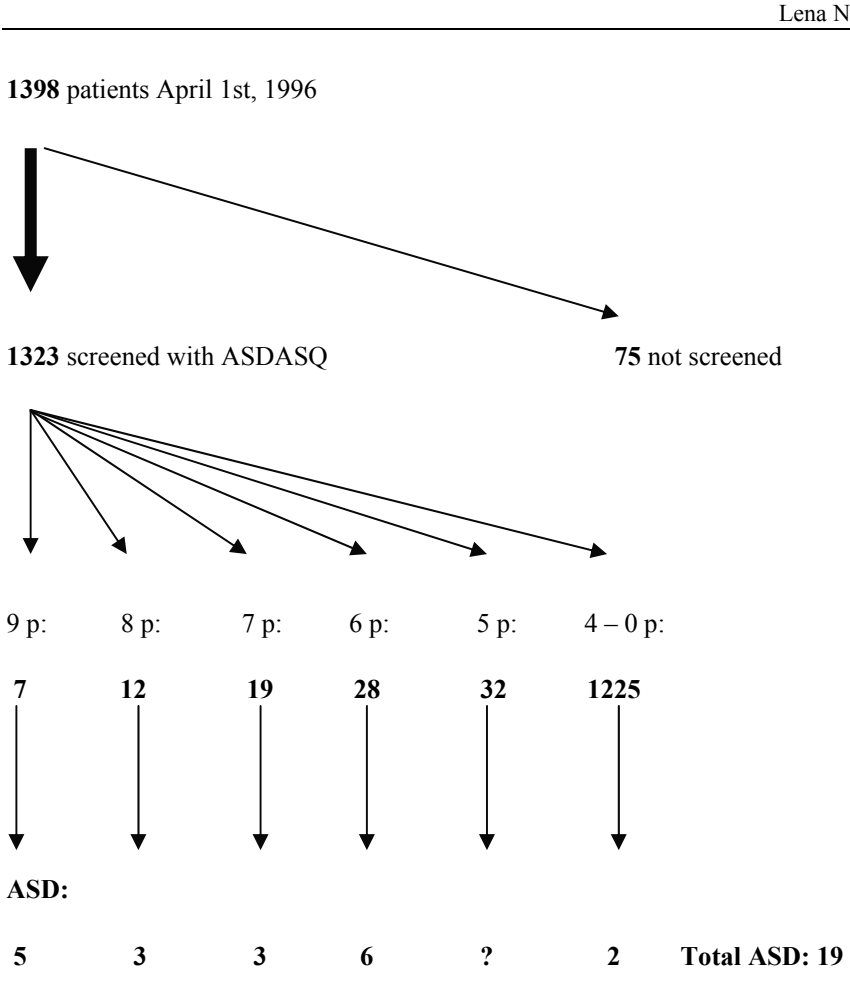


Figure 1. Study I. Procedure

3.2.2 Study II – Screening for ADHD in adult psychiatry

The first step of this study was the screening for ADHD symptoms in a group of adult patients treated in psychiatric out-patient services. Since an essential feature of ADHD in adults is its chronicity, i.e. impairing symptoms that have been present since before age seven are required for diagnosis, the screening questionnaire given to the patients needed to be one for retrospective assessment of childhood symptoms.The only such scale available was the Wender Utah Rating Scale (WURS). We used the 25 WURS questions considered most valid for an ADHD diagnosis, the WURS-25, for

scoring. Cut-off for possible ADHD in this study was set at a score of 30 on the WURS-25, which is lower than the recommended cut-off of 36 points (Ward, Wender & Reimherr, 1993), in order to ensure that patients who might not have remembered all their childhood symptoms would be offered an examination. It has been shown that adults with ADHD tend to retrospectively mitigate the impact of their childhood symptoms (Mannuzza, Klein, Klein, Bessler & Shrout, 2002; Miller, Newcorn & Halperin, 2010).

Recruitment of patients started April 1st, 2001 and ended June 11th, 2001. All out-patients, except those making their first visit, were, in connection with the visit, to be informed by the secretaries about the study and those who did not decline participation were given an envelope with written information and a form to sign for written consent together with the screening questionnaire and a stamped return envelope. This procedure was continued until 406 patients (of whom 8 refused participation) had been asked to participate. Later, it was discovered that another 145 patients meeting inclusion criteria had made visits during the recruitment period but, for administrative reasons, they had never been invited to participate. The screening was not done anonymously, since the next step would be an invitation to a clinical examination.

The medical records and registered diagnoses of all patients offered and not actively refusing participation (n=398) were scrutinized for ADHD diagnoses. In addition, the staff treating the patients were informed about the diagnostic criteria of ADHD, and asked if any of the patients might, in their opinion, qualify for an ADHD diagnosis.

Of the 398 patients, 141 (43 men, 98 women) gave their written consent to participate in the screening, and returned a completed WURS questionnaire. The drop-out group (n=257) was analyzed regarding age and gender and did not differ significantly from those who participated in the screening. Fifty-seven individuals consenting (10 men, 47 women) scored 30 or above on the WURS-25. These 57 patients were invited (by letter) to a one-day clinical examination by a psychiatrist (LN) and an experienced clinical psychologist (MH). Participants in the clinical part of the study were offered compensation for loss of income for the day of examination. Some patients declined to come, and one patient never showed up in spite of having booked appointments twice. In the end, 47 patients were examined.

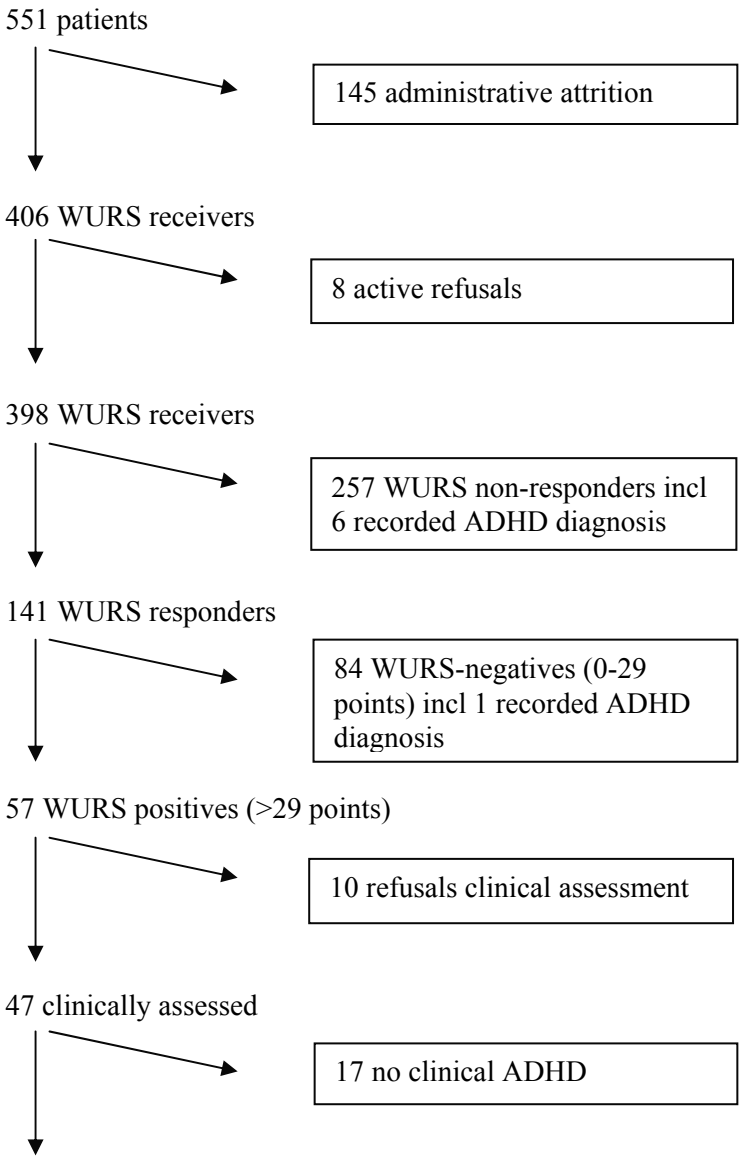


Figure 2. Study II. Procedure

The patients first underwent a clinical interview lasting around 90 minutes, with special emphasis on childhood and current symptoms in accordance with the DSM-IV ADHD diagnostic criteria. The Montgomery-Åsberg Depression Rating Scale (MADRS) was used to examine depressive symptoms. The patients completed self-report scales, namely the Autism Quotient (AQ) for autistic traits, the Alcohol Use Disorders Identification Test (AUDIT), The Sheehan Disability Scale, and a brief screening questionnaire, constructed for use in the present study covering the use of illegal drugs. The patients were tested with an extensive battery of psychological tests, including the Wechsler Adult Intelligence Scale-Revised (WAIS-R), the Trail Making Test (TMT), FAS, Tower Of London (TOL), Colour Word Test (CWT), Rey Complex Figure Test (RCFT) and Test Of Variables of Attention (TOVA). They were also given the DSM-IV/ICD-10 Personality Questionnaire (DIP-Q). At the end of the assessment day the patients were informed about the results of the examination, and were, in cases meeting criteria for ADHD, informed about this. The examinators also took care to discuss the patient's opinion on the diagnosis. All patients who met criteria for ADHD agreed with the examiners on the diagnosis. The procedure of Study II can be followed in Figure 2.

3.2.3 Study III – Impact of ADHD/ASD diagnosis in adult age

Since this study aimed to estimate the impact of a developmental disorder diagnosis received in adulthood, patients were not included until at least one year had elapsed after the completion of their diagnostic assessment. Thus the study group had been examined and, in the cases where this was applicable, diagnosed with ADHD, ASD or TS one to almost four years (mean 29 months) earlier. The diagnostic process had contained the parts deemed clinically relevant for each patient, but always included a detailed developmental history taken by two experienced clinicians, psychiatrist and psychologist, and in the majority of cases also extensive neuropsychological testing and/or a collateral interview. All patients had been asked about their housing, economical maintenance, work/occupation, contacts with health care and habilitation services, and medication.

The questionnaire constructed for the study contained questions concerning the above-mentioned circumstances, together with questions about the patient's opinions on the benefit of the diagnostic evaluation, satisfaction with social circumstances and any changes occurring after the diagnostic evaluation. The questions about opinions, satisfaction or change were answered on a scale from 1 to 5, with 1="not at all/much worse" and 5="totally/much better". The patients were also supplied with a Global

Assessment of Functioning (GAF) scale (APA, 1994) and asked to do a GAF self-assessment. The questionnaire, intended for anonymous completion, was mailed to each participant. In the same questionnaire participants were asked if they allowed the researchers to contact a person, close relative or friend, a so-called significant other (SO), and if so, to submit name and address to this person. Eighty-five patients agreed to this part of the study.

The SOs were contacted by mail and sent a questionnaire containing 21 questions largely consistent with questions in the patient questionnaire. The SOs were asked to do a GAF assessment of the probands, and to answer questions concerning the practical and emotional burden caused by the proband's impairment. The latter questions were graded from 1 to 5, with 1="not at all/much worse" and 5="totally/much better".

3.2.4 Study IV – Register study of ASD and ADHD

This study was performed in an adult psychiatric clinic with a long (since 1985) tradition of registering every out-patient visit or in-patient episode. Over the past 25 years, the organization of services and of registration has varied, and thus, for this study, data from several patient registers had to be scrutinized by the secretary responsible for the clinic's patient register. Data on all patients found to have been diagnosed with ADHD or ASD were collected into one file, de-identified by deleting name, address and social security number, and then exported into SPSS for statistical analysis. Psychiatric diagnoses in the registers were mostly coded according to ICD-10, but for patients diagnosed before 1995, diagnoses were coded according to ICD-9, and a few even ICD-8, here converted to ICD-9 (Socialstyrelsen, 2011a). All psychiatric diagnoses (category F in ICD-10) were grouped into 9 categories/diagnostic groups as shown in Table 1.

For each patient, calendar year when ADHD or ASD was first diagnosed was noted, and records for visits to out-patient clinics and for number of days as in-patient were summed for each of the twenty years investigated. Calendar year thus was the time unit used.

3.2.5 Statistical analyses

In study I, inter-rater and test-retest correlations were determined by Kendall's tau-b and Spearman rank correlations (Altman, 1991). Cohen's Kappa coefficients (Landis & Koch, 1977) were computed for the different items in order to estimate the adjusted levels of agreement between two ratings. Absolute test-retest stability was computed by means of Wilcoxon matched-pairs signed rank test (Altman, 1991). Internal consistency was calculated by means of Cronbach's alpha (Cronbach, 1990). Estimates of

sensitivity and specificity for the ASDASQ were also calculated (Altman, 1991).

In study II and III SPSS 15.0 and in study IV SPSS 17.0 was used for all demographic statistics, and the Mann-Whitney U test (Altman, 1991) for comparing means. Ninety-five percent confidence levels were calculated when appropriate.

Diagnostic group		ICD-9 code	ICD-10 code
1	ADHD and equivalents	314	F90
2	ASD and equivalents	299	F84
3	Mental retardation	317, 318, 319	F70-F79
4	Psychotic disorders	295, 297, 298	F20-F29
5	Affective disorders (incl bipolar)	296, 311	F30-F39
6	Anxiety disorders	300	F40-F42
7	Personality disorders	301	F60-F61
8	Psychoactive substance use related disorders	291W, 292, 303, 304, 305	F10-F19
9	Other psychiatric disorder	294W, 307, 309, 310, 312, 313, 315	F01, F06, F07, F09, F43-F45, F48, F50, F51-F53, F63, F68, F69, F81, F89, F91- F95, F98

Table 1. Study IV. ICD-Diagnostic groups

4 RESULTS

4.1 Overall findings

The studies demonstrated convincingly that although ADHD is clearly very common among adult psychiatric patients, the diagnosis is still usually not registered. ASD also occurs, albeit in a smaller number of patients, and is probably underdiagnosed as well. The rates of registered diagnoses of ASD and ADHD were considerably higher during the last decade than during the 1990s, but the underdiagnosis of ADHD, in particular, was striking even as recently as in 2009. The study of effects/impact of making a diagnosis of ADHD or ASD in adult age proved to be fraught with problems, and conclusions on the basis of results obtained in this substudy can only be tentative and speculative.

In the following, more detailed results of each substudy will be presented separately.

4.1.1 Study I – Screening for ASD in adult psychiatry

The screening instrument ASDASQ had good internal consistency and mostly acceptable to good inter-rater and one-year test-retest agreement. The sensitivity and specificity was 0.90 and 0.96, respectively.

Of all the screened patients (95% of the patients who at the time of the study were treated as out-patients in this particular clinic), 1.4% (n=19) were given an ASD diagnosis after clinical examination of those who scored 6 or above on the ASDASQ and for whom analysis of the psychiatric records had not rendered examination unnecessary. Fourteen of the patients with ASD were male, giving an M:F ratio of 2.8:1. There was an aggregation of patients with ASD in one of the out-patient centres catering to the needs only of patients with long-standing severe problems, mostly psychotic disorders. Among those patients, the frequency of ASD was 3.2%. The most common prior diagnosis was schizophrenia (295X, 295D, 295H), which applied in five cases. In three of these cases clear symptoms of schizophrenia had almost certainly been present, while in the other two it was dubious if a true comorbidity with schizophrenia was on hand. However, the issue of comorbidity or misdiagnosis was not pursued in these few patients. Nine patients scoring 6 to 9, and with highly probable ASD, were not examined since they refused, were not possible to locate or were too ill (n=3) to be

disturbed at the time of the study, and eight – those scoring 5 points with probable ASD – were not interviewed for administrative reasons. Two patients scoring below the tentative cut-off of the screening instrument were diagnosed with ASD while in treatment. Taken together, these findings suggest that it is highly probable that the frequency of ASD in adult psychiatric patients is higher than the 1.4% minimum prevalence obtained in this study.

4.1.2 Study II – Screening for ADHD in adult psychiatry

Of 141 patients participating in the screening, 57 had WURS-25 scores of 30 points or more, and were therefore invited to a clinical examination. Ten patients (all female) scoring 30 or above on the WURS-25 and thus suspected of having ADHD and invited to clinical examination refused this part of the study, or never came for the agreed-upon appointment. Of the 47 patients who accepted and who did show up, 30 (nine male, 21 female) were diagnosed with ADHD and 17 were found not to meet ADHD criteria. Of the 30 diagnosed patients, 24 had no formerly assigned ADHD diagnosis. Two of the patients who did not have ADHD (both female) had very high scores on the WURS-25; 73 and 70 (out of a maximum possible score of 100).

The opinion of staff was that 48 (12%), 25 women and 23 men, of the 398 patients invited to and not actively refusing the screening, met criteria for ADHD. Thirty-two of these patients belonged to the drop-out group (n=257) and amounted to 12.5% of this group, while the screened group (n=141) contained 16, amounting to 11.3% of this group. Twelve of the 48 patients belonged to the group invited to clinical assessment, which resulted in ADHD diagnoses in 11 of these cases.

Among the screened patients with WURS-25 scores below 30, one had a registered diagnosis of ADHD. The number of patients with diagnosed ADHD in the screened sample thus was 31, and the prevalence of ADHD in this group (n=141) of psychiatric patients was 21.9%. Of all the screened women (n=98) 22 (22.4%) had ADHD. A slightly smaller percentage, 20.9%, of the screened men (9 out of 43) were found to have ADHD.

When the medical records and the administrative patient register were scrutinized, it was found that 6 patients, 2 men and four women, among the 257 who were not screened had been diagnosed with ADHD, yielding a total of 37 patients with known ADHD in the material of 398 who were invited to screening. Of the 134 men 11 (8.2%) had diagnosed ADHD and 26 (9.8%) of the 264 women. If all patients visiting the clinic – the group invited to

participate (n=406) and those who, for administrative reasons, were not invited to participate (n=145) – are taken into account, the total number of patients in treatment during the study period was 551, and the prevalence of patients with diagnosed ADHD would be 6.7%. If only those who were possible to examine, i.e. the screened group (n=141), are considered, 21.9% had ADHD.

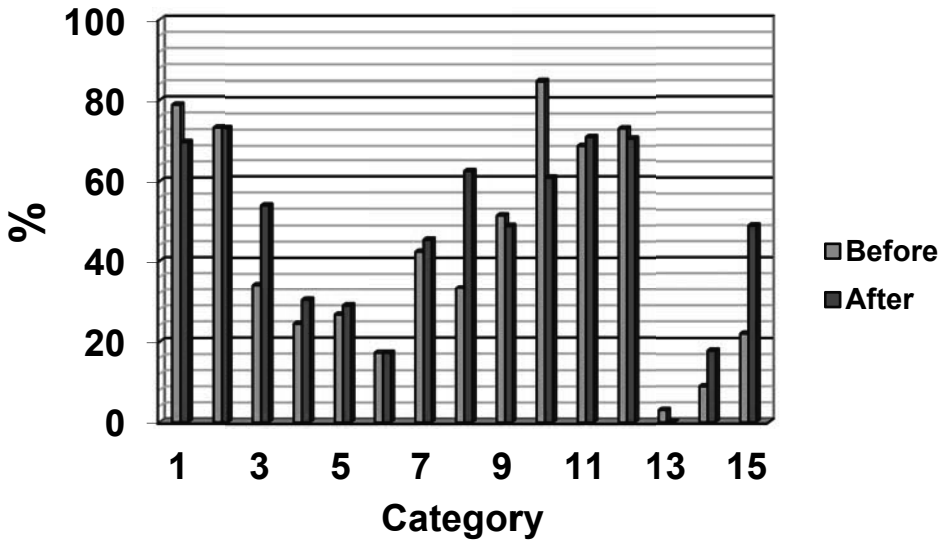
Among the patients diagnosed with ADHD (n=37) the most common registered main diagnosis was affective disorder in 35% of the cases, followed by maladaptive reactions in 19%.

4.1.3 Study III – Impact of ADHD/ASD diagnosis in adult age

A little more than half of the targeted group, 121 patients (53.7%), agreed to participate in the study and returned the questionnaire. However, every patient had not answered every question, and very few had done the GAF self-assessment. Of the 121 responders, 33 were patients examined but not diagnosed with any developmental disorder (42% of the "no new diagnosis" group), 45 were patients with ADHD (54% of the ADHD group), 41 were patients with ASD (66% of the ASD group) and 2 were patients with TS only (100% of the group with TS only).

The largest changes noted by the patients were in respect of medication (the ADHD group, where 11 of 45 patients had received stimulant treatment after diagnosis), or independent living and contact with habilitation services (the ASD group). Changes in life circumstances and health care contacts are shown in Figure 4. The mean score for having experienced a positive change in life after the diagnostic assessment was higher in the two groups diagnosed with ADHD and ASD, respectively, than in the group for whom no new diagnoses were assigned. The ADHD and ASD groups also rated the usefulness of the evaluation and their satisfaction with their present situation higher than the "no new diagnosis group". The ADHD group rated the professionalism of the evaluation higher than the comparison group did, while the ASD group had the highest rating for getting help as expected after diagnosis. Most of the patients with ADHD thought they had been diagnosed correctly. The patients with ASD were more satisfied with their income than the other two groups, although only 17% were working.

Of the patients included, 85 (70.2% of the participants) allowed a contact with a SO, and 60 SOs, for the most part parents, of 59 patients responded. The opinions of SOs, to a large extent and especially among the ASD group´s SOs, were more positive than those of the patients. The ASD group's SOs



Categories:
1: Percent living independently; 0 new diagnosis.
2: Percent living independently, ADHD.
3: Percent living independently, ASD.
4: Percent with income from work, 0 new diagnosis.
5: Percent with income from work, ADHD.
6: Percent with income from work, ASD.
7: Percent with psychotropic medication, 0 new diagnosis.
8: Percent with psychotropic medication, ADHD.
9: Percent with psychotropic medication, ASD.
10: Percent in contact with health care, 0 new diagnosis.
11: Percent in contact with health care, ADHD.
12: Percent in contact with health care, ASD.
13: Percent in contact with habilitation services, 0 new diagnosis.
14: Percent in contact with habilitation services, ADHD.
15: Percent in contact with habilitation services, ASD.

Figure 4. Study IV. Social and health care data before and 12 to 44 months after diagnostic examination

noted a positive change in social relations with the patient, as well as in contacts with services. On the scale 1 to 5, SOs of patients who did not meet

criteria for ADHD or ASD noted higher mean scores (signifying heavier burden) for practical (3.36) as well as emotional (3.73) burden than did the SOs of patients with ADHD (2.59 and 3.07, respectively) or ASD (2.60 and 3.20, respectively). The mean GAF ratings by SOs were lower (=larger impairment) in the "no new diagnosis" group (GAF last year: 58.7) than in the ADHD (GAF last year: 69.8) or ASD (GAF last year: 63.2) group.

4.1.4 Study IV – Register study of ADHD and ASD

Of the patients diagnosed with ADHD, most (60.9%) were assigned F90.0, while another 29.5% were diagnosed with national ICD-10 code variants, namely F900A (DAMP), F900B (ADHD), F900C (ADD) or F900X (ADHD-NOS) (Socialstyrelsen, 2011b). F90.9 (hyperkinetic disorder, unspecified) was assigned in 7.1%, and 2.5% (11 individuals) had other diagnostic codes (314, 314X, F90.1, F90.8).

Of the diagnoses in the autism spectrum, ICD-10 Asperger's syndrome namely F84.5 was by far the commonest diagnosis, assigned in 69.3% of cases. Childhood autism, F84.0, was diagnosed in 13.0%, and atypical autism (F84.1) and pervasive developmental disorder not otherwise specified (F84.9) in 6.7% and 5.6% respectively. Another 5.5% (13 individuals) had diagnostic codes 299, 299W, 299X or F84.8 in the register. In a small number of patients (n=14; 4 female and 10 male), the two diagnoses ASD and ADHD had been given concomitantly. In the further analyses, these patients were classified only among the patients with ASD, on account of the autism spectrum disorders being regarded as pervasive and thus "more important" than ADHD in the diagnostic hierarchy, albeit both being developmental disorders. The DSM-IV ADHD criterion "does not occur exclusively during the course of a pervasive developmental disorder" reflects an opinion that ADHD symptoms may be associated features of ASD, but not vice versa (APA, 1994). This opinion has been questioned, and the criteria subsequently suggested to be changed in the DSM-5.

In the register there were more males than females with an ADHD or ASD diagnosis. The difference was larger in the ASD group with a male preponderance of 2.3:1 while in the ADHD group it was 1.6:1. In both groups the mean age at diagnosis was around 30 years, and the age at first contact with adult psychiatry in the mid-twenties. Even though a large group of patients was diagnosed with ADHD (51.0% of ADHD patients) or ASD (47.8% of ASD patients) within the same calendar year as their first contact with the adult psychiatric clinic, the mean number of calendar years between first contact and ADHD diagnosis was more than 3 in both groups, with a

large variation. In a few cases, the developmental disorder diagnosis had not been made until after decades of psychiatric contact.

The majority of the patients diagnosed with developmental disorders had had out-patient contact only – 30% of the patients with ADHD and 43.3% of the ASD patients had been subject to in-patient treatment during the twenty-year period studied. The number of new ADHD and ASD diagnoses made per year at the studied clinic went up during the twenty years studied. In the 1990s, few developmental disorder diagnoses were made. During this decade, ASD (n=37) was a more common diagnosis than ADHD (n=15). However, since the beginning of the 2000s, the number of ADHD diagnoses made in the clinic had been rising to around 0.80% of all patients seen in 2009, while the number of ASD diagnoses peaked in 2000, and since then had been more level, around 0.15-0.25% of all patients seen per year.

Eight patients diagnosed with ADHD, all male, and 8 patients, 6 male and 2 female, with ASD had died before December 31st 2009. The mortality in the ADHD group thus was 1.8% and in the ASD group 3.0%. Ages at death were 22 to 44 years for the ADHD patients and 22 to 56 years for the ASD patients.

The yearly percentage of the total patient group in contact with the clinic who had ADHD or ASD, diagnosed or later to be diagnosed, rose continually, from 0.09% (ADHD) and 0.29% (ASD) in 1990 to 2.72% (ADHD) and 1.31% (ASD) in 2009. The rise was much steeper in the number of ADHD patients than in the number of ASD patients in contact with adult psychiatry.

Other psychiatric diagnoses than the so-called index diagnosis were registered in 61.3% of the ADHD cases and 60.0% of the ASD cases. ADHD was counted as “another” diagnosis in ASD cases, but not vice versa. The most common coexisting diagnoses in the ADHD group were affective disorders, which were registered in 27.3% and second most common (not counting “other disorders”, see below) were disorders related to alcohol or substance use, 21.3%. Among the ASD patients, psychotic disorders were registered in 21.1%, followed by affective disorders in 17.4%. Anxiety disorders had been diagnosed in 18.3% of ADHD patients and 17.0% of ASD cases, and personality disorders in 16.2% and 14.5%, respectively. Mental retardation was registered in 11.5% of ASD cases and 2.1% of ADHD cases. Alcohol or substance use related disorders were registered in no more than 4.8% of the ASD patients. In both groups, the frequency of “other psychiatric diagnoses”, comprising a number of diagnoses not possible to group under any of the other eight labels was around 22% (Table 1).

5 DISCUSSION

5.1 General findings

Three of the four studies, I, II and IV, focussed on the presence, and number of, ADHD (paper II and IV) and ASD patients (paper I and IV) among adult psychiatric patients. The studies show that adults, sometimes even middle-aged or elderly persons, treated in psychiatry are afflicted by these developmental disorders. The first three studies also show that it is possible to diagnose developmental disorders in adults, even though a crucial part of the diagnostic criteria is the requisite that some symptoms and impairment should have been present since early childhood. That ADHD and ASD are, eventually, becoming diagnostic alternatives also in adult psychiatry becomes evident in the fourth study which shows that these diagnoses are indeed made with increasing frequency in adult psychiatry, and that the number of adults with ADHD and ASD in contact with psychiatric services is steadily rising. A majority of the patients with these developmental disorders who are in contact with adult psychiatry are concomitantly diagnosed with other psychiatric disorders. The majority of ADHD and ASD patients in adult psychiatry are treated as out-patients only.

The combined results from studies I, II, and IV, taken with the evidence from studies published by other authors, indicate that ASD, and particularly ADHD, still usually remain undiagnosed/unregistered in adult psychiatry, in spite of the clear upwards trend in diagnosing the conditions that is evident from the 1990s into the 2000s.

The patients diagnosed with ADHD or ASD participating in the third study indicated that they had experienced a more positive change in life after the diagnostic evaluation than those who did not receive any of these diagnoses (comparison group). In the areas where there was any difference between the ratings of the group diagnosed with ADHD or ASD, respectively, and the comparison group, the ratings were more positive in the diagnosed groups. This was also the case among SOs, and, even if the differences were small it may be inferred that an ADHD or ASD diagnosis received in adulthood, after a careful examination, will not be harmful to the patient. Concrete changes noted by patients after the evaluation were more independent living (ASD), more contacts with habilitation services (ASD) and more access to medication, especially stimulants (ADHD).

5.1.1 General discussion of methodology

In clinical studies of psychiatric patients, there is usually a compliance problem. At least partly owing to their psychiatric symptoms and/or medication effects – anxiety, suspiciousness, tiredness, cognitive dysfunction – patients may choose not to participate, or refrain from any active choice. This problem is evident in studies II and III, where the patients were either given (study II) or sent (study III) a questionnaire. In study II, only 34.8% of those who were asked to participate (n=406) in screening gave their written consent and returned the screening questionnaire. In study III, 53.7% returned the questionnaire and agreed to participate. The higher, albeit still not very high, number of consenting participants in study III may be due to these patients being a somewhat less heterogeneous group, where all had been going through an examination, performed by two of the researchers who were named in the letter of information sent with the questionnaire. The patient group in study II comprised patients treated by a variety of professionals with different methods for a multitude of diagnoses. In step 2 of that study, another 10 persons who were invited to clinical examination dropped out. In study I, the screening of the patients was made by staff and with a questionnaire designed to be quick and easy to use for psychiatric staff members. This procedure gave a very small attrition, only 5%. However, in the next step of this study, nine of the patients scoring above cut-off and with, on the basis of information in the medical records, suspected ASD could not be examined since they refused, could not be located or were too ill. One reason for this attrition may have been that the screening questionnaire (ASDASQ) selects patients with severe behavioural disturbances, which may include some with ongoing psychotic illness. Another eight patients with ASDASQ scores of 5 and suspected ASD were not interviewed for economical reasons.

The questionnaire sent to the patients in study III was extensive, comprising 32 questions and including a self evaluation with the GAF scale. To fill in the questionnaire may have proven too difficult or time-consuming for many of the patients, an assumption that is supported by the fact that several of the respondents did not answer all the questions, and only a few had made the GAF evaluation. The follow-up time in study III was short, only one to almost four years, which is not a very long time compared to the many years these adult patients have had the developmental disorder. In psychiatry in general, and especially when developmental disorders or chronic illness are studied, longer follow-up times will provide a more adequate picture of patients' circumstances in real life.

In the first study, diagnostic decisions (ASD, or not ASD) were made by the first author (LN) who performed all patient and collateral interviews. Diagnoses were confirmed with an oral case presentation to two senior very experienced colleagues who were blind to caseness, diagnosis, and to the scores on the ASDASQ. However, these senior professionals did not themselves meet the patients and had to rely on the descriptions given by the first author.

In studies II and III, the diagnostic procedures were performed by the first author (LN) in close collaboration with a very experienced clinical psychologist (MH). In study II, the diagnostic procedure was the same for the 47 examined patients, and was extensive. However, it is a limitation that no collateral interviews were made and that the developmental history consequently was taken only from the patients themselves. The patients in study III had all been subjects to a clinical examination for a suspected developmental disorder (ADHD, ASD or TS). This examination always comprised an extensive developmental history, in most cases taken from the patient and a parent or other relative, and a clinical assessment, made by the psychologist, of overall cognitive capacity. In many of the cases, a more detailed neuropsychological assessment (most often the WAIS-R, frequently supplemented with other tests) had been deemed necessary or useful by the psychologist. The examinations thus had contained different procedures, but always the developmental history, and always checking of DSM-IV diagnostic criteria, except for Asperger's syndrome, where the Gillberg and Gillberg criteria were used. The material thus was assessed and diagnosed according to good (excellent) clinical practice.

In study IV, only register data was used. The data was collected and double checked by the secretary responsible for the clinic's register, who had been working with the patient register in the same clinic since the 1980s and thus had very good knowledge of the different registers needed, since administrative and organisational changes had occurred, to collect all the data from the 20 years studied. The data thus collected was double-checked and then de-identified by erasing name, address and social security number. It was then again checked for incongruities by the first author, to assure highest possible quality of data. However, the diagnoses are registered by many secretaries and made by a great number of psychiatrists with differences in expertise, and thus reflect common clinical practice in psychiatry, rather than being based on strict research criteria. The diagnoses for the study were collected on a specific date, since diagnoses in some instances are changed in the register months in retrospect.

5.1.2 General discussion of limitations and strengths

The level of attrition poses a serious limitation, especially in studies II and III, but also in study I. It is a limitation of study I that it was not completed, as intended, with clinical examinations also of the patients scoring 5 on the ASDASQ and suspected of having ASD.

The diagnostic procedure in study II lacks the taking of a developmental history from another informant than the patient. The comparison group used in study III, comprising patients who had been examined for but not diagnosed with any developmental disorder, was small, and it poses a problem to find a control group for a study of the possible benefit of receiving a diagnosis. The diagnostic examination procedure used for the patients in study III was not standardized and homogenous, but varied according to the patient's clinical needs. The questionnaires used in study III were constructed for this study, not validated, and probably unnecessarily lengthy and complicated.

The supposed heterogeneity of diagnostic practice in everyday clinical work is a limitation to study IV. The use of calendar year as the time unit allows for great variation, one to 23 months, in the time range "within the next calendar year", which is a limitation. However, more precise time measurements were not practically feasible.

In study I, the limited attrition (5%) in the screening is a strength, as is the conservative diagnostic assessment, which, whenever possible, included a collateral interview regarding early development. In studies II and III, the clinical diagnostic work with the 47 patients examined (study II) and 231 patients originally included (study III) was done by the same two experienced senior clinicians (LN and MH), implying that diagnoses were well substantiated. In study II all 47 patients, who had agreed to participate in the clinical part of the study, were examined with exactly the same procedure, whereas in study III assessment procedures were chosen with priority for the patient´s needs and wishes, since the patients were referred for clinical reasons. It may thus be a limitation of study III that details in procedures may have differed, while on the other hand this reflects the clinical reality.

5.1.3 Discussion of results obtained in each of the four studies

I. The prevalence of ASD in adult psychiatric out-patients was fairly low, 1.4% of all patients treated at a certain time. This is not far above the

estimated prevalence in the population, namely 1%. The ASD rate may well be regarded as a minimum prevalence, since, (a) in the centre for treatment of patients with long-standing and severe impairments, mostly psychotic disorders, the estimated prevalence of ASD was at least 3.2%, and (b) several of the whole group of targeted patients with strongly suspected ASD were not examined for various reasons, and hence were not included in estimates of overall prevalence. The study comprised the patients who were regarded as being in contact with the clinic on a certain date, and it is possible that over time, the prevalence would be higher. The "original psychiatric" diagnoses assigned to individuals with ASD varied considerably, schizophrenia being diagnosed in about one fourth of the cases. The ASDASQ appeared to be useful for screening for autistic-like behaviours in large psychiatric populations by staff – it is quick and easy to use, and has acceptable psychometric properties.

II. ADHD is common in adult psychiatric out-patients, and may well be a background factor, possibly predisposing, to other psychiatric disorders. The attrition in this study was substantial, but even if the 37 cases with ADHD actually clinically diagnosed were the only cases of ADHD in the studied population (which is highly improbable), the prevalence of ADHD in adult psychiatric out-patients would still be 6.7%, i. e. above that in the general population. If only the screened cases were counted (more reasonable), the minimum prevalence would be 21.9%. It is not unlikely that the rate of ADHD among those in the attrition group may have been substantially higher than among those who were clinically assessed (cf. Stormark, Heiervang, Heimann, Lundervold & Gillberg, 2008), suggesting that the "true" rate of ADHD among adult psychiatric patients might be higher even than 21.9%. In either case, it seems safe to assume that the prevalence of ADHD in psychiatric patients is higher, probably very much higher, than in the population at large. It should be noted that 10 screen-positive patients in study II never were examined. However, it should also be noted that two of the patients with very high WURS-scores in the screening did not have ADHD, but other disorders. The attrition groups (257 and 145 patients, respectively) have been analysed in all possible ways, given ethical considerations. There is no reason to believe that the prevalence of ADHD in the non-responding group, or in the administrative attrition, would be substantially lower than among the responders; in fact, as argued above, it is more likely that the non-responders would contain a relatively large proportion of ADHD cases. The diagnostic procedure used for the cases examined in the study was exhaustive, with the only exception that collateral interviews were not done.

III. Since the attrition in this study was almost 50%, it is difficult to draw definite conclusions about the hypothesis that patients who get an ADHD or ASD diagnosis in adulthood experience this as beneficial. This study had other severe methodological shortcomings, namely that the questionnaire was not validated and probably difficult to fill in and that the comparison group was small, heterogeneous and far from perfect as a control group. The conclusions that can be drawn from this study are that it is difficult to measure the impact of a diagnosis as such, but that a substantial group of adults, as well as their SOs, found the diagnostic procedure a positive experience. The greatest changes noted after the examination were more independent living (which may have been an effect of increasing age) and more contacts with habilitation services in the ASD group, and more access to medication among the ADHD patients. The SOs had a positive view of the diagnostic procedure and had noted an overall positive change in both groups. The SOs rated their emotional burden, caused by the patient's impairment, as greater than the practical burden.

IV. The rate of newly diagnosed ADHD and ASD in the adult psychiatric clinic that was studied rose during the 20 years studied. The rise was steeper regarding ADHD diagnoses. The percentage with ADHD or ASD, respectively, of all patients who were in contact with adult psychiatry rose as well, but still was far below the number that would be expected on the basis of the results obtained in studies I and II. Around half of the patients got their ADHD or ASD diagnosis within the same calendar year as their first contact with the clinic, but extreme diagnostic delays, more than 10 years, were noted in some cases. In each group, around 60% had concomitant diagnoses. The majority of each group was treated as out-patients only. In-patient treatment was more common in the ASD group, where psychotic disorders were more commonly diagnosed than among ADHD patients. Only a small group, 14 (2%) of 707 patients, had concomitantly diagnosed ADHD and ASD. This may be due to the clinicians mostly (but apparently not always) adhering to the diagnostic rules in the DSM-IV, stipulating that the two disorders may not be diagnosed concomitantly, or there may be other reasons.

6 CLINICAL CONCLUSIONS

The importance of cognitive capacities (in a broad sense and comprising not only those intellectual abilities measured by the Wechsler scales and expressed through "IQ", but also capacity for reciprocal social understanding as well as the capacity to control one's attention and activity) for mental health has been elucidated from time to time, but still seems to often be neglected in clinical adult psychiatry. With the increase in research and knowledge about certain developmental disorders, particularly ADHD and ASD, in child psychiatry, also clinicians working with adults have realized that patients seeking psychiatric help may have developmental disorders underlying and adding to their psychiatric illnesses. In some cases, it may even be the developmental disorder that gives the patient problems leading to their seeking psychiatric help. Some individuals may actually be "erroneously" diagnosed as having generalized anxiety disorder or personality disorder, when in fact their only "real" problem is their ADHD or ASD.

As mentioned above, among others the Swedish psychiatrist Sjöbring recognized cognitive capacities as important factors in personality disorders. Sjöbring's four personality variables include K for capacity (kapacitet in Swedish) (Sjöbring, 1973). The DSM-IV general diagnostic criteria for personality disorders comprise 4 areas where the patient's functioning may be compromised, and one of these areas, although not often taken into account, is the cognitive function. It is not an extraordinary thought that an adult who, for some reason, is lacking in capacity will have problems in adapting to the complex and varying demands of today's society. Adults with cognitive impairments will experience problems in academic, occupational and relational circumstances, and often find themselves unable to deal with the problematic situations. It is not surprising that individuals in these situations experience stress, anxiety, low self-esteem and low mood. Some of these individuals become psychiatric patients, with or without a psychiatric illness in combination with their cognitive impairment, and often present with complicated clinical pictures or treatment-resistant disorders. To fully understand the situation of these patients and to give the optimal, individualized treatment and support, it is essential for psychiatric staff to get a clear picture of the person's capacities and of his/her development from early childhood. When a developmental history is taken, it is quite often found that criteria for ADHD or ASD are met, also when the patient is adult. The present studies show that ASD and, especially, ADHD are overrepresented among adult psychiatric patients and need to be taken into

account in diagnostic considerations. They also indicate that ASD and ADHD are still underrecognized and overlooked in adult psychiatry.

These categorical diagnoses, however crude, may be helpful. Patients with an ADHD diagnosis can benefit from treatment with central stimulants, and from other therapeutic and supportive efforts. One beneficial factor, often mentioned by the patients, may be the diagnostic label per se, since it gives the patient a concept to relate to instead of only feeling odd and maladjusted. Some adults with ADHD and ASD, respectively, have written books or given talks about the value of the diagnostic label for their own self-esteem, and for explaining their behaviour to others. The ADHD and ASD diagnoses, respectively, give people around the individuals affected useful clues to what to expect and how to communicate. In Sweden, patients with an ASD diagnosis have access to habilitation services.

ESSENCE has recently been described as a relevant concept for child psychiatry and developmental medicine. However, some of the symptoms of ESSENCE may persist into adulthood and cause adaptation problems, and in these patients even more ESSENCE symptoms are often revealed if a developmental history is taken.

It is an old truth that in psychiatry there are very few, if any, single symptoms that point to only one single diagnosis. Anxiety or concentration difficulties are examples of symptoms that are encountered in many adult patients with different diagnoses, psychiatric as well as somatic. This means that any single symptom of cognitive or emotional dysfunction may be a sign of one (or more) of several diagnoses, or of vulnerability to psychiatric disorder. Along this line of thinking, the implications of ESSENCE ought to be borne in mind also by mental health professionals working in services for adults. Also, it should be recognized that a number of adults, while presenting with some or several impairing ESSENCE symptoms, do not fit into any of the present diagnostic categories. These individuals should not be denied assessment and help.

Another old truth is that patients with the same diagnosis may have differing and varying needs. Services for adults are, like in child psychiatry and paediatrics, increasingly set up to serve discrete diagnostic categories of patients. For example, clinics for patients with affective disorders are separate from clinics/professional teams for patients with ADHD and/or ASD or clinics for patients with psychotic disorders/schizophrenia. In adults and children alike, psychiatric syndromes often overlap and one patient may need expertise in several fields to get his/her problems adequately assessed and addressed. For patients with cognitive problems, a common but often

overlooked phenomenon in adult psychiatry, this fragmentation of services is not helpful and may contribute to a worsening of problems. It is also a troubling consequence of this differentiation that a patient must have a certain diagnosis to be eligible for a certain treatment, even though many psychiatric treatments as far as we know are beneficial across diagnostic “boundaries”.

7 IMPLICATIONS FOR RESEARCH

While ADHD for a long time has been among the most studied diagnostic categories in child and adolescent psychiatry, the research interest in adults with ADHD is fairly new, but very rapidly increasing. Since ADHD is very common among adult psychiatric patients, it is important to study comorbidity and differential diagnostic issues, for example in relation to anxiety disorders, mood disorders and suicidal behaviour, personality disorders and psychotic disorders. It would also be of interest to study the possibility of prevention of psychiatric illness (including disorders related to the use of psychotropic substances) and psychosocial maladaptation in adulthood, given that the developmental disorder can be recognized and the diagnosis assigned in childhood. Long time follow-up studies of various treatments of adults with ADHD, as well as of concomitant treatment of coexisting psychiatric disorders, are required. More research into pharmacological enhancement, with central stimulants or other substances, of different aspects of executive functioning, not only in ADHD but in many other disorders as well, would be of great interest. The clinical pictures of ADHD in the elderly and the needs of this group of adults need elucidation.

The research into ASD is still to a great extent concentrated on children with the disorders. There remains much to be done concerning adults with ASD and, not least, elderly individuals with ASD. Longer term, meaning several decades, follow-up studies, with a focus on subjective quality of life rather than the conventional outcome measures, are needed. The relationship between ASD and concomitant psychiatric disorders, especially psychotic disorders and personality disorders, needs to be studied. One area of so-called comorbidity that needs further studying is ADHD and ASD, especially the qualitative aspects of the attention deficits of the presumably different disorders. In studies of relationships between what we today conceptualize as different disorders, the "borderline" cases of ASD – the broad autistic phenotype as well as atypical autism/PDD-NOS – should be of special interest.

It goes without saying that the search for reliable biological markers for ASD as well as ADHD must continue, with the hope of finding ways to make these categorical diagnoses, if they are to be used, more precise. It may well be that other diagnostic or classifying dimensions - as expressed by the 2009 NIMH (National Institute of Mental Health) task force for research domain criteria: "the effort is to define basic dimensions of functioning (such as fear circuitry or working memory) to be studied across multiple levels of analysis, from genes to neural circuits to behaviours, cutting across disorders as

traditionally defined" (NIMH, 2011) - will be found and validated, rendering the present categories obsolete.

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