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The ESSENCE in child psychiatry: Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations☆

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ABSTRACT

Co-existence of disorders – including attention-deficit/hyperactivity disorder, oppositional defiant disorder, tic disorder, developmental coordination disorder, and autism spectrum disorder – and sharing of symptoms across disorders (sometimes referred to as comorbidity) is the rule rather than the exception in child psychiatry and developmental medicine. The acronym ESSENCE refers to Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations. It is a term I have coined to refer to the reality of children (and their parents) presenting in clinical settings with impairing child symptoms before age 3 (−5) years in the fields of (a) general development, (b) communication and language, (c) social inter-relatedness, (d) motor coordination, (e) attention, (f) activity, (g) behaviour, (h) mood, and/or (i) sleep. Children with major difficulties in one or more (usually several) of these fields, will be referred to and seen by health visitors, nurses, social workers, education specialists, pediatricians, GPs, speech and language therapists, child neurologists, child psychiatrists, psychologists, neurophysiologists, dentists, clinical geneticists, occupational therapists and physiotherapists, but, usually they will be seen only by one of these specialists, when they would have needed the input of two or more of the experts referred to. Major problems in at least one ESSENCE domain before age 5 years often signals major problems in the same or overlapping domains years later. There is no time to wait; something needs to be done, and that something is unlikely to be just in the area of speech and language, just in the area of autism or just in special education.

1. Introduction

While in the past, child psychiatry had little interest in operationalised diagnosis, recent trends have made categorical diagnosis an integral part of everyday clinical and research practice (Sonuga-Barke, 2009). So focused are we now on the dichotomous distinction between disorder and not disorder that clinics become more and more specialised and cater to the needs of children with "autism only", "attention-deficit/hyperactivity disorder/ADHD only" or "Tourette syndrome only". This has led to a situation in which the diffuseness of disorder has come to be underestimated.

At the same time, rather belatedly, there is a growing realisation that co-existence of disorders and sharing of symptoms across disorders (so called comorbidity, a misnomer if ever there was one) is the rule rather than the exception (e.g. Kadesjö & Gillberg, 2001). I pointed this out more than a quarter of a century ago (Gillberg, 1983), but, in clinical practice, this insight has not led to new approaches to addressing the needs of children and families with "complex needs". Instead, diversification has boomed.

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There are legislational, scientific, and clinical attempts to separate out children with autism spectrum disorders (ASD) from those who do not have ASD, all aiming to provide better societal guidelines, more focused attempts at finding the causes, and autism-specific services. Children with ADHD are targeted in similar ways, even though legislation has yet to catch up with them. The same holds for children with language impairments (often erroneously referred to as "specific" language impairment (SLI); erroneous because the impairments are almost never specific), visual impairments and hearing deficits (children who may, or may not, have additional impairments as regards general cognition, motor performance, ASD or ADHD).

There is good evidence that ASD and ADHD can be separate and recognisable "disorders", but, equally, there is mounting evidence that they often overlap, constitute amalgams of problems, and that in some families they separate together and probably represent different aspects of the same underlying disorder (Reiersen, Constantino, Volk, & Todd, 2007).

With growing insight that early onset childhood problems, such as those reflected in children who are diagnosed in early childhood as suffering from ASD or ADHD, have long-term, indeed probably often, lifetime consequences (Billstedt, Gillberg, & Gillberg, 2005; Cederlund, Hagberg, & Gillberg, 2010; Rasmussen & Gillberg, 2000), the incentive to screen and diagnose these conditions has become a main priority for clinicians and administrators hoping to alter the often negative course inherent in cases who have had little or no intervention (or indeed an exclusionary attitude on the part of those "responsible") during the course of growing up. The question to be addressed is: would making discrete diagnosis (of, say, ASD or ADHD) before age 5 years contribute to a better understanding, better intervention, and more positive outcome in children who present with problems that potentially could be indices of these disorders.

2. What is ESSENCE?

The acronym ESSENCE refers to Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations. It is a term I have coined to refer to the reality of children (and their parents) presenting in clinical settings with impairing child symptoms before age 3 (−5) years in the fields of (a) general development, (b) communication and language, (c) social interrelatedness, (d) motor coordination, (e) attention, (f) activity, (g) behaviour, (h) mood, and/or (i) sleep. Children with major difficulties in one or more (usually several) of these fields, will be referred to and seen by health visitors, nurses, social workers, education specialists, pediatricians, GPs, speech and language therapists, child neurologists, child psychiatrists, psychologists, neurophysiologists, dentists, clinical geneticists, occupational therapists and physiotherapists, but, in the vast majority of cases they will be seen only by one of these specialists, when, in fact, they would have needed the input of two or more (occasionally even all) of the experts referred to.

The syndromes encompassed under the ESSENCE umbrella acronym are listed in Table 1.

Most of these syndromes are conceptualised as more or less discrete disorders in the DSM-IV-TR, and in the ICD-10. Here, they are listed, not because I believe they exist "in their own right" (even though occasionally they do show up as isolated conditions in individuals), but because they currently drive development in the whole field of child health, and all of them have links to one or more of the other conditions on the list.

2.1. An example from the field of SLI

In a recent population study, Miniscalco identified 25 children with "specific language impairment" (SLI) at age 2.5 years (Miniscalco, Nygren, Hagberg, Kadesjö, & Gillberg, 2006). They had been screened by child health nurses and had both screened positive (on one or more of the items (i) fewer than twenty-five communicative words, (ii) comprehension difficulties, (iii) articulation difficulties) *and* been deemed to have some degree of speech and language impairment after formal testing made by a pediatric speech and language therapist (SLT). They were contrasted with 80 children from the general population without SLI and followed as regards speech and language development for a period of 5 years (seen by an SLT at ages 4, 6 and 7.5 years). When they were 7.5 years they were, in addition, examined by a neuropsychiatric team, who remained blind to the original assessments. At this age, more than 70% of the children with SLT had ASD, ADHD,

Table 1
Syndromes encompassed under the ESSENCE acronym.

Syndrome	Prevalence	Key reference
ASD/PDD	1%	Gillberg and Wing (1999)
ADHD	5%	Swanson, Wigal, and Lakes (2009)
ODD	4%	Pliszka (2000)
SLI	6%	Miniscalco et al. (2006)
LD	1.5%	Gillberg and Söderström (2003)
NVLD	?	Rourke (1988)
Tic disorders/Tourette syndrome	1%	Comings (1990)
Bipolar disorder	?	Biederman et al. (2003)
Behavioural phenotype syndromes	.7%	O'Brien (2000)
Rare epilepsy syndromes	.01%	Aicardi, Bax, and Gillberg (2009)
Reactive attachment disorder	?	Minnis et al. (2009)
Total taking overlap into account	7–10%	Gillberg (1995)

mental retardation, or borderline learning disability (or combinations of these). None of them had been suspected of having any of these problems at the original diagnosis of SLI. By age 4 and 6 years, only a small fraction had been recognised to suffer from ASD or ADHD, and an even smaller proportion had received appropriate interventions for such problems.

What can we conclude on the basis of these and similar findings from previous studies? Children with SLI at 2.5 years are a large group—several per cent are affected according to UK and Swedish studies (Law et al., 2006; Miniscalco, Westerlund, & Lohmander, 2005). When a child is recognised as having SLI in a child health setting he/she is usually referred for a hearing test and assessment and possibly speech and language therapy to a pediatric SLT. The results of the study referred to indicate that this might not be appropriate. It would probably be reasonable to characterise the problem signalled by the SLI as belonging to the ESSENCE group and refer the child for multidisciplinary evaluation by a community pediatrician, a psychologist *and* an SLT.

2.2. An example from the field of ASD

Two decades ago, our group demonstrated that autism diagnoses made before age 3 years were relatively stable over time, 75% still meeting criteria for ASD at follow-up years later (Gillberg et al., 1990). However, in 25% this was not the case, but all the children in this latter group met criteria for another developmental disorder, such as non-autism learning disability or ADHD. Other groups (e.g. Chawarska, Klin, Paul, Macari, & Volkmar, 2009) have found similar results. In a new study of more than 300 preschool children with a clinical diagnosis of ASD, the vast majority met research DSM-IV criteria for autistic disorder, Asperger's disorder, or pervasive developmental disorder not otherwise specified at follow-up after 2 years. However, about one in 10 was not diagnosed with ASD, but had other developmental disorder diagnoses, such as non-autism learning disability or ADHD (Fernell et al., 2010). Rates of speech and language problems, ADHD, DCD, gastrointestinal problems, epilepsy, and learning disability in the ASD group varied from about 10% to 60%, but this had not been revealed in connection with the original clinical diagnosis of ASD. The findings provide good support for the notion that these were children suffering from ESSENCE, and, depending on the inclination, interest, and training of the professional first seeing the child because of ESSENCE problems, the child may first have been diagnosed with SLI, ADHD, learning disability or ASD, and any number of the comorbid problems might have been missed.

2.3. The early symptoms of ESSENCE

The "typical" symptoms of ESSENCE are listed in Table 2. These symptoms should not be seen as "specific" for ESSENCE. Rather, they should be considered markers for the (very likely) presence of a neurodevelopmental disorder that (very likely) will continue to cause symptoms long after their clinical surfacing in the first few years of life.

3. Scope of the problem

The estimated prevalence rates of the syndromes subsumed under the ESSENCE acronym are listed in Table 1. Most of the disorders listed have been epidemiologically surveyed during the early or middle school ages, and only a few have been the subject of prevalence studies in the preschool years. Even though all of the syndromes are present (and usually symptomatic) from the preschool years, many cases will not have come to the attention of clinicians before school age. Thus, the sum prevalence of about 10% of the general population of children suffering from these syndromes, may not reflect how many children come to clinical attention during the preschool period. On the basis of preschool studies of ASD, ODD and ADHD (Fernell et al., 2010; Kadesjö, Hägglöf, Kadesjö, & Gillberg, 2003), a reasonable estimate would be that about 5–7% of children under age 6 years would meet "criteria" for ESSENCE (i.e. have clinical symptoms of a syndrome and have presented at a clinic with a view to diagnosis and intervention). Boys would be extremely overrepresented in this group, even though they probably would not outnumber girls by more than 2–3:1 had parents, teachers and clinicians been more aware that girls with ASD, ADHD, ODD, and SLI, while meeting full criteria for these disorders, might have a slightly/clearly different pattern

Table 2
Symptoms (causing major impairment) signalling ESSENCE in the first 4 years of life.

Symptom	Reference
Motor abnormality	Gillberg (1995)
General developmental delay	Gillberg (1995)
Speech and language delay	Law et al. (2006)
Social interaction/communication problems	Wing (2005)
Behaviour problems	Richman, Stevenson, and Graham (1975)
Hyperactivity/impulsivity	Spencer, Biederman, and Mick (2007)
Hypoactivity	Lundervold, Posserud, Sørensen, Ullebø, and Gillberg (submitted for publication)
Inattention/does not listen	Bishop et al. (1999)
Sleep problems	Stores (2006)
Feeding difficulties	McDougall, Drewett, Hungin, and Wright (2009)

of comorbidity (Kopp, Berg Kelly, & Gillberg, 2009; Mahone & Wodka, 2008; Pinkhardt et al., 2009). Girls, as a group, tend to be less violent, less motorically active, more socially adept, and better at using language skills for communication. All of these factors contribute to masking the early symptomatic presentation of disorders such as ASD, and ADHD. With better awareness about the presence of such disorders in preschool girls, more and more female cases are likely to come to attention over the next several years.

4. ASD

ASD is no longer considered a rare condition (Baird et al., 2006), rather, its prevalence during the school years is believed to be slightly higher than 1% of the general population of children. Boys are clearly much more often affected than girls, at least if we are referring to the clinically impairing variant of the autism phenotype. Skuse (2009) has argued that the autism phenotype might be equally common in males and females, and that other factors are responsible for the large discrepancy in male:female ratios seen in clinical and epidemiological populations. However, others (including Baron-Cohen, 2005) have proposed that the autistic phenotype is an expression of the "extreme male brain", which would make the male preponderance in ASD a very real thing and not due to gender roles, comorbidity or other factors making boys more likely to be diagnosed with the condition.

ASD is a group of multifactorially determined conditions, and there are almost as many different causes as there are cases (Gillberg & Coleman, 2000). The prefrontal, temporal, brainstem and cerebellar regions of the central nervous system are usually affected. These areas constitute a functional network, "the default network", which appears to be critically differently functioning in ASD (Buckner & Vincent, 2007; Iacoboni, 2006; Monk et al., 2009). ASD with some degree of cognitive impairment is probably associated with life-long disability in the vast majority of cases (e.g. Billstedt et al., 2005), but it is unclear to what extent higher functioning individuals with ASD (including the group with Asperger syndrome) continue to show pervasive impairments in adult life (e.g. Cederlund et al., 2010), even though there are indications that persistence of some problems throughout life are more common than not. There is now good evidence that early intensive training programmes have lasting beneficial effects on a number of aspects of the disorder.

ASD is almost never an isolated phenomenon. Co-existing problems and disorders are the rule. These include learning disability (including non-verbal learning disability), epilepsy, motor control problems, ADHD, depression, and anxiety, gastrointestinal problems, and sleep disorders. These problems and disorders are sometimes the reason for referral to a specialist for evaluation. For instance, it is not uncommon for an extremely hyperactive child to be referred for evaluation of ADHD, but the full appraisal, once considered, will reveal that the child's main diagnosis is ASD, and it may, or may not, be motivated to diagnose co-existing ADHD.

5. ADHD (and oppositional-defiant disorder)

ADHD (with or without ODD) is a very common condition, affecting at least 5% of school age children (Faraone, Sergeant, Gillberg, & Biederman, 2003). In about 60% of the cases it is associated with ODD, which is usually symptomatic already around 3 years of age (Kadesjö et al., 2003). Again, boys are affected much more often than girls, and, particularly in the preschool period it is unusual for a girl to be recognised as having the condition (unless it is in the context of having another diagnosis, such as ASD or learning disability). It appears that at least half of individuals diagnosed in childhood with ADHD continue to have impairing ADHD in adult life, and that the majority have some remaining problems, even if they do not meet full criteria for "clinical" ADHD (Dopheide & Pliszka, 2009; Rasmussen & Gillberg, 2000). There is evidence that several aspects of the disorder can be positively affected by short- and long-term interventions combining a psychoeducational and pharmacological approach (Ghuman, Arnold, & Anthony, 2008; Vaughan, Fegert, & Kratochvil, 2009). There are indications, that at least when it comes to certain associated conditions (such as ASD), "comorbidity" needs to influence intervention choice in important ways in order to achieve the best possible outcome (Ollendick, Jarrett, Grills-Taquechel, Hovey, & Wolff, 2008). Preschool ODD, perhaps the most common of all the associated problems in the field of ADHD, indicates a much increased risk that the child may go on to develop conduct disorder, which, in turn, is a strong predictor of later antisocial personality disorder. Recognising and intervening for ODD in ADHD would probably ameliorate prognosis in a number of cases. Similarly, recognising and intervening for DCD in ADHD, has the potential of improving outcome even further. DCD in ADHD is also a strong predictor/marker for associated ASD (Kadesjö & Gillberg, 1999).

ADHD is largely genetic (Curatolo, Paloscia, D'Agati, Moavero, & Pasini, 2009), but a very similar phenotype can develop after various types of brain damage/environmentally caused brain dysfunction (Strang-Karlsson et al., 2008). The brain develops differently in children with ADHD than in typically developing children, with loss of the prefrontal component of normal asymmetrical brain development (Shaw et al., 2009). There is also growing evidence that the brain's dopamine-dependent reward system is dysfunctional in ADHD (Volkow et al., 2009). Interestingly, there is now good evidence that ASD and ADHD are clearly related in some families, and that CNS connectivity genes involved in ASD may also be relevant for the development of ADHD symptoms (Kopp et al., 2009; Mulligan et al., 2009; Sharp, McQuillin, & Gurling, 2009).

ADHD, like ASD, is usually not a discrete disorder. Instead, even in the community, not just in clinics dealing with severely impaired individuals, "co-morbidity" is the rule (Kadesjö & Gillberg, 2001). ODD, DCD, depression, anxiety, ASD, substance use disorder, and conduct disorder are all relatively or very common co-existing disorders.

6. Learning disability, non-verbal learning disability, and dyslexia

Learning problems, including learning disability, borderline intellectual functioning, non-verbal learning disability, and precursors of dyslexia (including phonological awareness problems) are common in the preschool period, and affect several per cent of both boys and girls. More often than not, such learning problems co-exist with other neurodevelopmental/neuropsychiatric disorders, such as ADHD, ASD and ODD. There is currently a clinical diagnostic substitution trend, at least in the UK, Scandinavia, and the US (Bishop, Whitehouse, Watt, & Line, 2008; Coo et al., 2008; Fernell et al., 2010; Howlin, 2008), leading to fewer children being diagnosed with learning disability and more being labelled as suffering from ASD. The problem with this trend is that the very real learning problems suffered by many individuals with ASD and ADHD may go undiagnosed for long periods of time. In the past, the opposite was often true. Non-verbal learning disability is common in Asperger syndrome (Cederlund & Gillberg, 2004; Klin, Volkmar, Sparrow, Cicchetti, & Rourke, 1995), but often not recognised, much less diagnosed. This is unhelpful for those who are clearly impaired by "both conditions". Many individuals with Asperger syndrome – and their parents and teachers – benefit greatly from a better understanding of the particular neuropsychological profile (with its characteristic peaks and troughs) associated with non-verbal learning disability. The reverse is also true, and Asperger syndrome is often missed by neuropsychologists who specialise in non-verbal learning disability. Phonological awareness problems, a common precursor of dyslexia, are frequent in ADHD (with or without associated autistic symptoms), but are often missed, once the "overshadowing" diagnosis of ADHD/ASD has been established (Asberg, Kopp, Berg-Kelly, & Gillberg, 2009). Many of these clinical problems, stemming from the overfocus on one or other of all the preschool neurodevelopmental disorders, could be avoided if clinicians were more aware of the implications of ESSENCE, and had several different diagnoses (and associated/comorbid diagnoses) in mind whenever examining a child presenting with impairing symptoms of ESSENCE.

7. Developmental coordination disorder

DCD has recently become the subject of more intense systematic study, after having been virtually neglected as an important clinical problem and focus of research. It is quite common, affecting about 5% of all school age children (Gillberg & Kadesjö, 2003), the majority of whom should be recognisable before age 5 years. However, currently, it is rare for a child to be given this diagnosis before school age. There is now a need for all child psychiatrists to be trained in the field of motor coordination assessment, and for pediatricians and other "non-psychiatry" physicians to keep abreast of developments in the field of ASD and ADHD, the two psychiatric disorders that appear to be most commonly associated with DCD. A Swedish population-study has suggested that there might be a specific connection between ADHD and ASD, and that it is mediated by DCD (Kadesjö & Gillberg, 1999): children with ADHD who also have DCD (about half the group of all with ADHD) have a very high risk of having impairing autistic symptomatology, whereas those without DCD have a low risk, and a much higher risk for ODD and conduct problems.

8. Tics and Tourette syndrome

Tics are extremely common in middle childhood and probably affect at least 15% of all children at some time. Severe, chronic motor and vocal tics (the combination that is referred to as Tourette syndrome) are much less common, probably affecting about 1% of all school age children (Kadesjö & Gillberg, 2000). Tics fluctuate in intensity and over time, which means that even some severely affected individuals may not actually show any tics during consultation. Tics are rarely diagnosed in the preschool years, but various forerunners of Tourettés disorder (such as impulsivity and a variety of obsessive compulsive phenomena) are usually present long before the typical, sometimes striking, even dramatic, tics occur or surface at early school age. Tourettés disorder is considered to be a strongly genetic disorder (but more heterogeneous than previously believed) (Keen-Kim & Freimer, 2006; State, Pauls, & Leckman, 2001).

One of the clinically most important aspects of Tourette syndrome (and other severe motor or vocal tic disorders) is its strong association with ADHD and OCD (Debes, Hjalgrim, & Skov, 2009). Almost all severely handicapped children with Tourette syndrome are affected by either ADHD or OCD or both, and are usually more impaired by these "comorbid" conditions than by the tic disorder itself. These associated problems, particularly ADHD (and perhaps particularly extremes of impulsive-hyperactive behaviours), are often apparent already during the preschool years, and they, rather than the tics, are what will lead to referral for clinical neurodevelopmental/neuropsychiatric examination.

9. Bipolar disorder

Pediatric bipolar disorder is still a somewhat controversial diagnosis (Biederman et al., 2003). However, it is becoming increasingly recognised that bipolar disorder can present with symptoms already in the preschool years. Children with "ADHD" and/or depression who have a family history of bipolar disorder may actually be presenting with prodromal signs and symptoms of a bipolar disorder (Chang, 2008). Extremes of irritability, mood swings, and even classic manic symptoms may onset in the first several years of life and signal the possibility of an underlying bipolar disorder. ADHD and ASD can both occur in conjunction with bipolar disorder (and can probably overshadow the affective disorder). Longitudinal systematic study of large groups of children with ESSENCE will help clarify the prevalence and importance of pediatric bipolar disorder.

10. Behavioural phenotype syndromes

As many as 0.7–0.8% of all preschool children may be affected by one (or more) of the "rare disorders", also referred to as behavioural phenotype syndromes (Gillberg, 2009, chap. 23–25). Examples of such disorders are the fragile X syndrome, 22q11deletion syndrome, tuberous sclerosis and Smith-Lemli-Opitz syndrome. Each of these disorders is really "rare" (occurring, usually in fewer than 1 in 2000 children), but given that there are hundreds of them, taken as a group they are actually quite common. The majority of these syndromes have a large subgroup – usually the majority – with some degree of cognitive impairment, although it is important to point out that there are quite a number of affected individuals who do not have learning disability, and some have high IQ (e.g. most individuals with Marfan syndrome and about half the group with 22q11deletion syndrome). Large subgroups of individuals within each category of the rare disorders in addition have ASD or ADHD or both, and other individuals may have other neuropsychiatric/neurodevelopmental problems that are symptomatic from a very young age (Hagerman et al., 2009; Niklasson, Rasmussen, Óskardòttir, & Gillberg, 2009; Sikora, Pettit-Kekel, Penfield, Merkens, & Steiner, 2006). Indeed it is very common for such problems to be the original reason for referral. In our centre we see quite a number of cases each year, in which the behavioural phenotype syndrome (and the genetic abnormality usually underlying it) has been missed.

11. Rare epilepsy syndromes

Landau-Kleffner syndrome or "verbal auditory agnosia with seizures" is a relatively rare syndrome which often presents in the preschool years and which is sometimes "misdiagnosed" as ASD, ADHD or both. Children with Landau Kleffner syndrome very often meet criteria for one or both of these types of conditions, but it is essential that the underlying epileptic syndrome not remain undiagnosed. Pulsed steroids, and, in certain cases, surgical treatments may be indicated (Cross & Neville, 2009). The overlap with the syndrome referred to as Continuous Spike Wave activity during Slow-wave sleep (CSWS) is considerable, and it is probably more a matter of the child's age than of any intrinsic difference between Landau-Kleffner syndrome (preschool children) and CSWS (older children) which of the named conditions gets a label in the individual case.

Infantile spasms (Saemundsen, Ludvigsson, & Rafnsson, 2008) and Dravet syndrome with SCN1A mutations (Arzimanoglou, 2009) carry high risks of intellectual disability, ASD and ADHD. It is important that such additional diagnoses are not overlooked in the follow-up of preschool children with these rare epilepsy syndromes, given that clinical experience suggest beneficial effects of ASD and ADHD interventions even in the presence of the severe underlying seizure disorder. Other rare epilepsy syndromes with onset in the preschool period is usually of such devastating character that making additional diagnoses of neuropsychiatric disorders such as ASD and ADHD is often not discussed, nor indeed relevant. However, just occasionally, epilepsies of the Lennox-Gastaut type (and other, even rarer conditions) can be sufficiently well controlled and ASD or ADHD type problems so pronounced that the issue of ESSENCE might be raised. In such instances it would not be appropriate to conclude that given the nature and severity of the epilepsy syndrome an additional diagnosis of ASD, ADHD, or another ESSENCE behaviour disorder would makes little difference. There is sufficient anecdotal support for the notion that even in cases considered "hopeless", interventions targeting ASD and/or ADHD may drastically improve quality of life for affected families.

12. Reactive attachment disorder

There is emerging evidence that reactive attachment disorder as defined under the DSM-IV-TR exists as a relatively distinct problem (Minnis et al., 2009). It can be recognised in the preschool years (Zeanah, Keyes, & Settles, 2003), and separated from – although symptomatically overlapping with – ADHD during the early school years (Minnis & Follan, in press). It also is associated with severe pragmatic language problems that are not explained by the occasional co-occurrence with ASD (Sadiq et al., submitted for publication). It is of considerable interest that a large subgroup of children meeting symptomatic criteria for reactive attachment disorder have not been severely abused or deprived in early childhood (Minnis, Marwick, Arthur, & McLaughlin, 2006). A brief screen for the disorder is available for school age children (Minnis et al., 2007), but there is a need for development of more refined screening and diagnostic tools for preschoolers. The disorder should be considered in all children who have suffered severe maltreatment or deprivation in the early years, and, perhaps also in all children with any kind of impairing ESSENCE symptom who show the possibly discriminating feature of cuddliness with strangers (Minnis & Follan, in press).

13. Overlap, co-existence and "comorbidity"

The word comorbidity is inadequate when it comes to describing and delineating the reality and meaning of the co-occurrence of phenomena, problems, symptoms, syndromes and disorders and diseases in the clinical and research field of ESSENCE. Most clinicians and researchers attach different meanings to the word comorbidity (Caron & Rutter, 1991). Using the word in a literal sense, one would assume that a person diagnosed with "comorbid" ASD and ADHD would have two different morbid ("disease") conditions. These morbid conditions could have different etiologies, the same etiology, or have no known etiology ("idiopathic"). In actual fact, when we talk about comorbidity, what we are usually referring to is

"co-existence", "association", "overlap", "additional problems" or suchlike. When the word comorbidity has been used here (usually within quotes), it has been "in that sense".

The syndromes subsumed under the ESSENCE label constitute collections of symptoms – sometimes, but certainly not always, operationalised under rigidly structured algorithms – that, at the current state of our knowledge, appear to delineate clinically meaningful conditions. However, as our knowledge base increases, so the algorithm barriers for making the specific diagnoses will need to be reviewed, and, quite often, changed. This has happened over the past 30 years in ASD and ADHD. The DSM-V is going to introduce another, probably major, change in how these categories are conceptualised, operationalised, algorithmised, and diagnosed. There is growing realisation that (a) most so called syndromes, including ASD, are, at least to some extent, partly arbitrary end- or cut-off-points on normal distribution curves, and depending on where you draw the line you may be referring to autistic disorder or Asperger syndrome; (b) most syndromes comprise a mixture of symptom collections from end- or cut-off points of different normal distribution curves, so that, at intersections, some individuals affected will meet criteria for ASD, others for ASD with ADHD, and others still for ADHD "only"; (c) most syndromes can be "mimicked by" (or may have actually be modelled around) more circumscribed brain disorders (genetic or environmental) or diffuse or unspecific/specific brain injury/dysfunction (temporary or chronic) caused by a variety of factors including the effects of myelin disorder after extreme prematurity, periventricular bleeding after perinatal asphyxia, thalidomide – or extremes of alcohol – exposure in fetal life, and exposure to products included in diets currently considered to be "normal", or, at least, not harmful. Against this background, it should come as no surprise that the introduction of the term ESSENCE, as suggested by the definition of the acronym, is nothing but an attempt to acknowledge this state of affairs, and the fact that there is a need to implement this approach to thinking about the problems in the whole wide field of child health and development services.

14. The implications of ESSENCE

What then are the implications of introducing a term such as ESSENCE? Let me list them, in no specific order, but with the most important conclusion summarised at the end:

(1) ESSENCE is a new acronym but not a new way of thinking about early onset childhood problems that continue to affect children's development long after the preschool period;
(2) ESSENCE is introduced so as to detract from the current trend towards compartmentalising syndromes in child and adolescent psychiatry and developmental medicine to the extent that "things" such as ASD and ADHD are considered "boxes" that are exclusive and separable from each other;
(3) ESSENCE is a term that draws attention to the fact that there is no easy way out in terms of diagnosis in preschool children who present with ESSENCE symptoms. All children presenting with an ESSENCE problem need to be considered from the point of view of multiproblem and multidisciplinary assessment;
(4) Children with ESSENCE need to get a holistic approach – on first presenting to services – to diagnosis and intervention. If the child suffers from ASD, it is likely that he/she also suffers from LD, ADHD, etc., and if the child suffers from ADHD, it is likely that he/she also suffers from ODD and DCD. The approach to diagnosis is likely to be unhelpful if it is exclusively directed to the diagnosis of one of these "disorders";
(5) The overlap of problems encountered in the field of ESSENCE indicates that we are not dealing with discrete disorders or syndromes, but with brain dysfunctions/neurodevelopmental problems that reflect circuitry breakdown, network dysfunctions and decreased/aberrant/increased connectivity, or, indeed, in quite a number of cases, "normal" brain function variants, and, that, therefore, it would be inappropriate to diagnose one problem and not consider the implication of the other(s). Currently, there is a trend towards compartmentalisation, services and clinics being developed specifically for ASD or ADHD or Tourette syndrome. This does not appear to be a helpful approach. In the future, as we learn more about the extent of normality, and as we teach a growing generation of children that we are all different, there may not be a need for lumping diagnoses (such as ESSENCE), but for specific diagnosis of genetic and environmental contributors to the problems encountered in each individual case;
(6) Taken together, all of the above would appear to combine to suggest the obvious solution. There is a need for Child ESSENCE Centres (rather than Community Pediatrics, GP centres, CAMHS, SLT-services, Special Education Units, Child Neurology, ASD, ADHD, Tourette or Affective disorder centres) to be organised for all preschool children, catering to the diagnostic, intervention planning, and follow-up requirements that are clearly warranted for all preschool children presenting with a major ESSENCE symptom. There is abundant evidence that major problems in at least one ESSENCE domain before age 5 years signals major problems in the same or overlapping domains several years later. There is no time to "sit down and wait"; something needs to be done, and that something is unlikely to be "just" in the area of speech and language. "just" in the areas of ASD or ADHD or "just" in special education.

14.1. Lumping, splitting, splitting, lumping, or both?

Progress in medical research usually leads to refinement of diagnostic criteria and increasingly sophisticated methods of subgrouping according to etiology, with important consequences for intervention. Superficially, this much-accepted view of cutting-edge medicine could be seen as support for a "splitter" approach to medical progress. The introduction of the

ESSENCE label could, by some, be taken to mean a step backwards in development in child psychiatry, given its implicit support for a "lumper" view. However, lumping of ESSENCE is only meaningful and, I would suggest, very helpful, if clinicians and researchers start by approaching the area of early child developmental problems by accepting that splitting in a state-of-the-art way (making refined and individualised diagnosis and intervention plans) will only be possible if there is anything to start splitting from (i.e. from a "lumped" group of cases). Also, if splitting occurs already in the mind of the original beholder/referrer (i.e. delayed language is seen as the "property" of the SLT, social interaction problems is seen as the "property" of the "autism centre", and delayed overall development with behaviour problem is seen as the "business of the learning disability psychiatrist") this would lead to inadvertent delay in recognising that the child with ESSENCE very likely will have more than one problem (i.e. ASD with ADHD, ASD with ADHD and epilepsy, ADHD with DCD and reactive attachment disorder, etc.). In summary, the introduction of the ESSENCE-mode of thinking about problems to do with deviations from normal child development, should not be taken as support for lumping rather than splitting, but for the order in which those two aspects of diagnosis is approached.

References

Aicardi, J., Bax, M., & Gillberg, C. (2009). *Diseases of the nervous system in childhood*. Cambridge: MacKeith Press.

Arzimanoglou, A. (2009). Dravet syndrome: From electroclinical characteristics to molecular biology. *Epilepsia,* Suppl. 8: 3–9.

Asberg, J., Kopp, S., Berg-Kelly, K., & Gillberg, C. (2009). Reading comprehension, word decoding and spelling in girls with autism spectrum disorders or AD/HD: Performance and predictors. *International Journal of Language and Communication Disorders, 2*, 1–16.

Baird, G., Simonoff, E., Pickles, A., Chandler, S., Loucas, T., Meldrum, D., & Charman, T. (2006). Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: The Special Needs and Autism Project (SNAP). *Lancet, 368*, 210–215.

Baron-Cohen, S. (2005). Testing the extreme male brain (EMB) theory of autism: Let the data speak for themselves. *Cognitive Neuropsychiatry, 10*, 77–81.

Biederman, J., Mick, E., Faraone, S. V., Spencer, T., Wilens, T. E., & Wozniak, J. (2003). Current concepts in the validity, diagnosis and treatment of paediatric bipolar disorder. *International Journal of Neuropsychopharmacology, 6*, 293–300.

Billstedt, E., Gillberg, I. C., & Gillberg, C. (2005). Autism after adolescence: Population-based 13–22-year follow-up study of 120 individuals with autism diagnosed in childhood. *Journal of Autism and Developmental Disorders, 35*, 351–360.

Bishop, D. V., Bishop, S. J., Bright, P., James, C., Delaney, T., & Tallal, P. (1999). Different origin of auditory and phonological processing problems in children with language impairment: Evidence from a twin study. *Journal of Speech, Language, and Hearing Research, 42*, 155–168.

Bishop, D. V., Whitehouse, A. J., Watt, H. J., & Line, E. A. (2008). Autism and diagnostic substitution: Evidence from a study of adults with a history of developmental language disorder. *Developmental Medicine and Child Neurology, 50*, 341–345.

Buckner, R. L., & Vincent, J. L. (2007). Unrest at rest: Default activity and spontaneous network correlations. *Neuroimage, 37*, 1091–1096.

Caron, C., & Rutter, M. (1991). Comorbidity in child psychopathology: Concepts, issues and research strategies. *Journal of Child Psychology and Psychiatry, 32*, 1063–1080.

Cederlund, M, & Gillberg, C. (2004). One hundred males with Asperger syndrome. A clinical study of background and associated factors. *Developmental Medicine and Child Neurology, 46*, 652–660.

Cederlund, M., Hagberg, B., & Gillberg, C. (2010). Asperger syndrome in adolescent and young adult males. Interview, self- and parent assessment of social, emotional and cognitive problems. *Research in Developmental Disabilities, 31*, 287–298.

Chang, K. D. (2008). The bipolar spectrum in children and adolescents: Developmental issues. *Journal of Clinical Psychiatry, 69*, e9.

Chawarska, K., Klin, A., Paul, R., Macari, S., & Volkmar, F. (2009). A prospective study of toddlers with ASD: Short-term diagnostic and cognitive outcomes. *Journal of Child Psychology and Psychiatry, 50*, 1235–1245.

Comings, D. E. (1990). *Tourette syndrome and human behavior*. Hope Press.

Coo, H., Ouellette-Kuntz, H., Lloyd, J. E., Kasmara, L., Holden, J. J., & Lewis, M. E. (2008). Trends in autism prevalence: Diagnostic substitution revisited. *Journal of Autism and Developmental Disorders, 8*, 1036–1046.

Cross, J. H., & Neville, B. G. (2009). The surgical treatment of Landau-Kleffner syndrome. *Epilepsia,* Suppl. 7: 63–67.

Curatolo, P., Paloscia, C., D'Agati, E., Moavero, R., & Pasini, A. (2009). The neurobiology of attention deficit/hyperactivity disorder. *European Journal of Paediatric Neurology, 13*, 299–304.

Debes, N. M., Hjalgrim, H., & Skov, L. (2009). The presence of comorbidity in Tourette syndrome increases the need for pharmacological treatment. *Journal of Child Neurology, 24*, 1504–1512.

Dopheide, J. A., & Pliszka, S. R. (2009). Attention-deficit-hyperactivity disorder: An update. *Pharmacotherapy, 29*, 656–679.

Faraone, S. V., Sergeant, J., Gillberg, C., & Biederman, J. (2003). The worldwide prevalence of ADHD: Is it an American condition? *World Psychiatry, 2*, 104–113.

Fernell, E., Hedvall, A., Norrelgen, F., Erikssson, M., Höglund-Carlsson, L., Barnevik-Olsson, M., Svensson, L., et al. (2010). Developmental profiles in preschool children with autism spectrum disorders referred for intervention. *Research om Developmental Disabilities, 31*, 790–799.

Ghuman, J. K., Arnold, L. E., & Anthony, B. J. (2008). Psychopharmacological and other treatments in preschool children with attention-deficit/hyperactivity disorder: Current evidence and practice. *Journal of Child Adolescent and Psychopharmacology, 18*, 413–447.

Gillberg, C. (1983). Perceptual, motor and attentional deficits in Swedish primary school children. Some child psychiatric aspects. *Journal of Child Psychology and Psychiatry, 24*, 377–403.

Gillberg, C. (1995). *Clinical child neuropsychiatry*. Cambridge: Cambridge University Press.

Gillberg, C. (2009). Developmental and neuropsychiatric disorders of childhood. In J. Aicardi (Ed.), *Diseases of the nervous system in childhood* (3rd ed., pp. 889–932). London: Mac Keith Press.

Gillberg, C., & Coleman, M. (2000). *The biology of the autistic syndromes* (3rd ed.). Cambridge: Cambridge University Press.

Gillberg, C., Ehlers, S., Schaumann, H., Jakobsson, G., Dahlgren, S. O., Lindblom, R., et al. (1990). Autism under age 3 years: A clinical study of 28 cases referred for autistic symptoms in infancy. *Journal of Child Psychology and Psychiatry, 31*, 921–934.

Gillberg, C., & Kadesjö, B. (2003). Why bother about clumsiness? The implications of having developmental coordination disorder (DCD). *Neural Plasticity, 10*, 59–68.

Gillberg, C., & Söderström, H. (2003). Learning disability. *Lancet, 362*, 11–21.

Gillberg, C., & Wing, L. (1999). Autism: Not an extremely rare disorder. *Acta Psychiatrica Scandinavica, 99*, 399–406.

Hagerman, R. J., Berry-Kravis, E., Kaufmann, W. E., Ono, M. Y., Tartaglia, N., Lachiewicz, A., Kronk, R., Delahunty, C., Hessl, D., Visootsak, J., Picker, J., Gane, L., & Tranfaglia, M. (2009). Advances in the treatment of fragile X syndrome. *Pediatrics, 123*, 378–390 (review).

Howlin, P. (2008). Autism and diagnostic substitution. *Developmental Medicine and Child Neurology, 50*, 325.

Iacoboni, M. (2006). Failure to deactivate in autism: The co-constitution of self and other. *Trends in Cognitive Sciences, 10*, 431–433.

Kadesjö, B., & Gillberg, C. (1999). Developmental coordination disorder in Swedish 7-year-old children. *Journal of the American Academy of Child and Adolescent Psychiatry, 38*, 820–828.

Kadesjö, B., & Gillberg, C. (2000). Tourette's disorder: Epidemiology and comorbidity in primary school children. *Journal of American Academy and Child Adolescent Psychiatry, 39*, 1466.

Kadesjö, B., & Gillberg, C. (2001). The comorbidity of ADHD in the general population of Swedish school age children. *Journal of Child Psychology and Psychiatry, 42*, 487–492.
Kadesjö, C., Hägglöf, B., Kadesjö, B., & Gillberg, C. (2003). Attention-deficit-hyperactivity disorder with and without oppositional defiant disorder in 3-7-year-old children. *Developmental Medicine and Child Neurology, 45*, 693–699.
Keen-Kim, D., & Freimer, N. B. (2006). Genetics and epidemiology of Tourette syndrome. *Journal of Child Neurology, 21*, 665–671.
Klin, A., Volkmar, F. R., Sparrow, S. S., Cicchetti, D. V., & Rourke, B. P. (1995). Validity and neuropsychological characterization of Asperger syndrome: Convergence with nonverbal learning disabilities syndrome. *Journal of Child Psychology and Psychiatry, 36*, 1127–1140.
Kopp, S., Berg Kelly, K., & Gillberg, C. (2009, on-line). Girls with social and/or attention deficit: A descriptive study of 100 clinic attenders. *Journal of Attention Disorders*.
Law, J., Dockrell, J. E., Castelnuovo, E., Williams, K., Seef, B., & Normand, C. (2006). Early Years Centres for pre-school children with primary language difficulties: What do they cost and are they cost-effective? *International Journal of Communication Disorders, 41*, 67–81.
Lundervold, A. J., Posserud, M. B., Sørensen, L., Ullebø, A. K., & Gillberg, C. (submitted for publication). Processing speed in hypoactive 7–9 years old children with internalizing or/and externalizing disorders.
Mahone, E. M., & Wodka, E. L. (2008). The neurobiological profile of girls with ADHD. *Developmental Disability Research Review, 14*, 276–284.
McDougall, P., Drewett, R. F., Hungin, A. P., & Wright, C. M. (2009). The detection of early weight faltering at the 6–8-week check and its association with family factors, feeding and behavioural development. *Archives of Disease in Childhood, 94*, 549–552.
Miniscalco, C., Nygren, G., Hagberg, B., Kadesjö, B., & Gillberg, C. (2006). Neuropsychiatric and neurodevelopmental outcome at school age 6 and 7 years of children who screened positive for language problems at 2.5 years. A community-based study. *Developmental Medicine and Child Neurology, 48*, 361–366.
Miniscalco, C., Westerlund, M., & Lohmander, A. (2005). Language skills at age 6 years in Swedish children screened for language delay at 2(1/2) years of age. *Acta Paediatrica, 94*, 1798–1806.
Minnis, H., & Follan, M. (in press). Forty-four Juvenile Thieves revisited: From Bowlby to reactive attachment disorder. *Child, Care Health and Development*.
Minnis, H., Green, J., ÓConnor, T. G., Liew, A., Glaser, D., Taylor, E., Follan, M., Young, D., Barnes, J., Gillberg, C., Pelosi, A., Arthur, J., Burston, A., Connolly, B., & Sadiq, F. A. (2009). An exploratory study of the association between reactive attachment disorder and the attachment narratives in early school-age children. *Journal of Child Psychology and Psychiatry, 50*, 931–942.
Minnis, H., Marwick, H., Arthur, J., & McLaughlin, A. (2006). Reactive attachment disorder—A theoretical model beyond attachment. *European Child and Adolescent Psychiatry, 15*, 336–342.
Minnis, H., Reekie, J., Young, D., O'Connor, T., Ronald, A., Gray, A., & Plomin, R. (2007). Genetic, environmental and gender influences on attachment disorder behaviours. *British Journal of Psychiatry, 190*, 490–495.
Monk, C. S., Peltier, S. J., Wiggins, J. L., Weng, S. J., Carrasco, M., Risi, S., & Lord, C. (2009). Abnormalities of intrinsic functional connectivity in autism spectrum disorders. *Neuroimage, 47*, 764–772.
Mulligan, A., Anney, R. J., O'Regan, M., Chen, W., Butler, L., Fitzgerald, M., et al. (2009). Autism symptoms in attention-deficit/hyperactivity disorder: A familial trait which correlates with conduct, oppositional defiant, language and motor disorders. *Journal of Autism and Developmental Disorders, 39*, 197–209 (Erratum in: Journal of Autism and Developmental Disorders, 39, 210–211).
Niklasson, L., Rasmussen, P., Óskardòttir, S., & Gillberg, C. (2009). Autism, ADHD, mental retardation and behavior problems in 100 individuals with 22q11 deletion syndrome. *Research in Developmental Disabilities, 30*, 763–773.
O'Brien, G. (2000). Behavioural phenotypes. *Journal of the Royal Society of Medicine, 93*, 618–620.
Ollendick, T. H., Jarrett, M. A., Grills-Taquechel, A. E., Hovey, L. D., & Wolff, J. C. (2008). Comorbidity as a predictor and moderator of treatment outcome in youth with anxiety, affective, attention deficit/hyperactivity disorder, and oppositional/conduct disorders. *Clinical Psychology Review, 28*, 1447–1471.
Pinkhardt, E. H., Kassubek, J., Brummer, D., Koelch, M., Ludolph, A. C., Fegert, J. M., & Ludolph, A. G. (2009). Intensified testing for attention-deficit hyperactivity disorder (ADHD) in girls should reduce depression and smoking in adult females and the prevalence of ADHD in the longterm. *Medical Hypotheses, 72*, 409–412.
Pliszka, S. R. (2000). Patterns of comorbidity with attention-deficit/hyperactivity disorder. *Child and Adolescent Psychiatry Clinics of North America, 9*, 525–540.
Rasmussen, P., & Gillberg, C. (2000). Natural outcome of ADHD with Developmental Coordination Disorder at age 22 years: A controlled, longitudinal, community-based study. *Journal of American Academy of Child and Adolescent Psychiatry, 39*, 1424–1431.
Reiersen, A. M., Constantino, J. N., Volk, H. E., & Todd, R. D. (2007). Autistic traits in a population-based ADHD twin sample. *Journal of Child Psychology and Psychiatry, 48*, 464–472.
Richman, N., Stevenson, J. E., & Graham, P. J. (1975). Prevalence of behaviour problems in 3-year-old children: An epidemiological study in a London borough. *Journal of Child Psychology and Psychiatry, 16*, 277–287.
Rourke, B. P. (1988). Socioemotional disturbances of learning disabled children. *Journal of Consulting and Clinical Psychology, 56*, 801–810 (Review).
Sadiq, A., Slator, L., Law, J., Gillberg, C., Skuse, D., & Minnis, H. (submitted for publication). A comparison of the pragmatic skills of children with reactive Attachment Disorder and High functioning Autism.
Saemundsen, E., Ludvigsson, P., & Rafnsson, V. (2008). Risk of autism spectrum disorders after infantile spasms: A population-based study nested in a cohort with seizures in the first year of life. *Epilepsia, 49*, 1865–1870.
Sharp, S. I., McQuillin, A., & Gurling, H. M. (2009). Genetics of attention-deficit hyperactivity disorder (ADHD). *Neuropharmacology, 57*, 590–600.
Shaw, P., Lalonde, F., Lepage, C., Rabin, C., Eckstrand, K., Sharp, W., Greenstein, D., Evans, A., Giedd, J. N., & Rapoport, J. (2009). Development of cortical asymmetry in typically developing children and its disruption in attention-deficit/hyperactivity disorder. *Archives of General Psychiatry, 66*, 888–896.
Sikora, D. M., Pettit-Kekel, K., Penfield, J., Merkens, L. S., & Steiner, R. D. (2006). The near universal presence of autism spectrum disorders in children with Smith-Lemli-Opitz syndrome. *American Journal of Medicine Genetics A, 40*, 1511–1518.
Skuse, D. H. (2009). Is autism really a coherent syndrome in boys, or girls? *British Journal of Psychology, 100*, 33–37.
Sonuga-Barke, E. (2009). Gained in translation: How can we facilitate science-driven innovations in child mental health therapeutics? *Journal of Child Psychology and Psychiatry, 50*, 655–656.
Spencer, T. J., Biederman, J., & Mick, E. (2007). Attention-deficit/hyperactivity disorder: Diagnosis, lifespan. Comorbidities, and neurobiology. *Journal of Pediatric Psychology, 32*, 631–642.
State, M. W., Pauls, D. L., & Leckman, J. F. (2001). Tourette's syndrome and related disorders. *Child and Adolescent Psychiatric Clinics of North American, 10*, 317–323.
Stores. (2006). Sleep disorders. In C. Gillberg, R. Harrington, & H. C. Steinhausen (Eds.), *Clinician's deskbook of child and adolescent psychiatry* (pp. 304–338). Cambridge: Cambridge University Press.
Strang-Karlsson, S., Räikkönen, K., Pesonen, A. K., Kajantie, E., Paavonen, E. J., Lahti, J., Hovi, P., Heinonen, K., Järvenpää, A. L., Eriksson, J. G., & Andersson, S. (2008). Very low birth weight and behavioral symptoms of attention deficit hyperactivity disorder in young adulthood: The Helsinki study of very-low-birth-weight adults. *American Journal of Psychiatry, 65*, 1345–1353.
Swanson, J. M., Wigal, T., & Lakes, K. (2009). DSM-Vand the future diagnosis of attention-deficit/hyperactivity disorder. *Current Psychiatry Reports, 11*, 399–406.
Vaughan, B., Fegert, J., & Kratochvil, C. J. (2009). Update on atomoxetine in the treatment of attention-deficit/hyperactivity disorder. *Expert Opinion on Pharmacotherapy, 10*, 669–676.
Volkow, N. D., Wang, G. J., Kollins, S. H., Wigal, T. L., Newcorn, J. H., Telang, F., et al. (2009). Evaluating dopamine reward pathway in ADHD: Clinical implications. *Journal of the American Medical Association, 302*, 1084–1091 (Erratum in: Journal of the American Medical Association, 302, 1420).
Wing, L. (2005). Reflections on opening Pandora's box. *Journal of Autism and Developmental Disorders, 35*, 197–203.
Zeanah, C. H., Keyes, A., & Settles, L. (2003). Attachment relationship experiences and childhood psychopathology. *Annals of the New York Academy of Sciences, 1008*, 22–30.