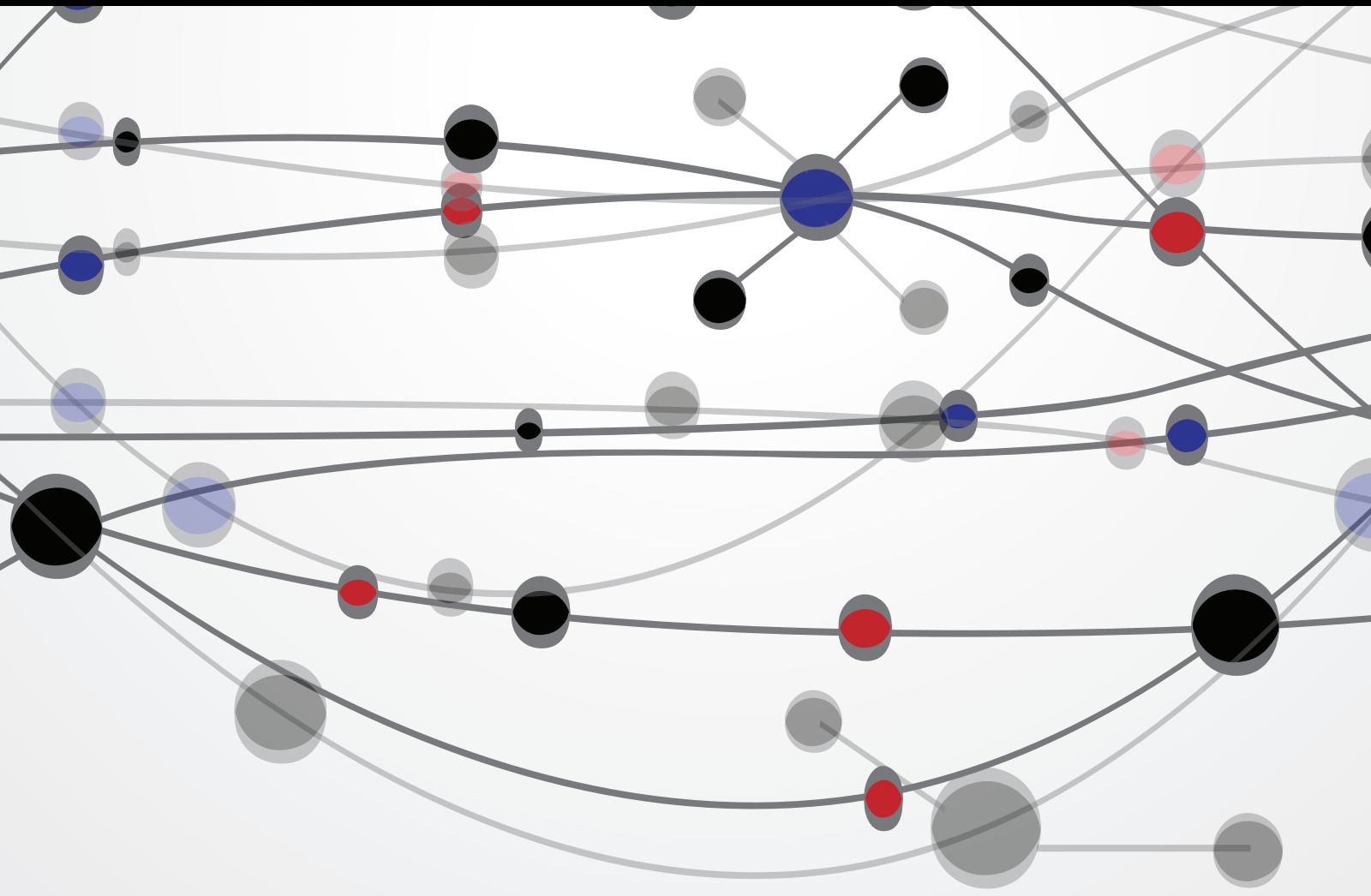
The Scientific World Journal

# Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations

Guest Editors: Christopher Gillberg, Elisabeth Fernell, and Helen Minnis



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*Editorial*

# Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations

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This special issue is devoted to the concept of ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations). It is an acronym that one of us coined some years ago [1] with a view to highlighting the clinical reality of children (and their parents) presenting in first, second, or third tier clinical settings with, usually complex, impairing developmental symptoms already in early childhood. The children are reported to have problems in the fields of (a) general development, (b) communication and language, (c) social interrelatedness, (d) motor coordination, (e) attention/"listening," (f) activity, (g) behavior, (h) mood, and/or (i) sleep. Children with major difficulties in one or more (usually several) of these fields will be seen by health visitors, nurses, social workers, education (including preschool) 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.

Categorical diagnosis is an integral part of everyday clinical and research practice. We are so insistent on the distinction between disorder and not disorder (normalcy) that clinics and clinicians become more and more specialized and cater to the needs of children with "Autism Spectrum Disorder/ASD only," "Attention-Deficit/Hyperactivity Disorder/ADHD only," "Language Disorder only," "Reactive Attachment Disorder/RAD only," or "Tourette syndrome only." This has led to a situation in which the typical clinical diffuseness of disorder has come to be underestimated.

At the same time, there is growing acceptance that coexistence of disorders and sharing of symptoms across disorders (so-called comorbidity, a misnomer if ever there was one, seeing as we are usually not dealing with completely separate coexisting disorders) are the rule rather than the exception (e.g., [2]). This was pointed out more than a quarter of a century ago [3], but, in clinical practice, this insight has not led to new approaches when trying to address the needs of children and families with "complex needs." Instead, diversification has boomed.

There are legislational, scientific, and clinical attempts to separate out children with certain disorders/diagnosis; for example, ASD from those who do not meet criteria for the disorder/diagnosis. The goal is usually provide better societal guidelines, more focused attempts at finding the causes, and more 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 Disorder, visual impairments, and hearing deficits (children who may, or may not, have additional impairments as regard to general cognition, motor performance, ADHD, or ASD).

ASD and ADHD, long treated and, believed to be, completely separate and recognizable "disorders," are now increasingly often diagnosed "together" within the same individual, and there is growing awareness that they sometimes overlap, constitute amalgams of problems, and that in some families they separate together and probably represent different aspects of the same underlying disorder [4].

The overlap, shared and nonshared symptoms and etiologies of these named disorders are in focus in this special issue.

There are 14 papers altogether in the volume. They deal with a variety of ESSENCE-related issues ranging from maltreatment and RAD (and the difficult issue of how to study the effects of early intervention aiming to stop maltreatment and provide safe and nurturing care), through autism from preschool to adult life (including a study showing that autism diagnosed early in life is always comorbid with other disorders, and a literature review indicating that pain sensitivity is, in fact, *not* decreased in autism), language delay (which can only be screened for by face-to-face assessment), eating problems (that are shown to be comorbid with ASD and ADHD symptomatology in a very high proportion of cases), and cerebral palsy (in which the prevalence of mental health problems, including ADHD, appears to currently be grossly underestimated) to more general mental health problems (and the use of child psychiatric and school psychology services that is associated with such problems). Methodologies covered in the special issue range from longitudinal population-based screening and clinical assessment studies, through randomized controlled trials and large-scale epidemiological twin research, to position and PRISMA-guideline systematic review papers. There is a wealth of information for clinicians and researchers alike, and it is expected that the issue on ESSENCE will prove to be a landmark in the development of new approaches to screening and intervention for children and adults affected by neurodevelopmental disorders. ESSENCE affect about one in ten individuals across the planet, and we are dealing with a huge public health problem. ESSENCE, from now on, must be given highest priority both in clinical research and practice.

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*Elisabeth Fernell*
*Helen Minnis*

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*Research Article*

# Autism in Preschoolers: Does Individual Clinician's First Visit Diagnosis Agree with Final Comprehensive Diagnosis?

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Comprehensive clinical diagnosis based on all available information is considered the "gold standard" in autism spectrum disorders (ASD). We examined agreement across independent assessments (clinical judgment) of 34 young children (age 24–46 months) with suspected ASD, assessed by a multidisciplinary team, and final comprehensive clinical diagnosis. Agreement across settings and between each clinician's assessment and final diagnosis was moderate. The poorest fit was found at assessment in connection with psychological evaluation and the best with preschool observation and parent interview. Some individual clinicians had good and others had poor fit with final diagnosis. Disagreement across assessments was pronounced for girls. The findings suggest that multidisciplinary assessments remain important and that comprehensive clinical diagnosis should still be regarded as the gold standard in ASD.

## 1. Introduction

In an international perspective, there is now a strong focus on autism spectrum disorders (ASD) and the importance of its early diagnosis in toddlers and preschool children. Early identification of problems and early intervention are important for the child's positive development [1, 2]. ASD is usually congenital and involves early childhood symptomatic restrictions in reciprocal social communication and stereotyped behaviors [3]. It occurs at different levels of general intelligence, with a prevalence of about one percent of the general population, about 0,8% in preschool children [4], and a much raised male : female ratio [5–7]. In a newly published Swedish study [8], preschool girls and boys were recruited through population screening, assessed for suspected ASD, and matched by chronological and developmental age. No significant differences were found in their developmental profiles, a result contrary to earlier studies [9]. Therefore, there is still a need for further research in gender differences in ASD, to develop diagnostic instruments that are appropriate for both girls and boys.

The definitions for diagnosis in the field of ASD—or Pervasive Developmental Disorders (PDD) as they are referred to in most diagnostic manuals—are currently based on the International Classification of Diseases, Tenth Revision (ICD-10) [10] or the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) [11]. The DSM-5 (http://www.dsm5.org) introduces the concept of an autism "spectrum", and this is the first time that what was previously considered a distinct diagnostic *category* will be referred to as *a spectrum of disorders*. Clinical judgment by experienced clinicians is seen as crucial in the diagnostic process and considered the gold standard for diagnosis [12]. Diagnosing young children is often a complex process, and the early identification of core symptoms is very important. Clinicians need to have good knowledge regarding common developmental disorders and medical/psychiatric conditions in young children and of normal "age-typical" child development [3, 6, 13]. Symptoms of ASD in 2-year-old children may differ (even markedly) from symptoms identified at the age of 4 or 5 years. For instance, in a 2-year-old, particular types of repetitive and stereotyped behaviors and interests may be less obvious than a few years later, whereas other behaviors and interests

may show the opposite trajectory. Even if standardized assessments are very important, clinical experience/judgment is suggested to be more reliable regarding young preschool children [14].

There is a high degree of phenotypical variation in ASD, and no single instrument or algorithm, for example, Diagnostic Interview for Social and COmmunication disorders (DISCO) [15] or Autism Diagnostic Observation Schedule (ADOS) [16], can be used to "finalize" the diagnosis, particularly since there are many other factors, including chronological age, overall developmental/cognitive level, and "comorbidity," that need to be taken into account [17].

Certain difficulties, including problems pertaining to joint attention, have been suggested to be strong predictors of ASD. However, there are many children with ASD who do not fail to respond to joint attention and even those who do appear to initiate it [18]. This means that joint attention tests in themselves cannot be used as "diagnostic arbiters" for ASD. In order to collect even the minimum (=sufficient) amount of information about the child, needed to arrive at an appropriate clinical diagnosis, multidisciplinary diagnostic assessments can be very important. Interviews with parents or other caregivers and free-field structured observation of the child in social settings, in addition to formal test instruments, are suggested to be very important in the diagnostic process, not least in young children. It is also generally agreed that clinical assessments for ASD should be done by clinicians with extensive experience [17].

ASD is one of the diagnostic categories subsumed under the umbrella concept of Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations (ESSENCE). ESSENCE refers to developmental problems, presenting as "syndromes" in clinical settings before 5(-6) years of age [6]. Symptoms are classifiable as stemming from problems in terms of (a) general development, (b) communication-language, (c) social inter-relatedness, (d) motor coordination, (e) attention, (f) activity, (g) "general" behavior; (h) mood, and/or (i) sleep. If problems in one of these fields have been identified, it has become commonplace to refer the child to a specialist within a specific field, when in reality the child would have required a more multidisciplinary approach to assessment and intervention. If the child shows major problems in at least one of the problems listed before 5(-6) years of age, there is a high risk of major problems in the same or overlapping area several years later. Often, these "overlapping" problems nowadays go unnoticed, undiagnosed, and untreated for years. However, evidence exists to indicate that, whenever a diagnosis of ASD is made, there is a need to also be on the look-out for attention-deficit/hyperactivity disorder (ADHD), tic disorders, intellectual developmental disorder (IDD) [19], speech and language disorder, epilepsy and other "medical disorders," and so forth, at the same time [6, 20]. There is no good reason to wait for the identification of the whole range of non-ASD problems that exist in virtually all young children with ASD at the earliest possible age.

All of this would suggest an even stronger rationale for a multidisciplinary assessment in all children suspected of suffering from ASD at a young age. Conversely, however, due to the high prevalence of suspected ASD (about one percent of the general population of toddlers), there is a need to find out which "autism specific" assessments carry the highest potential of predicting the "true positive" gold standard clinical ASD caseness; is it the doctor's medical examination, the psychologist's testing, the autism observation assessment at the clinic, the detailed parent diagnostic interview, or free-field observation in the child's preschool? Or are we still in need for multidisciplinary assessment?

Taking these partly opposing needs (multidisciplinary versus focused "lean") into account, we designed a study of ASD in preschoolers, nested in the context of an ASD general population cohort, looking at agreement across a variety of separate autism focused assessments and the ability of each of these to predict final conjoint comprehensive clinical ASD diagnosis.

*1.1. Aim of the Study.* The aims of the present study were to evaluate (1) the agreement between different, independent, expert clinicians' first clinical impression of young children with suspected ASD and (2) the agreement between their assessment and the final clinical comprehensive ASD diagnosis. We argued that getting a handle on these issues would have the potential of providing guidance regarding the extent of assessment needed in young children with suspected ASD, and of the status of clinical global impressions vis-à-vis certain formal tests.

## 2. Methods

This is a substudy of the larger general population AUtism Detection and Intervention in Early life project (AUDIE), at the Child Neuropsychiatry Clinic (CNC), a study performed in collaboration with Child Health Care Services and Autism Habilitation Centres in Gothenburg [7]. The overall aim of the AUDIE project is to (a) identify all 0–3-year-old children with symptoms of ASD and other developmental disorders in the general population, (b) provide comprehensive clinical assessment and diagnosis without delay, and (c) offer early intervention without delay. All Gothenburg children are screened for language/communication problems and ASD by specially trained well-baby nurses in well-baby clinics at 2.5 years of age and earlier. All children screening positive at 2.5 years or raising suspicion of ASD at any other age below 4 years are referred for ASD in-depth assessments to the CNC. All cases diagnosed with ASD are then referred to the Autism Habilitation Centers for intervention.

*2.1. Participants.* Thirty-four children (6 girls, 28 boys), with an age range of 24–46 months (mean age 34 months, mean Griffiths' developmental quotient (DQ) 82, range 33–128), participated in the study. They had all screened positive for ASD and had been referred for suspected ASD to the CNC, where they underwent comprehensive neuropsychiatric assessment, comprising six different assessment settings (and 12 different assessors representing four different types of profession; see below). All 34 children were seen during a limited time period. Forty-two children had originally been targeted, but eight had to be excluded because data from three

or more of the six assessments were missing. No divisions by ethnicity or socioeconomic status were made in this study.

### 2.2. Assessments and Test Instruments Used

*2.2.1. Medical-Psychiatric Neurological Examination by Physician.* One of four physicians met the child and the parents at the CNC, observing and interacting with the child in the room and obtaining a medical/developmental/psychiatric history from one or both parents. A neurological examination/brief neuropsychiatric observation assessment of the child was also made. This examination took about 1.5 hour.

*2.2.2. Griffiths' Developmental Scales Assessment by Psychologist.* One of four psychologists administered the Griffiths' developmental scales I and II [21] which measure the rate of development for children from birth to eight years of age. It consists of six subscales: (a) gross motor; (b) personal-social; (c) hearing-speech; (d) eye-hand coordination; (e) performance and (f) practical reasoning. The combined result of the subscales provides a developmental quotient (DQ). The test took about 45–60 minutes to be completed.

*2.2.3. Language Assessment by Speech and Language Pathologist.* One of two speech and language pathologists (SLP) performed the language assessment. Language comprehension was tested with the Reynell Developmental Language Scales III (RDLS) [22], where the Swedish version has norms for 2.0–4.11-year-old [23]. The RDLS contains 62 test items, sorted into 10 different domains, from comprehension of single words to sentences of increasing complexity/difficulty. Expressive language was measured, whenever possible, with formal language tests, and spontaneous speech was transcribed. The SLP assessment took about one hour to be completed.

*2.2.4. DISCO by Physician or Psychologist.* One physician or one of two psychologists made a parent interview, using the Diagnostic Interview for Social and COmmunication disorders (DISCO) [15], which is a semistructured interview, designed for eliciting systematic information regarding development and behaviors from the start of life until current time, so as to allow well-founded classification of ASD in accordance with a variety of diagnostic systems [24]. In our study at least one of the child's parents participated in the interview. It took 2–4 hours to be completed.

*2.2.5. ADOS Assessment by Education Specialist and Psychologist.* One of two education specialists plus one of four psychologists administered the Autism Diagnostic Observation Schedule (ADOS) [16]. The ADOS is a standardized, semistructured play-based assessment of communication, reciprocal social interaction, play, and behavior. There are four modules, based on expressive language level. One test manager interacted with the child, and one other professional observed the child during the test. Immediately after the ADOS, both professionals jointly scored the child's performance according to the manual, which has an algorithm for ASD diagnosis cutoff. The ADOS took about 40–50 minutes of the child's time to be performed.

*2.2.6. Preschool Observation/Observation at Home by Education Specialist.* One of two education specialists from the assessment team observed the child in group activities and free play in accordance with a protocol based on the symptom areas covered by the ADOS. The classrooms were designed for typically developing children, and the number of children in the groups ranged 15–30 children. During the observation, the preschool teachers were with the children as they normally would in everyday situations. The observation took about 45–60 minutes to be performed and was followed by an interview with the teachers regarding the child's abilities and behavior in different situations in preschool, meaning that the total time for the education specialist was on average 2 hours. Eight of the children in the study did not attend a preschool, so the education specialist observed the child in the home for about one hour, with one or more family members around.

*2.3. Diagnostic Process.* In addition to the above-described instruments, the Vineland Adaptive Behavior Scales [25] (performed by the psychologist) and the CGAS [26] (jointly made by the assessment team) were used in the diagnostic process in all cases. However, these two instruments were not included in this study and were made *after* the individual clinician's first clinical assessments had been documented.

To avoid bias, all six assessments were performed by the different professionals working independently of each other, and this required specific logistics. Under "ordinary" clinical diagnostic conditions, the same professional might well perform both a preschool observation and the ADOS at the clinic, meaning that fewer individual members would have to be included in the assessment team. Here, we had to involve several different clinicians, in order to guarantee blindness across different assessment ratings. The results from each of the six assessments were included on the basis of assigning a final comprehensive conjoint clinical diagnosis. The clinicians remained blind to all other assessment results until the consensus diagnostic case conference, which was held after the completion of all assessments as listed, approximately 4–6 weeks after the first assessment. On the basis of all available information, the assessment team made consensus clinical diagnoses according to the DSM-IV criteria for disorders first evident in childhood or adolescence and CGAS ratings.

The number of clinical examiners involved in the study was four psychologists, four physicians, two SLPs, and two education specialists. All clinicians except for one had worked in the field >10 years.

*2.4. Procedure.* In order to avoid bias, different examiners performed all the assessments independently of each other and were blind to any other prior information obtained by other clinicians. The examiner knew only the child's name, age, and gender and the fact that the child had screened positive for ASD at a well-baby clinic check-up. Prior to

start of the data collection, the examiners were given oral and written instructions. A separate coding sheet for each examiner's independent assessment of ASD [(1) ASD; (2) ASD probable or possible; or (3) no ASD] was completed at the end of the child's first visit to that examiner. On the coding sheet, there was also a box for notes regarding any other comments the examiner might want to make about the child's problem. The completion of the coding sheet was done before any summaries of formal assessments were made, such as before scoring the ADOS, the DISCO, or Griffiths'. The coding sheet was then put in an envelope, sealed, stored, and opened only after the full diagnostic process had been completed. In addition, the clinicians were instructed not to reveal any information about their stored clinical impression to anybody else (including child, parent, teacher, or any other clinician).

*2.5. Statistical Methods.* Sensitivity and specificity with 95% confidence interval were analyzed for each individual rater with final clinical diagnosis as the golden standard. Agreement across individual assessors and final clinical diagnosis was analyzed by percent agreement and the weighted kappa statistic with 95% confidence interval. Systematic differences across assessors and clinical diagnoses were analyzed using sign test. All significance tests were two-sided and conducted at the 0.05 significance level.

*2.6. Ethics.* This study was approved by the Human Ethics Committee of the Medical Faculty at the University of Gothenburg, Sweden. Informed consent was obtained from at least one of the parents/responsible carers for each patient.

## 3. Results

Twenty-five of the children were clinically comprehensively diagnosed with ASD (16 autistic disorder, 9 pervasive developmental disorder not otherwise specified (PDDNOS)/ atypical autism). Five children had autistic traits (1–4 symptoms of DSM-IV autistic disorder), and 4 children had no ASD/no autistic traits.

*3.1. Assessment Setting: ASD Codes versus Final ASD/No ASD Diagnosis.* The main results are presented in Table 1. The sensitivity versus final clinical diagnosis was the highest for DISCO (0.74), lowest for DQ (0.40) and all other assessments between 0.60 to 0.86. The specificity was much higher, over 0.89 for all raters except for language. Corresponding 95% confidence intervals were rather wide due to the small number of subjects. The DQ assessment setting (Griffiths' testing) yielded the poorest agreement (47%), weighted kappa 0.28 with comprehensive clinical diagnosis, and also showed systematically less ASD than the clinical diagnosis ($P = 0.007$). For all other assessments the percent agreement was between 58% and 68% and weighted kappa between 0.33 and 0.43.

The DQ assessors "underestimated" almost half (44%) of the children in terms of diagnostic "level" in relation to clinical diagnosis (final clinical diagnosis showed more ASD), whereas the parent interviewers (DISCO) "underestimated" a much smaller proportion (22%) in this respect. In contrast, the DQ assessors "overestimated" only 9% and the parent interviewers 19%.

The number of girls in the study was low, and gender differences were not statistically analyzed due to this. Nevertheless, we consider it to be of interest that the DQ assessors failed to agree with the final clinical diagnosis in all six girls participating in the study. The ADOS assessors agreed in 1/6 (17%), the SLP in 2/5 (40%), the child psychiatrist/neurologist in 3/6 (50%), the educator specialist in 4/6 (67%), and the parent interviewer (DISCO) in 3/4 (75%). All the girls were clinically comprehensively diagnosed with ASD.

*3.2. Individual Assessors' Codes versus Final ASD/No ASD Diagnosis.* We found a very considerable degree of variability as regards agreement between individual assessor diagnostic codes and final diagnosis, both between and within different professional categories (Table 2). Of the 12 clinical assessors who had assessed five or more children, two of them had more than 80% agreement with final diagnosis and five had less than 50% agreement.

In addition, we found that the algorithm diagnosis in the ADOS differed from the consensus clinical diagnosis in 7/34 cases (4/7 "less ASD," 3/7 "more ASD"). For the DISCO it differed in 8/34 cases (1/8 "less ASD," 7/8 "more ASD").

## 4. Discussion

This study found only moderate agreement between "blind" clinical assessors' individual preliminary diagnosis and the final comprehensive conjoint clinical diagnosis based on all available evidence elicited at the various clinical evaluations. Also, agreement across types/classes of raters was not perfect. A tendency for "best fit" with final conjoint clinical ("gold standard") was found using assessment made immediately after preschool/home free-field observation of the child, and the poorest was that of assessment of clinical diagnostic status made in connection with highly structured DQ assessment. On the other hand the low reliability obtained in spite of the comprehensive assessment performed, casts doubts on the feasibility and usability of the diagnosis of ASD in toddlers and may indicate the need for a broader diagnosis before the age of 4 (developmental disorder) in agreement with ESSENCE [6]. In doubtful cases that should be confirmed at a later stage.

When interpreting these results, it is important to consider how the environmental assessment conditions vary. The psychologist's primary role was to evaluate the child's developmental level and basic abilities. In order to be able to do this, the assessment situation had to be more structured than everyday situations, meaning fewer items of distraction, fewer people in the room, and so forth. The SLP assessment setting was similar in this respect, but the focus here was on the child's language and communication, which is one of the main problems in a child with ASD and therefore may be somewhat easier to uncover by language assessment rather than by general developmental assessment. The ADOS and

Table 1: Sensitivity, specificity, and agreement of measurements between assessments and clinical diagnosis (all subjects).

| Assessment | Sensitivity ASD clinical diagnosis (95% CI) | Specificity ASD clinical diagnosis (95% CI) | Weighted kappa (95% CI) | *n* (%) agreement | Clinical diagnosis more ASD | Clinical diagnosis less ASD | *P* value systematic changes between raters and clinical diagnosis |
|---|---|---|---|---|---|---|---|
| Medical/neurologic-psychiatric | 0.64 (0.43; 0.82) | 0.89 (0.52; 1.00) | 0.40 (0.17–0.64) | 21 (62%) | 9 (26%) | 4 (12%) | 0.2668 |
| DQ | 0.40 (0.21; 0.61) | 1.00 (0.66; 1.00) | 0.28 (0.09–0.47) | 16 (47%) | 15 (44%) | 3 (9%) | 0.0075 |
| Language | 0.63 (0.41; 0.81) | 0.78 (0.40; 0.97) | 0.33 (0.08–0.59) | 19 (58%) | 9 (27%) | 5 (15%) | 0.4240 |
| DISCO (parent interview) | 0.74 (0.52; 0.90) | 0.89 (0.52; 1.00) | 0.40 (0.20–0.59) | 20 (63 %) | 7 (22%) | 5 (16%) | 0.7744 |
| ADOS | 0.60 (0.39; 0.79) | 1.00 (0.66; 1.00) | 0.43 (0.21–0.64) | 21 (62%) | 10 (29%) | 3 (9%) | 0.0923 |
| Preschool/home | 0.68 (0.46; 0.85) | 0.89 (0.52; 1.00) | 0.44 (0.18–0.69) | 23 (68%) | 8 (24%) | 3 (9%) | 0.2266 |

The sensitivity and specificity are calculated on the dichotomous variables ASD/no ASD, where "no ASD" also contains the classification "probably/possible ASD." Weighted kappa, % agreement, clinical diagnosis more ASD, clinical diagnosis less ASD, and *P* value are all calculated at the 3-point division; ASD, ASD probable/possible; and no ASD.

Table 2: Individual assessor's agreement with final diagnosis.

| Assessor | Same code as final diagnosis/ number of assessments |
|---|---|
| Medical/neurologic-psychiatric | |
| 1 | 14/20 (70%) |
| 2 | 2/2 (100%) |
| 3 | 1/3 (33%) |
| 4 | 4/9 (44%) |
| DQ | |
| 1 | 2/3 (67%) |
| 2 | 3/9 (33%) |
| 3 | 2/9 (22%) |
| 4 | 9/13 (69%) |
| Language | |
| 1 | 19/31 (61%) |
| 2 | 0/2 (0%) |
| DISCO | |
| 1 | 14/17 (82%) |
| 2 | 2/6 (33%) |
| 3 | 4/9 (44%) |
| ADOS | |
| 1 | 8/15 (53%) |
| 2 | 13/19 (69%) |
| Preschool/home | |
| 1 | 11/19 (58%) |
| 2 | 12/15 (80%) |

One child did not have language evaluation, and 2 did not have the DISCO.

the medical evaluation are more unpredictable for the child, and both may require more flexibility on the part of the child. Given that negative reactions to new events and lack of flexibility are typical of autism, problems in these domains would perhaps be easier to detect than in a more structured environment.

Even though not significantly different in respect of diagnostic validity, preschool/home observation might be seen to be the most "informative" assessment setting of the six examined in this study. This does not mean to say that it is the "optimal" situation for the child, but it does provide the opportunity to see his/her functioning in everyday life. In the "free-field" preschool/home setting, the child's social communication problems become more obvious compared to typically developing peers. A proper assessment in this setting requires, of course, that the assessor has experience and knowledge of typical child development [13]. In Sweden, preschool groups of about 20 children are the rule; in this environment the child is expected to interact with other people, develop in play and everyday skills, and adapt to different routines, all of which tend to be difficult for a child with ASD. Therefore, it is not surprising that it was this kind of assessment that tended to lead to the best agreement with the final clinical diagnosis. In line with our findings, observation of young children in social settings has previously been suggested to be important [17].

The clinical impression and preliminary diagnostic assessment made after DISCO interview with a parent (before scoring for algorithm diagnosis) also corresponded quite well with final diagnosis. In particular "in the hands" of a medical doctor (who was "right" in 82% of the 17 cases she coded) with vast experience in the use of this particular instrument, the DISCO, to a very considerable degree, focuses on the parental experience of the child's functioning in everyday life. This further confirms earlier studies showing that information from parents and other caregivers is important in assessments of young children [17].

Assessment of the child's general development and cognitive ability is considered important in all neuropsychiatric assessments. On the basis of the present results we would argue that, in addition, it is important to observe the child in social, natural settings and that it is not sufficient to evaluate the child only in structured situations at the clinic. A previous study [27] showed high agreement between "textbook" ADOS observation at-the-clinic results and results obtained at preschool observation. When, as in the present

study, clinical judgment is added in, one can speculate that the preschool observation of the child in interaction with his/her peers and the information from the preschool teachers together pick up the symptoms of ASD in a more meaningful way than the ADOS does. Observation of the child in the preschool can also provide information that can form the basis for an educational action plan and specific ASD appropriate interventions. This, of course, does not mean that ADOS is not an important instrument. Furthermore, some children do not attend preschool, or there could be other reasons why preschool observation cannot be made. Further clinical experience suggests that in some cases it may be crucial to include both preschool observation and clinic ADOS testing, for example, when ASD symptoms are less striking or when parents need "hands-on" information from watching the ADOS testing in order to better understand their child's problems.

Despite the very limited number of girls in our study ($n = 6$), we found it to be of some interest that not one of the assessors estimated any of the girls as having greater problems than what the final diagnosis suggested. In addition, the assessment of diagnostic ASD status made immediately after DQ testing did not agree with final clinical diagnosis in any of the cases. If only one or two of the six different assessments had been used for assigning clinical ASD diagnoses, most of the girls in our study would have been "missed." This should be a subject for further research as regards differences between girls and boys with suspected ASD.

It is important to underline that the individual clinical assessment was made at the first meeting with the child. For some of the tests used (e.g., the DQ evaluation) the clinician would see the child more than once, and he/she might later receive additional information that could change the clinical appraisal of the child. We also have to consider that there could be a variation between the assessors with regard to being more or less "careful" to evaluate the degree of problems, when he/she saw the child for the first time. The fact that the children's problems varied with regard to DQ and autism symptoms and were more or less obvious at the first meeting with the child could also have affected the results.

We are aware that there is a problem related to the confounding factor of the final comprehensive diagnosis being formulated on the basis of input from all the clinicians whose individual first impressions were then compared with the final diagnosis. However, none of the individual clinicians had the "final say" in respect of final diagnosis, and it would be clinically—and ethically—difficult, if not impossible, to design a study that would involve a completely independent comprehensive clinical diagnosis based on as many separate pieces of evidence which are needed when making a "comprehensive autism diagnosis based on all available evidence."

We used a rather small sample in our study, which reduces the possibility of generalization of our results to other clinical or community populations of preschool children. We also had a very small number of cases of children diagnosed with "no ASD," limiting the possibility to conclude whether or not we can distinguish cases with milder symptoms of ASD from no ASD. Due to these limitations, it is important to consider the results cautiously and not to make too strong conclusions. However, we believe our findings add to those of earlier studies [12, 14], suggesting the view that clinical judgment is a crucial complement to formal tests. We also believe that it is important to make observations of the child in situations where the child's general behavior is as representative as possible. As emphasized by Huerta and Lord [17], multidisciplinary evaluations are important.

Additional research with larger samples is needed in the field. We also propose that it is important to further examine how gender might possibly be important as a confounder in terms of getting a "correct" ASD diagnosis at young ages if children are assessed for ASD only by one or two examiners, however skilled they might be in diagnosing the disorder. As described in previous studies, stereotyped behaviors and so forth can be more obvious in children older than the participants in the current study [14], meaning that some symptoms might be easier to detect in some ages than in other ages. Multidisciplinary assessment by several team members would seem to be important when aiming to arrive at a valid clinical diagnosis. Interestingly, we found that one in seven to one in eight preschool children with a suspicion of ASD would be "misdiagnosed" if only the ADOS, the DISCO, or both had been used.

Finally, we conclude that clinical ASD experience among assessing clinicians is of utmost importance. Extensive experience and good knowledge of typical development in young children would also be needed.

*4.1. Limitations.* There are some obvious limitations, and, as previously mentioned, these need to be considered when interpreting our results. We had no comparison group, which means that we do not know how the results might have turned out if we included a more "mixed" sample. The sample was small, and, for this reason and because of the limitations previously discussed, the results have to be considered with caution. Also, within the context of the present study we could not perform a specific interrater reliability study across clinicians within the same professional category, for example, between the different education specialists. However, for the education specialists doing observations in preschool we have previously published the results of just such study [27], and we found that percent agreement ranged from 83% to 94% and weighted kappa from 0.82 to 0.93. In spite of these limitations, we do consider the results to be of interest for clinicians aiming to formulate guidelines for the diagnostic process for preschool children suspected of suffering from ASD.

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*Review Article*

# Pain Sensitivity and Observer Perception of Pain in Individuals with Autistic Spectrum Disorder

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The peer-reviewed literature investigating the relationship between pain expression and perception of pain in individuals with ASD is sparse. The aim of the present systematic PRIMSA review was twofold: first, to see what evidence there is for the widely held belief that individuals with ASD are insensitive to pain or have a high pain threshold in the peer-reviewed literature and, second, to examine whether individuals with ASD react or express pain differently. Fifteen studies investigating pain in individuals with ASD were identified. The case studies all reported pain insensitivity in individuals with ASD. However, the majority of the ten experimental studies reviewed indicate that the idea that individuals with ASD are pain insensitive needs to be challenged. The findings also highlight the strong possibility that not all children with ASD express their physical discomfort in the same way as a neurotypical child would (i.e., cry, moan, seek comfort, etc.) which may lead caregivers and the medical profession to interpret this as pain insensitivity or incorrectly lead them to believe that the child is in no pain. These results have important implications for the assessment and management of pain in children with ASD.

## 1. Introduction

Autistic Spectrum Disorder (ASD) describes a range of conditions classified as pervasive developmental disorders (PDDs) in the Diagnostic and Statistical Manual of Mental Disorders (DSM). PDDS include autism, Asperger syndrome, pervasive developmental disorder not otherwise specified (PDD-NOS), childhood disintegrative disorder, and Rett syndrome. However, typically only the first three are considered part of the autism spectrum [1]. ASDs have an onset in early childhood and adverse, often lifelong, effects on communication, socialisation including tendencies toward restricted interests and/or repetitive behaviours [2]. Often associated with these symptoms are sensory-perceptual anomalies which occur in approximately 70% of cases [3]. To determine the prevalence of autism and related disorders, the Centers for Disease Control (CDC) conducted a study examining 8-year-old children living in 14 sites in the United States and found that 1 in 150 children are living with an ASD [4]. Despite the numerous studies attempting to clarify the pathogenesis of ASD, the causes remain uncertain [5].

Individuals with ASD may experience sensory abnormalities related to sight, hearing, touch, smell, and/or taste that include an increased sensitivity to pain. The processing of these types of incoming information might be distorted; rain might sound like gunfire, clothing might feel like sandpaper, or fingers shampooing a scalp might feel like sharp metal [6]. Such unusual responsiveness to the environment has been suggested to be partly due to stimulus overselectivity, the tendency of individuals with ASD to respond only to a very limited amount of the relevant sensory information [7]. Both hyposensitivity and hypersensitivity are exhibited in the same individual [3, 8–10]. Stereotyped and self-injurious behaviours (SIBs) are also exhibited in significant numbers of individuals with ASD [11–15] which has been associated with apparent pain insensitivity [16]. As many as 70% of ASD patients may show self-injurious behaviour at some point in their lives, but this is typically found in more severely affected individuals and takes on many forms including head banging, scratching, bruising, and biting [17]. However, the role of pain in relation to self-injury is unclear [18–22].

Numerous biochemical theories have been put forward to explain the apparent pain insensitivities in individuals with ASD. Certain repetitious activities such as rocking, arm flapping, or pacing produce an increase (or build up) of the level of released endorphins which can lead to a reduction of the sensation of pain, which may explain why children with an ASD who have physical accidents report feeling less pain when the accidents take place later in the day [23]. A number of researchers have also suggested that excessive brain opioid activity could explain the apparent pain insensitivity of ASD and contribute to or even determine the pathogenesis of ASD [24–30]. The opioid hypothesis for ASD postulates that this "hyperfunction of the endogenous opioid system" may actually explain some, if not all, of the symptoms associated with ASD including (1) reduced socialisation (and aloofness), (2) reduced clinging in animals, (3) diminished crying, (4) repetitive stereotyped behaviours, (5) promotion of convulsive activity, (6) insensitivity to pain, (7) episodes of motor hyperactivity alternating with hypoactivity, and (8) affective lability [27].

To date, relatively little research on the sensitivity to painful stimuli, or the expression of pain, in infants, children or adults with ASD has been conducted. Accurate pain assessment, in order to provide appropriate and timely care, can be a challenging task especially in children with ASD [31]. However, pain assessment strategies for children with ASD are poorly understood [32] and relatively little is written about the relationship between pain and ASD in the pain literature [33]. Due to communication and assessment difficulties, there is a greater likelihood that their pain may go unrecognised and untreated (e.g., [34, 35]). Another potential barrier to assessing pain in children with ASD is the prevailing belief, frequently based on anecdotal observation or clinical impression, that pain insensitivity is a common feature in children with ASD (e.g., [2, 36–40]). Parents, caregivers, and mental health professionals have reported that some children with ASD appear to withstand painful stimuli (bumps, cuts, etc.) show absence of nociceptive reflexes (e.g., absence of hand withdrawal reflex when burning oneself), or lack of protective body position in cases of broken legs or arms [41]. However, nearly all of the support for this notion of pain insensitivity is derived from anecdotal reports and limited clinical observations [24–29, 42–44]. Despite the lack of systematic studies of pain sensitivity and reactivity in ASD, the presence of pain insensitivity in ASD has been given further validation because of its inclusion as an associated feature in standard diagnostic texts. In DSM-IV and DSM-IV-TR "a high threshold for pain" is described [2, 45] while in DSM-III the "ignoring of pain" is described (APA, 1987). Not only are children with ASD considered to have "reduced pain sensitivity," but they have also been described as "not feeling pain as intensely as others" [27], having an "indifference to pain" [44] and having a "high threshold for pain" [2]. The belief that children with ASD are insensitive to pain may bias observers' judgements of pain in these children [46].

It is important to understand the behaviours observers can use to assess pain in children and adults with ASD and to understand the potential bias of pain sensitivity information on observers' judgements of pain. Over the last decade there has been a plethora of studies investigating pain expression and perception in individuals with intellectual disabilities or individuals with developmental disabilities (often the exact diagnostic nature of these groups is not specified) (i.e., [47–50]). By contrast, peer-reviewed literature investigating the relationship between pain expression and perception of pain in individuals with ASD is sparse. Research on pain in children with developmental disabilities has almost exclusively relied on observational or behavioural assessment measures [51, 52]. The present systematic review was carried out using PRISMA guidelines [53] to primarily identify and examine the evidence for the widely held belief that individuals with ASD are insensitive to pain or have a high pain threshold. Additionally, this review will examine whether individuals with ASD react or express pain differently.

## 2. Method

Internet-based bibliographic databases (PsycINFO and PubMed) were searched to access studies which examined pain in individuals with ASD only (authors reported no comorbidity in their sample). Studies which investigated pain in individuals with ASD who also had another disorder, such as mental retardation, were not included because the present review was specifically interested in the impact *pure* ASD has on pain sensitivity and expression of pain. Studies which investigated pain in individuals with ASD on a psychological/behavioural level were included. Numerous studies were excluded as they explored more medical issues related to ASD such as gastrointestinal symptoms (i.e., bowel inflammation and alterations in intestinal microflora).

It is commonly reported in the literature that sensory disturbances can feel painful to individuals with ASD. For instance, rain might sound like gunfire and the individual finds this so painful that they have to cover their ears. However, studies which discussed these types of painful experiences were not included as the present review is interested in what is considered to be well-known painful events to the majority of individuals, such as needles in the skin and high and cold temperature. The process of eliminating nonrelevant papers can be seen in the flowchart (following PRISMA guidelines, [53]) (Please see Figure 1 for the Flowchart). Duplicates were excluded prior to the retrieval of references. Searches on the two databases were originally conducted on October, 18, 2012 and updated on February, 6, 2013. The following search criteria were entered into PubMed: ["pain" (title/abstract) AND "autis∗" (title/abstract)] which returned a total of 126 references. The following search criteria were entered into PsycINFO: ["pain" (all text) AND "autis∗"] which returned a total of 148 references. Combining the abstracts returned on these two databases, there was a total of 274 abstracts. In addition to these database searches, numerous permutations of ASD and pain were entered into Google Scholar and thoroughly searched for any additional articles not found in the database searches. For instance, [Asperger AND pain]; [autism AND pain]; [ASD and pain]. These searches only returned one additional article which was an abstract of a pilot study (the findings of which have not

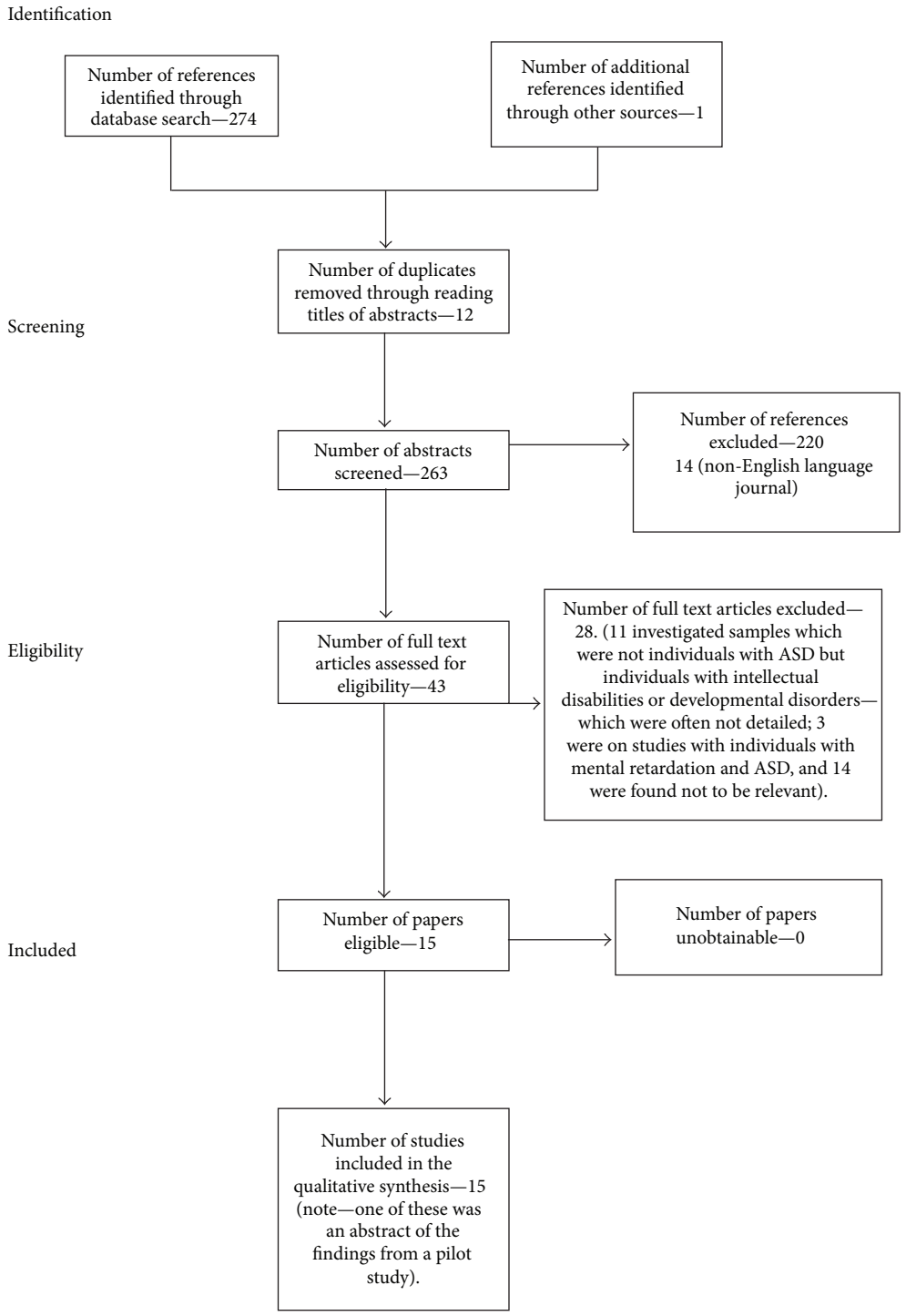


Figure 1: Flow of information through Systematic Review.

since been published in a peer-reviewed article to the authors knowledge).

Abstracts for each reference were obtained and screened using the following criteria.

*Inclusion Criteria*

(1) Human study population.

(2) Investigated psychological/behavioural pain response in individuals with ASD.

*Exclusion Criteria*

(1) Paper not published in English.

(2) Dissertations.

(3) Book reviews.

(4) Studies which investigated a sample that comprised of individuals with a disorder other than ASD (for instance, developmental disabilities or intellectual disabilities) or ASD with a comorbidity (i.e., ASD and mental retardation) were excluded.

*Screening*. In the first stage, papers were rejected which

(i) investigated medical issues (such as intestinal inflammation) or clinical psychopharmacology aspects of ASD,

(ii) were not published in the English language.

For the next stage, papers were rejected which were not studies that involved a sample of individuals with ASD.

In addition, review papers and book chapters which were clearly reviews were excluded. Full documents were obtained for the remaining records.

## 3. Results

Five case studies and ten experimental studies were found in the PRISMA search that investigated some aspect of pain in individuals with ASD.

*3.1. Case Studies.* Table 1 details the five case report studies which explored pain perception, expression, or observer perception of pain in individuals with ASD.

Pain experts might be underrecognising signs and symptoms of ASD in their patients, a notion which led Bursch et al. [33] to explore this in two patients (Tony and Gregg) who displayed signs and symptoms indicative of possible ASD. Tony's mother reported a possible sensory disturbance in early childhood in that he liked to belt his trousers extremely tightly, which most children would have found painful, but Tony liked the sensation. His mother reported that he once grabbed a hot frying pan and did not seem to respond in a way typical of someone in pain. Despite both adolescents showing obvious signs and symptoms indicative of an ASD, review of previous medical records and parental interviews suggested that health care professionals did not identify the need for evaluation of these unusual characteristics. This is clinically useful to recognise because any type of pain might be exacerbated by sensory processing abnormalities and/or persistent arousal that often characterise patients with ASD [54, 55].

Elwin et al.[56] reviewed 17 works published in English or Swedish and 10 autobiographies to explore hyper- and hyposensitivity in individuals with ASD in the context of verbal expression. The autobiographies were written by individuals who all had an ASD diagnosis. The authors found much evidence to suggest pain insensitivity (hyposensitivity) in individuals with ASD in that pain could be indistinctly experienced. Several authors indicated that they had a very high pain threshold. For instance, one individual reported "Injuries could easily go undetected. In there, I was given a punch in the stomach, every day, though usually only one. Perhaps I was not much fun to hit because I had a very high pain threshold, and even when I did hurt I never showed what I felt. I did not know that was what you should do" [57, page 92]. They also found evidence of pain sensitivity (hypersensitivity). However, for the purposes of the present review we have excluded this as from the descriptions given in the paper by Elwin et al. [56], this was pain which was experienced as a result of sensory abonormalities not specifically related to what would typically be defined as a painful event (such as bodily injury or needle injection). They reported cases where the individual reported feeling excruciating pain racking through her head in response to a fog horn.

Rutherford [58] described the development of an infant (N.F.) who was later diagnosed with ASD in direct comparison to the development of his twin, from the prenatal period to the age of four years, through the examination of personal journals and medical records kept by the mother of the twins. Several differences in development between the twins, some as early as six months of age, were found and of particular interest was the observation that N.F. frequently showed insensitivity to pain which was exhibited as early as six months of age. Differences reemerged by the age of four years, at which point N.F. would wake up frequently during the night, sometimes as many as nine times. He would cry and yell during these times and his mother thought that he appeared to be in extreme pain.

Autoextraction of teeth (self-extraction of a tooth) is an unusual form of self-injurious behaviour (SIB) and is rarely seen in children with ASD. Ross-Russell and Sloan [17] present the case of a seven-year-old boy with mild ASD who experienced unexplained dental pain and subsequently went on to extract his own lower right deciduous canine tooth. He has also demonstrated SIB in the form of head banging. He was brought to the clinic complaining of pain of about one week's duration that was increasing in intensity, was present most of the time, and was not sensitive to hot, cold, or sweet stimulus. Within 24 hours the patient was again back at the clinic as the pain had not resolved with ibuprofen and by this time his lower right deciduous canine was very slightly mobile. The tooth had normal root anatomy and no evidence of alveolar bone loss was evident but by the next day the patient had extracted his lower right deciduous canine tooth, which was witnessed by his mother. He claimed it had been "itching" him until he got it out. This case indicates that the patient was insensitive to pain to some degree.

Mieres et al. [32] describe how a nurse and a physical therapist in an interprofessional (IP) school-based clinic worked together to meet the needs of a nine-year-old child with pervasive developmental disorder, not otherwise specified, with atypical classroom behaviours and declining student performance. The child denied pain of any type, using a 0- to 10-point visual analogue scale. The IP team noted that the student was speaking less to other students, faculty, and staff. Although such behaviour could be a sign of withdrawal, it may also be a sign of oral problems. As five weeks had passed without any change in the student's demeanor, the child was referred to a dentist who discovered a severe abscess affecting two teeth. The dentist reported that an abscess of this size without pain is unusual, given the size, the depth, and the

Table 1: Case report studies which explored pain perception, expression, or observer perception of pain in individuals with ASD.

| Author | Samples | Level of functioning of ASD sample | Aim of the study | Findings |
|---|---|---|---|---|
| Bursch et al. [33] | 2 patients with the signs and symptoms of ASD. | Does not specify. | Case report of 2 patients and their sensory abnormalities and pain perception as observed by family. | Reported evidence of lack of pain sensitivity in both patients. That is, "...once grabbed a hot frying pan and did not seem to respond in a way typical of someone in pain." |
| Elwin et al. [56] | 17 works published in English or Swedish and 10 autobiographies. | Does not specify for individuals. | To explore hyper- and hypo-sensitivity in individuals with ASD in the context of verbal expression. Using samples of published autobiographies as a data source. | Yes, self-reported pain insensitivity.<br><br>Pain could be indistinctly experienced, and several authors pointed out having a very high pain threshold. Injuries could easily go undetected. |
| Mieres et al. [32] | 9 year old with pervasive developmental disorder, not otherwise specified. | Does not specify. | To describe how a nurse and a physical therapist in an interprofessional (IP) school-based clinic collaborated to meet the needs of a child with PDD-NOS, with atypical classroom behaviours and declining student performance. | Yes: parental report of pain insensitivity. For this student, pain was an unreliable indicator of both a dental infection and piercing of skin by thorny objects. Child was referred to a dentist who discovered a severe abscess affecting two teeth. The dentist reported that an abscess of this size without pain is unusual, given the size, the depth, and the proximity to bone. |
| Ross-Russell and Sloan [17] | 7-year-old boy. | Mild ASD. | Report of a case of a young child with mild ASD who presented with unexplained dental pain and who subsequently went on to extract his own lower right deciduous canine tooth. | Yes, suggestion that this patient had pain insensitivity.<br><br>"He has also demonstrated SIB in the form of head banging. He was brought to the clinic complaining of pain of about one week's duration that was increasing in intensity which was present most of the time and was not sensitive to hot, cold or sweet stimulus. Within 24 hours the patient was again back at the clinic, as the pain had not resolved with ibuprofen, and by this time his lower right deciduous canine was very slightly mobile. No evidence of alveolar bone loss and the tooth had normal root anatomy. By the next day the patient had extracted his lower right deciduous canine tooth, witnessed by his mother. He claimed it had been 'itching' him until he got it out." |
| Rutherford [58] | Twins: boy who was diagnosed with ASD at 3 years and 1 month, and a girl who developed typically. | Does not specify. | Describes the development of an infant who was later diagnosed with ASD. Directly compares his development to that of his twin from a prenatal period through to the age of 4 years. Explored through examination of personal journals and medical records kept by the mother. | Yes: evidence of pain insensitivity—maternal observations.<br><br>N.F. frequently showed insensitivity to pain which was exhibited as early as 6 to 12 months of age. |

proximity to bone. The abscess required two 10-day rounds of antibiotics until the infection was completely remedied. Two months later, the same student arrived in the clinic and stated that he was "not able to concentrate and the noise was bothering him." Again, the student denied pain, using a 0- to 10-point pain scale, both verbal and pictorial. When given the same scale of 0 to 10 and instead asked, "How uncomfortable are you?" the student stated about a 7. Multiple superficial cuts and lacerations, some covered with bandaids, were seen bilaterally. When the mother was called from the clinic, she stated that over the weekend the student played in the sand dunes without shoes. She further stated that the other children playing with him left quickly after complaints of painful pinching in their legs and feet. The student continued to play in the dunes without any sign of discomfort and could not understand why the other children were complaining. Later, the mother discovered bleeding cuts on his feet and he was taken to a 24-hour clinic, where the physician removed 14 sand spurs. The student helped in the removal of the sand spurs without complaints of pain even when extractions were deep. However, the following morning, he complained of excessive noise, did not wish to be touched, and covered his head. The student stated at first that he had a 0 in a pain scale of 0 to 10. However, when asked, "How uncomfortable are you?" the student indicated a 7. For this student, pain was an unreliable indicator of both a dental infection and piercing of skin by thorny objects, preventing timely treatment.

In sum, the five reported case studies all seem to provide some support to the widely held belief that individuals with ASD are insensitive to pain or have a high pain threshold.

*3.2. Experimental Studies.* Table 2 details the experimental studies which explored pain perception, expression, or observer perception of pain in individuals with ASD. There were ten experimental studies identified in the search of which one was an abstract presenting the findings from a pilot study. The ten studies are split up into five different sections under the subheadings of "Facial Activity to Pain Stimuli in ASD" (no. 3); "Pain Sensitivity Experienced in ASD" (no. 4); "Embodied Pain in ASD" (no. 1); "Relationship between Opioid Hormone and ASD" (no. 1) and "Oversensitivity to Pain and Age of Diagnosis of ASD" (no. 1).

*3.3. Facial Activity to Pain Stimuli in ASD.* Facial activity has been found to be a major determinant of observers' judgements of pain in infants [59], children [60], and adults with cognitive impairments [61]. The widely held belief that children with ASD are less sensitive to pain compared to neurotypical children may bias observers' interpretation of pain expression/behavioural reactivity in these children. Messmer et al. [46] investigated whether the perceptions of pain in children with ASD could potentially be influenced by the belief that children with ASD are insensitive to pain. Twenty-seven undergraduate psychology students who had no previous experience with children with ASD were recruited at the University of British Columbia. The sample consisted of 23 females and four males, with a mean age of 20.11 years. Nineteen of the participants identified themselves as Caucasian, seven participants identified themselves as Asian, and one identified him/herself as "other." Observers received information that pain experience in children with ASD is either the same as, more intense than, or less intense than children without ASD. After viewing six video clips (which were obtained from a previous study by Nader et al. [62], described below) of children with ASD undergoing venepuncture, observers estimated pain intensity using a visual analogue scale. Venepuncture is a medical procedure which requires the use of a needle to puncture a patient's vein. Puncturing a vein provides direct access that allows for extraction of venous blood or insertion of medication or fluids directly into the blood stream and is the same basic procedure which is used to extract blood for blood donations. The sample of children with ASD used for the current study consisted of four boys and two girls between the age of three and seven. The clips consisted of the 10 seconds immediately preceding the injection and the 10 seconds immediately after needle insertion. Participants were randomly assigned to one of the three groups. Group A consisted of seven participants, and groups B and C consisted of 10 participants. Each group read a two-page booklet with information taken from "Children with Autism: A Parent's Guide Describing Features of Autism" [63]. Within the general account was a description of the pain experience of children with ASD. This description of pain in individuals with ASD was different for each group, saying either (a) "Children with autism appear to respond to pain in the same way that children without autism do"; (b) "Children with autism also appear to respond to pain differently than children without autism. In particular, they feel pain more than other children. This has been termed "pain hypersensitivity" and has recently been documented in research on children with autism"; or (c) "Children with autism also appear to respond to pain differently than children without autism. In particular, they seem to have a high tolerance for pain and do not appear to feel pain as much as other children".

After reading the booklet, participants watched six video clips of children with ASD undergoing venepuncture. The video clips had been previously coded for facial activity using the Child Facial Coding System (Child Facial Action Coding System Revised Manual, CFCS [64]). The CFCS is a facial coding system which was created as a way to assess pain experiences in children. Thirteen explicitly defined facial actions (e.g., brow lower, eye squeeze, and nose wrinkle) are coded, in terms of frequency and intensity, by a trained CFCS coder using stop-frame and slow-motion video editing equipment. After each video clip, participants rated the pain intensity of the child on a visual analogue scale (VAS), a 100 mm horizontal line anchored on the left by "no pain" and on the right by "worst possible pain." Participants placed a mark on the line to indicate how much pain they thought the child was feeling. The VAS is a valid measure for assessing pain intensity [65]. Mean pain intensity scores on the VAS were compared to the average facial pain activity scores from the CFCS. A Spearman rank order correlation suggested that the order of VAS ratings was highly correlated with the order of the CFCS scores ($rs = 0.943$, $P < 0.01$). In sum, the main findings of this study by Messmer et al. [46] were that children who received lower scores on the CFCS were judged

Table 2: Experimental studies which explored pain perception, expression, or caregiver/observer perception of pain in individuals with ASD.

| Author | Samples | Level of functioning of ASD sample | Aim of the study | Findings |
|---|---|---|---|---|
| Bandstra et al. [74] | 20 ASD (17 boys; 3 girls) & 20 TD controls (16 boys; 4 girls). Age range: 8–18 years. | High | Assessing self-report of pain using vignettes and also comparing this to parental reports. | No significant differences in pain intensity ratings between the ASD and controls.<br>No significant differences between the pain ratings of youths with ASD or their parents as compared with a sample of typically developing youths. |
| Cascio et al. [72] | 8 adults with ASD (clinical diagnoses of either Autistic or Asperger Disorder; all had IQ of at least 70 (7 males & 1 female (mean age 29.3 years, range 20–45). 8 adults without ASD (sex and age matched). (mean age 29.0, range 21–45). | High | To investigate tactile sensitivity in adults with autism using a variety of stimuli, in order to probe different submodalities of somatosensation.<br>Experiment specifically related to present review—thermal pain threshold. | Yes, significant difference—ASD group showed a greater degree of pain sensitivity.<br>For cold pain, there was a main effect of site ($F = 5.12$, $P = 0.0250$), and group ($F = 3.84$, $P = 0.0518$), with the ASD group displaying average cold pain thresholds of 16.68°C, compared to the control group average of 9.04°C.<br>For heat pain, there was a significant effect of group. The average threshold for the ASD group was 43.66°C, while that of the control group was 46.58°C. |
| Daughters et al. [79] | 5 children with a documented ASD (between the age 7–11 years). | Does not specify. | A pilot study to investigate pain and distress in children with autism during a dental cleaning procedure. | Children with ASD exhibited greater pain scores (M = 29.8) than children without ASD (M = 10.0). Greater levels of interfering distress behaviour were exhibited in the children with ASD. Moderate associations between severity of ASD symptoms and pain during the dental cleaning procedure ($r = .55$) and interfering distress behaviours ($r = .43$), with increased severity of the child's symptoms relating to higher levels of pain and distress. |
| Klintwall et al. [70] | Population-based group of 208 20–54-month-old children, diagnosed with ASD and referred to a specialised habilitation centre for early intervention. Children were sub-grouped (8 in total) based upon degree of ASD symptoms & cognitive level. | Subgroups (i.e., classic autism, nuclear autism)—but does not specify low or high functioning. | To describe sensory abnormalities in preschool children with an ASD, compared to different subgroups within the autism spectrum in terms of the presence of sensory abnormalities, and relate the findings to other clinically relevant symptom domains. | Yes: significant differences in pain sensitivity.<br>Under-reactivity to pain in 40% of the sample.<br>Under-reactivity to cold and heat were reported for 22% and 7%, respectively.<br>Children with self-injurious behaviours had more sensory abnormalities affected (M = 2.0, SD = 1.5, $n = 61$) than children with no such behaviours (M = 1.3, SD = 1.2, $n = 147$); $t(206) = 2.791$, $P = 0.006$. |
| Mandell et al. [89] | Survey data were collected in Pennsylvania from 969 caregivers of children who had ASD and were younger than 21 years regarding their service experiences. | Does not specify low or high functioning in terms of DSM and so forth. | Early diagnosis of children with ASD is critical but often delayed until school age. This study attempted to identify these factors among a community sample of children with ASD. | Oversensitivity to pain was associated with a 0.6-year increase in the age of diagnosis. |

Table 2: Continued.

| Author | Samples | Level of functioning of ASD sample | Aim of the study | Findings |
|---|---|---|---|---|
| Messmer et al. [46] | 6 ASD individuals (4 boys and 2 girls between 3 and 7 years). | Video clips of children with ASD undergoing venepuncture were obtained from a previous study [62]; see below for details. | To examine the influence of information about the pain experience of children with autism on observers' judgement of pain intensity in children with ASD and to examine the impact of facial activity on observers' judgement of pain intensity in children with ASD. | Facial activity had a significant impact on observers' estimates of pain intensity while pain sensitivity information did not. |
| Minio-Paluello et al. [85] | 16 right-handed men with ASD (aged 28.0 ± 7.2 years) and 20 neurotypical controls (aged 25.3 ± 6.7 years) age, sex, and IQ matched. | Mention levels of severity in terms of score on the AQ. | To explore whether people with AS differ from neurotypical control participants in their empathic corticospinal response to the observation of others' pain and the modulatory role played by phenomenal experience of observed pain and personality traits. | Participants with AS, compared with control participants, tended to judge the touch as more painful ($t = -1.82$, $P = 0.08$). |
| Nader et al. [62] | 21 3-year-old to 7-year-old children with ASD and 22 nonimpaired children. | Mean CARS score for the ASD group was 39.10 (SD = 4.98, range 30.5–47), which put the average for the group into the severely autistic range (CARS score >37). 9 fell into the mildly-moderately ASD range (CARS score 30–37), and 12 fell into the severely ASD range. | Aims of the study were to (1) characterise the behavioural response of children with ASD experiencing a venepuncture using objective observational measures of pain and distress, (2) examine parents' assessments of pain behaviour in children with and without autism, including comparison of the relationship of parental reports with behavioural measures, and (3) compare the behavioural reactions and parental assessments of children with ASD with children without ASD undergoing venepuncture. | In contrast with many of the other studies reported in this review, this study found evidence which indicates that individuals with ASD do not have an insensitivity to pain as manifested by a lack of behavioural response—children with ASD display a significant behavioural reaction in response to a painful stimulus.<br>Using FPS scores as a measure of parental assessment of pain response following the venepuncture, parents of children with ASD reported observing more pain in their children during the venepuncture (M = 4.29, SD = 1.45) compared with parents of the children without autism (M = 2.75, SD = 1.90; $t(41) = 2.97$, $P < 0.05$). Using the NCCPC as a retrospective measure of parental assessment of typical pain reactivity in their children, scores did not differ between the autism group (M = 60.33, SD = 13.50) and comparison group (M = 58.41, SD = 14.19; $t(41) = 0.46$, $P > 0.05$).<br>Parent reports of pain temperament in children with ASD (M = 2.72, SD = 1.32) were similar to parent reports of pain temperament in the children without ASD (M = 2.82, SD = 1.30; $t(38) = -0.23$, $P > 0.05$). |
| Nagamitsu et al. [88] | 19 Japanese children (17 boys, 2 girls, mean age 4.23 ± 1.18 years, range 2.00–6.42) with typical infantile autism. 23 controls—age-matched Japanese children (18 boys, 5 girls, mean age 3.78 ± 3.37 years, range 0–10.75). 3 patients with Rett syndrome (3 girls, ages 10–14 years). | Does not specify. | To clarify whether P-endorphin plays an important role in infantile autism, we determined the cerebrospinal fluid (CSF) levels of p-endorphin and evaluated the correlation between these levels and ASD symptoms. | Finding do not support the opioid hypothesis to explain pain sensitivity in ASD.<br>No significant correlation between CSF levels and clinical symptoms, including self-injurious behaviour, pain insensitivity, and stereotyped movement. However, CSF levels of p-endorphin were significantly higher in the patients with Rett syndrome than in the control ($P < 0.05$). Data suggest that neurons containing p-endorphin may not be involved in patients with infantile autism. |

Table 2: Continued.

| Author | Samples | Level of functioning of ASD sample | Aim of the study | Findings |
|---|---|---|---|---|
| Tordjman et al. [41] | 73 children and adolescents with ASD and 115 control matched for age, sex and pubertal stage. (ASD group 49 males and 24 females. ASD group total age 11.7 plus or minus 4.5; comparison group 75 males and 40 females. Total age 12.7 + or −5.9). | Individuals with "severe" ASD ($n = 39$). Individuals with "mild" to "moderate" ASD ($n = 39$). Normal controls ($n = 103$). | To examine behavioural and physiological pain responses, plasma b-endorphin levels, and their relationship in a large group of individuals with ASD. | No: individuals with ASD do not have decreased sensitivity to pain.<br>A high proportion of individuals with ASD displayed absent or reduced behavioural pain reactivity at home (68.6%), at day care (34.2%), and during venepuncture (55.6%). Despite their high rate of absent behavioural pain reactivity during venepuncture (41.3 versus 8.7% of controls, $P < 0.0001$), individuals with ASD displayed a significantly increased heart rate in response to venepuncture ($P < 0.05$) which was significantly greater than for controls (mean 6 SEM; 6.462.5 versus 1.360.8 beats/min, $P < 0.05$). Plasma b-endorphin levels were higher in the ASD group ($P < 0.001$) and were positively associated with ASD severity ($P < 0.001$) and heart rate before or after venepuncture ($P < 0.05$), but not with behavioural pain reactivity. |

Key:
AQ: Autism Spectrum Quotient [90].
CARS: The Childhood Autism Rating Scale [92].
CFS: Cerebralspinal fluid.
CNS: Central Nervous System.
PDD-NOS: Pervasive Developmental Disorder Not-Otherwise Specified.
TD: Typically developing.

to be experiencing a lower intensity of pain and children who received higher scores on the CFCS were judged to be experiencing a higher intensity of pain. Thus, Messmer et al. [46] found that observers' ratings of pain in children with ASD were *not* influenced by information regarding the pain experience in children with ASD and that they were able to use facial activity as one basis for estimating pain in children with ASD. This study also indicates that the children's experience of pain is communicated, at least to some degree, through their facial activity.

Nader et al. [62] conducted a study in order to examine the behavioural response of children with ASD during venepuncture using an objective observational measure of pain and distress. In addition to this objective measure, they also examined parents' assessments of pain behaviour in children with and without ASD, including comparison of the relationship of parental reports with behavioural measures. All of these measures were compared to the same assessment conducted on control children during the same procedure. Nader et al. [62] recorded behavioural distress and facial reactions of pain in 21 three- to seven-year-old children with ASD and 22 nonimpaired children during venepuncture. Parents provided observer reports of pain and facial activity was used as an objective behavioural measure of pain. Detailed coding of videotapes were performed using the Child Facial Coding System [64] (which was the objective measure also used in the study above by Messmer et al. [46]). An objective measure of distress was also used in the present study, namely, the Observational Scale of Behavioral Distress (OSBD). The OSBD [66] is a coding system designed to assess behavioural distress in children undergoing painful medical procedures. OSBD consists of eight operationally defined behaviours indicative of anxiety and/or pain behaviour in children.

Observer reports of pain from the parents were measured using the following two procedures. Histories of pain sensitivity were assessed by asking the parents to report on prior pain reactions of their children using the Non-Communicating Children's Pain Checklist (NCCPC) [67]. Parents were also asked to provide a summary report of their child's pain temperament by responding to the following statement: "My child is very sensitive to pain of bumps or cuts or other common hurts." The parent responded to this question on a scale of 1 = not typical/characteristic to 5 = very typical/characteristic. Lastly, the Faces Pain Scale (FPS; [68]) was given to the parents. This consists of seven faces showing gradual increases in pain expression from left to right (neutral to pain). The parents were asked to select the face that they felt represents the degree of pain experienced by their child during the venepuncture procedure.

Findings from the study by Nadar et al. [62] revealed that the behavioural responses of the children with ASD were overall similar to the comparison group, except the substantial facial pain reactivity instigated by the venepuncture in the children with ASD exceeded that found in the control group. The degree of concordance between parental report and observed pain responses were consistently better for the comparison group. For the ASD group, no significant correlation was observed between the FPS scores provided by the parents and the facial pain responses of the children, $r = -0.154$, $P > 0.05$. Interestingly, children with ASD who had been assessed by their parents as having a lower pain sensitivity and reactivity tended to show greater facial reactions and behavioural distress in response to the venepuncture. Using FPS scores as a measure of parental assessment of pain response following the venepuncture, parents of children with ASD reported observing more pain in their children during the venepuncture ($M = 4.29$, SD = 1.45) compared with parents of the children without ASD ($M = 2.75$, SD = 1.90; $t(41) = 2.97$, $P < 0.05$). Using the NCCPC as a retrospective measure of parental assessment of typical pain reactivity in their children, scores did not differ between the ASD group ($M = 60.33$, SD = 13.50) and comparison group ($M = 58.41$, SD = 14.19; $t(41) = 0.46$, $P > 0.05$). Parent reports of pain temperament in children with ASD ($M = 2.72$, SD = 1.32) were similar to parent reports of pain temperament in the children without ASD ($M = 2.82$, SD = 1.30; $t(38) = -0.23$, $P > 0.05$). In addition, although the ASD severity of the ASD group was well characterised and ranged from mild to severe, there was no information about level of intellectual functioning for this group. Overall, these findings demonstrate that children with ASD can display a significant behavioural reaction in response to a painful stimulus which is in contrast to the widely held belief in the literature that individuals with ASD are insensitive to pain. However, the study also shows that some of the caregivers did not interpret their child's pain expression accurately. Children with ASD, who had been assessed by their parents as having a lower pain sensitivity and reactivity, tended to show greater facial reactions and behavioural distress in response to the venepuncture. However, this is difficult to draw strong conclusions from this since it may be that the event was simply more distressing for the individuals with ASD rather than that they had any greater degree of pain sensitivity.

In another study, Tordjman et al. [41] examined behavioural and physiological pain responses, plasma beta-endorphin levels and their relationship in 73 children and adolescents with autism and 115 normal individuals matched for age, sex, and pubertal stage during blood drawing. Pain reactivity was assessed for patients in three different observational situations. (1) in day care, where two caregivers independently rated overall pain reactivity on a daily basis during the month preceding the blood drawing; (2) at home, where parents rated pain-related behaviour during the same month as the caregivers. In this situation, there were enough daily life situations involving pain to distinguish reactions to a variety of types of noxious and painful stimuli such as being burned, having internal pain (tooth pain, ear infection, headache, etc.), and other accidental painful stimuli (cutting, pinching, banging, etc.); (3) during the blood drawing at a medical centre, when a direct clinical observation was conducted by a nurse and child psychiatrist not belonging to the caregiver team. Normal controls were similarly assessed for pain reactivity to the venepuncture using the Pre-Linguistic Behavioral Pain Reactivity Scale (PL-BPRS) [69]. The scale looks at five different pain scenarios, namely, (1) paradoxical pain reactivity, the apparent pleasure reaction to a painful stimulus (such as smiling or laughing); (2) absence of pain reactivity,

absence of nociceptive reflexes (such as absence of hand withdrawal reflex when burning oneself or absence of arm withdrawal reflex from the needle during a blood drawing); (3) hyporeactivity to pain, incomplete pain reactivity or abnormally delayed reaction time to painful stimulus; (4) normal pain reactivity such as cries, screams, moaning, grimaces, reflexes of nociceptive withdrawal, lack of movement, body orientation, and glance towards the painful area, and lastly, (5) hyperreactivity to pain, disproportionate cries, and screams given the painful stimulus (with hypersensitive light touch). A checklist was used to indicate the presence or absence of SIB, aggressive behaviours directed against others, stereotyped behaviours, and social withdrawal during the blood drawing situation. Physiological measures included plasma b-endorphin levels analysis and a heart rate measurement to examine cardiovascular response to the blood drawing (with a stethoscope placed on the thorax considering that some patients can react negatively when their wrist is touched) immediately before and after the venepuncture (15-second measurement period).

Tordjman et al. [41] found that across the three observational situations, abnormal behavioural responses to painful stimuli were highly prevalent in individuals with ASD of low to moderate functioning. In general, there was a shift to hyporeactive or absent pain reactions in the ASD group. A high proportion of individuals with ASD displayed absent or reduced behavioural pain reactivity at home (68.6%), at day care (34.2%) and during venepuncture (55.6%). Although this pattern of observed behaviour is consistent with a number of previous studies, most prior reports did not distinguish pain reactivity from pain sensitivity. It is critical to keep this distinction in mind and not to conclude that absence of behavioural pain reactivity means absence of pain sensitivity. Despite their high rate of absent behavioural pain reactivity during venepuncture (41.3% versus 8.7% of controls, $P < 0.0001$), individuals with ASD displayed a significantly increased heart rate in response to venepuncture ($P < 0.05$). This response (Delta heart rate) was significantly greater than for controls (mean ± SEM; 6.4 ± 2.5 versus 1.3 ± 0.8 beats/min, $P < 0.05$). This strongly indicates that prior reports of reduced pain sensitivity in ASD are related to a different mode of pain *expression* rather than to an insensitivity or endogenous analgesia. Plasma beta-endorphin levels were higher in the ASD group ($P < 0.001$) and were positively associated with ASD severity ($P < 0.001$) and heart rate before or after venepuncture ($P < 0.05$), but not with behavioural pain reactivity. This is inconsistent with the opioid theory of ASD that would suggest that high levels of plasma beta-endorphin is associated with behavioural pain reactivity. In addition to the physiological response to the venepuncture, behavioural changes following the venepuncture or other painful stimuli occurring at home and day hospital (SIB, aggressive behaviours, stereotyped behaviours, social withdrawal) also suggest that children with ASD perceive pain, but do not express it in the same way that control children do.

The findings by Tordjman et al. [41] also show that a significant proportion of individuals with ASD did not display low/absent overall pain reactivity according to the parental, caregiver, and blood drawing evaluations. In fact, the majority (78%) of individuals with ASD were actually found to exhibit normal behavioural reactivity to burning; highlighting the importance of distinguishing different types of painful stimuli. Lastly, 22% of individuals with ASD displayed normal behavioural pain reactivity to the venepuncture and 15.9% displayed hyperreactivity which is in agreement with Nader et al. [62]. In sum, this study indicates that there may be different subgroups within the ASD population. One subgroup may experience pain insensitivity, another pain sensitivity, and the other normal pain sensitivity. However, there are numerous factors to consider when making such a conclusion at this early stage and this is outlined in the discussion. For instance, this present study found that the majority of individuals with ASD exhibited normal pain reactivity to burning. It may be that individuals with ASD may need to experience a particular high level of pain such as burning before they express normal pain reactivity. However, when the painful event is not so severe some individuals with ASD may have difficulty in expressing the pain.

*3.4. Pain Sensitivity Experienced in ASD.* Klintwall et al. [70] investigated sensory abnormalities in a population-based group of 208 20-54-month-old children, diagnosed with ASD and referred to a specialised habilitation centre for early intervention. Children were subgrouped (eight in total) based upon degree of autistic symptoms and cognitive level by a research team at the centre. Parents were interviewed systematically about any abnormal sensory reactions in the child. In the whole group, pain and hearing were the most commonly affected modalities. An interview according to the PARIS schedule (developed by Gillberg and colleagues within the "Paris Autism Research In Sib-pairs" study, [71]) was performed with one of the parents. This interview included structured questions about the child's sensory reactions to light, sound, smell, and so forth. However, for the purposes of this review their results for underreactivity to pain, underreactivity to heat, and underreactivity to cold are reported. Only clinically significant sensory abnormalities were scored as "present" in the study. Children in the most typical ASD subgroup (nuclear autism with no learning disability) had the highest number of affected modalities. There were no group differences in number of affected sensory modalities between groups of different cognitive levels or level of expressive speech, supporting the notion that sensory abnormality is very common in young children with ASD and providing further justification for inclusion of this symptom in the diagnostic criteria for ASD in the upcoming DSM-V. From the total group of 208 children, at least one type of major sensory abnormality was registered in 158 individuals (76%). The most commonly reported sensory abnormality was overreactivity to sound (44%) and underreactivity to pain (40%). Underreactivity to cold and heat was reported for 22% and 7%, respectively. Interestingly, children with self-injurious behaviours had a greater number of affected sensory abnormalities ($M = 2.0$, SD = 1.5, $n = 61$) compared to children with no such self-injurious behaviours ($M = 1.3$, SD = 1.2, $n = 147$); $t(206) = 2.791$, $P = 0.006$. Therefore, this study provides some support to the widely held belief that many

individuals (40%) with ASD are insensitive (under reactive) to pain.

Cascio et al. [72] recruited eight adults with high-functioning ASD (clinical diagnoses of either Autistic Disorder or Asperger Disorder; DSM-IVTR; [2]); there were seven males and one female (mean age 29.3 years, range 20–45). Eight adults without ASD were recruited from the community, selected to match each individual with autism on age and gender (mean age 29.0 years, range 21–45). Each participant completed a brief questionnaire, the Adult Sensory Profile [73] to determine whether groups differed in terms of their experience with sensory stimuli in everyday life. Cascio et al. [72] compared tactile sensation in adults with ASD compared to controls on two sites of the body: (1) the hairy skin of the right dorsal forearm and (2) the glabrous skin of the right thenar palm. A variety of tactile sensations were investigated. However, for the purposes of this review only those that were pain related are reported here. These were the thermal sensation—cold pain and heat pain. Participants were instructed to respond as soon as the stimulation reached a point of being "painfully or uncomfortably hot (or cold)." In order to alleviate any anxiety about the pain stimuli, participants were reminded that the device was limited to temperatures that are too mild to produce skin damage, and that their response triggered the return of the thermode to its baseline temperature. For cold pain, there was a main effect of site ($F = 5.12$, $P = 0.0250$), and group ($F = 3.84$, $P = 0.0518$), with the ASD group displaying average cold pain thresholds of 16.68°C, compared to the control group average of 9.04°C. For heat pain, there was a significant effect of group ($F = 6.79$, $P < 0.01$), and site ($F = 7.37$, $P = 0.0073$), and a significant group $x$ session interaction ($F = 8.18$, $P = 0.0048$). The average threshold for the ASD group was 43.66°C, while that of the control group was 46.58°C. Overall, the ASD group showed a greater degree of pain sensitivity to thermal pain at both sites recorded in this study as this group's cold and heat pain thresholds were lower compared to the control group.

Bandstra et al. [74] examined self-reported and parent-reported pain in 20 high-functioning youths with ASD (17 boys; 3 girls) and 20 typically developing controls (16 boys; 4 girls) ranging in age from 8 to 18 years and matched on age and IQ. This is the first study to assess the self-report of pain, using vignettes, in high-functioning children and adolescents with ASD. The Charleston Pediatric Pain Pictures (CPPP) are a series of 17 cartoon pictures depicting scenes of medical, play, and home situations [75]. Each drawing has a central figure of a young non-sex-specific child lacking facial expression, who is engaged in an activity. Thirteen of the 17 scenarios depict pain-provoking events and each has a short verbal vignette that describes the event taking place in the picture. One example of the 13 pain scenarios was: "You touched the hot stove and burned your hand. Show me how much hurt you would have". The amount of pain the participants would expect to feel was self-reported using the Faces Pain Scale-Revised (FPS, [76] and a Numeric Rating Scale (NRS) in a series of validated hypothetical pain situations depicted in cartooned images (e.g., scraping knee on pavement). The FPS-R is comprised of 5 line drawings of faces, presented horizontally, representing increasing levels of pain, typically from no pain (0) to extreme pain (10). In addition to the FPS-R, participants and their parents were asked to rate the pain of the hypothetical situations using an NRS. The NRS was provided using a 0 to 5 scale not only to ensure simplicity of the task for children in the study, but also to provide participants with the same number of response options as provided in the FPS-R. So children and adolescents were asked to provide ratings of their hypothetical pain using both the FPS-R and the NRS, whereas parents were asked to only provide ratings of their child's pain using the NRS. Findings revealed no differences between the pain ratings of youths with ASD or their parents as compared with a sample of typically developing youths.

The lack of differences in pain intensity ratings between the ASD and control youths in the study by Bandstra et al. [74] conflicts with other recent findings which showed greater facial and behavioural pain responses during painful medical procedures [41, 62]. Discrepancies between different measures of pain (e.g., behavioural versus self-report measures) are not unusual [77]; therefore it is possible that the self-report data obtained in this study represent a unique perspective on the subjective pain experience for youths with ASD. It is also possible that youths with ASD, although experiencing comparable levels of pain as typically developing children (as evidenced by the current data), express their pain in a more behaviourally and facially reactive manner (as evidenced in prior research). However, despite these issues, Bandstra et al. [74] highlighted the potential confounders that may have been present in the other major studies which did find increased facial pain response to the individuals with ASD. Specifically the study by Nader et al. [62] was confounded by its use of a bundling procedure (wrapping the child in a blanket for the purpose of constricting movement during the procedure) in preparation for the venupuncture procedure for the group of individuals with ASD and not the control group, a difference which could have accounted for the significantly greater pain responses evidenced by the children with ASD as compared with the controls in that study [62]. Also a recent study showing greater behavioural response in children with ASD also found higher levels of a physiological marker for stress in the ASD sample [41]. This indicates the possibility that the increased behavioural reactivity may not be an expression of pain; rather they are distressed at undergoing a medical procedure. Another important factor to consider in trying to understand pain in individuals with ASD is the degree of functioning of this group, which varies across the studies. For instance, Tordjman et al. [41] used a sample of nonverbal and low-functioning individuals with ASD, while Nader et al. [62] omitted any information about the level of functioning in their sample. The study by Bandstra et al. [74], on the other hand, used a high-functioning sample of children and adolescents with ASD. Also, Bandstra et al. [74] investigated pain responses in children aged 8 to 18 years, which represents a significantly older age group than the participants included in the study by Nader et al. [62]), for example, and aspects of the pain experience (e.g., ability to provide self-report) are known to change as typically developing children grow older [78]. Similar to the youth ratings, no differences emerged between the ASD and control groups for

parent ratings of the amount of pain they would expect their children to show. However, this finding does not necessarily mean that youths with ASD express their pain in the same way as typically developing youths. Rather, parents of the children in this group may have grown accustomed to their children's idiosyncratic pain expressions (e.g., angry responses) over time and have learned to interpret their child's cues accurately. Although group averages for parent and child ratings were similar, additional correlations demonstrated a lack of concordance between parent and child dyads which is not a surprising phenomenon in paediatric pain assessment. This finding may even provide further support for the argument that the pattern between parent and child pain ratings is consistent regardless of whether or not the child has ASD. Furthermore, the lack of concordance in ASD is important as it indicates that, as with typically developing children, it is important for clinicians to gather pain intensity ratings from youths with ASD, rather than only relying on parent report.

In their abstract, Daughters et al. [79] report their findings of a pilot study they carried out to examine pain and distress experienced by children with ASD during a dental cleaning procedure. The authors hypothesised that children with ASD would exhibit greater levels of behavioural distress and pain during the dental procedure compared to control children. Five children with a diagnosis of ASD and four control children participated in the study (ages 7–11 years) scheduled for a dental cleaning procedure (without sedation) took part in the pilot study. Prior to the dental cleaning procedure, caregivers were asked to complete a behavioural checklist to identify the severity of the child's stereotyped behaviours, social interaction, and communication difficulties. The dental cleaning procedures were videotaped and were later coded using a variation of the Brief Behavioral Distress Scale (BBDS), an observational measure of children's procedure-related distress. After the dental cleaning procedure, the caregivers were asked to complete the Non-Communicating Children's Pain Checklist-Revised (NCCPC) in order to assess their child's pain. The findings revealed that the mean pain scores during the dental procedure were indicative of pain for both groups. However, the children with ASD exhibited greater pain scores ($M = 29.8$) than children without ASD ($M = 10.0$). Greater levels of interfering distress behaviour were exhibited in the children with ASD compared to children without ASD. There were also moderate associations between severity of ASD symptoms and pain during the dental cleaning procedure ($r = 0.55$) and interfering distress behaviours ($r = 0.43$), with increased severity of the child's symptoms relating to higher levels of pain and distress. In sum, this pilot study indicates that individuals with ASD are more sensitive to pain during dental cleaning procedures.

*3.5. Embodied Pain in ASD.* Observing emotions or bodily sensations in another individual produces brain activations largely overlapping those which are activated during the direct experience of the same feelings. This overlap in activated brain regions between observed and directly experienced emotions or bodily sensations indicates that empathic brain responses may rely on resonant, mirror-like systems [80–82]. The idea that empathy for pain may be mediated by mirror systems emerged with the finding that neurons in the anterior cingulate cortex (ACC) fire in response to both pain in the self and the observation of pain in another [83]. Although ASD are often described in terms of reduced empathic abilities [84], evidence for reduced empathy in domains different from mentalising and perspective taking (for instance pain) is sparse. To investigate this, Minio-Paluello et al. [85] used a sample of sixteen right-handed men with Asperger's Syndrome (a type of ASD) (aged 28.0 ± 7.2 years) and 20 neurotypical controls (aged 25.3 ± 6.7 years) age, sex, and IQ matched.

Minio-Paluello et al. [85] used single-pulse transcranial magnetic stimulation (TMS) to explore a rudimentary form of empathy, called "sensorimotor contagion", elicited in neurotypical participants when they observe painful stimuli applied to the body of another person. The authors regard sensorimotor contagion to have taken place when there is a reduction of corticospinal excitability recorded from the specific body part that is vicariously affected by the observed painful stimulation, in this case, the hand muscles. This inhibition to observation of pain inflicted on another body is characteristic of the corticospinal inhibition found during actual noxious stimulation (when the pain is directly inflicted). So in the study carried out by Minio-Paluello et al. [85], participants underwent single-pulse TMS during observation of painful and nonpainful stimuli affecting another individual. Motor-evoked potentials (MEPs) induced by focal single-pulse TMS of the left primary motor cortex (M1) were simultaneously recorded from two right-hand muscles, the first dorsal interosseous (FDI), and the abductor digiti minimi (ADM). Four types of video clips (each lasting 1.8 seconds) were presented on a 19-inch screen. Video clips were (1) "static": static right hand; (2) "Pain": needle deeply penetrating the FDI muscle; (3) "Touch": cotton swab gently touching the FDI region; and (4) "Tomato": needle deeply penetrating a tomato. Thus, whereas participants' FDI muscle was vicariously involved by the painful stimulation, the ADM muscle served as a somatotopic control because it was not shown to be penetrated. Previous studies of TMS show that watching moving body parts or hands increased corticospinal excitability. In order to eliminate this confounding effect, the hands in the video were static in the clips and the syringe holder was not visible. In addition to these objective neurophysiological measures, participants were also asked to imagine how the pain would feel, if applied to them. The qualities of the imagined pain were measured using the McGill Pain Questionnaire (MPQ) [86], which is made up of Sensory (items 1–10, 17–19) and Affective (items 11–15, 20) subscales, and through the Hurts value, a rating between 0 and 10 indicating how much the participants thought the injection would hurt them.

Minio-Paluello et al. [85] found that when observing other's pain, participants with ASD, in contrast to neurotypical control participants, did not show any amplitude reduction of motor-evoked potentials recorded from the muscle vicariously affected by pain, nor did their neurophysiological response correlate with imagined pain sensory qualities. All experimental video clips were similarly rated by the two groups ($ps > 0.10$) except for the Static condition, which was significantly less arousing for ASD ($P < 0.02$). Participants

with ASD, compared with control participants, perceived themselves less able to identify with the model being touched ($t = 2.07$, $P = 0.050$) and tended to judge the touch as more painful ($t = -1.82$, $P = 0.08$). When asked to imagine how they would feel if receiving the painful stimulation shown in the videos and to rate the sensory and affective qualities of imagined pain, control participants and individuals with ASD gave similar ratings (all $ps > 0.33$). Therefore the lack of sensorimotor contagion in ASD cannot be explained by group differences in the imagined "painfulness" of the observed events. They were therefore able to correctly understand or identify how painful a particular event would be despite showing abnormal neurophysiological responses. Although participants with ASD did not embody others' pain, the observation of painful stimuli inflicted to the hand muscle of another person inhibited control participants' corticospinal representation of the same muscle (i.e., the FDI muscle). Those MEPs recorded from the ADM muscle are not modulated cannot be explained in the terms of reduced reactivity of this muscle. Indeed, when videos depict the ADM being penetrated by a needle, similar corticospinal inhibition of this muscle has been observed [87]. In sum, finding no embodiment of others' pain or reduced empathic abilities in individuals with ASD (as evidenced by reduced or absent sensorimotor contagion during the observation of pain affecting another person, the hand in the movie clips) provides neurophysiological evidence for reduced empathic resonance in people with ASD and suggests that their difficulties with empathy is mediated not only by cognitive dimensions but also by sensorimotor resonance with others.

*3.6. Relationship between Opioid Hormone and ASD.* Nagamitsu et al. [88] measured cerebralspinal fluid (CSF) levels of beta-endorphin, an opioid hormone, in 19 Japanese children (17 boys, 2 girls, mean age 4.23 years, range 2.00–6.42) with typical infantile autism (ASD). Some children presented with accessory symptoms such as self-injurious behaviour (3/19), pain insensitivity (8/19), and stereotyped movements (10/19). The controls consisted of 23 age-matched Japanese children (18 boys, 5 girls, mean age 3.78 years, range 0–10.75) who had undergone lumbar puncture for the diagnosis of a possible central nervous system (CNS) infection but whose CSF showed normal results. CSF levels of p-endorphin in three patients with the Rett syndrome (3 girls, ages 10–14 years) who presented with symptoms resembling those of infantile ASD were also recorded. In infantile autism, CSF levels of beta-endorphin did not differ significantly from those of age-matched controls. No significant correlation between CSF levels and clinical symptoms, including self-injurious behaviour, pain insensitivity, and stereotyped movement was found. However, CSF beta-endorphin levels were significantly higher in the patients with Rett syndrome than in the control ($P < 0.05$). Findings indicated that neurons containing beta-endorphin may not be involved in patients with infantile autism, therefore not supporting the relationship between dysfunction of brain opioid and ASD.

*3.7. Oversensitivity to Pain and Age of Diagnosis of ASD.* Mandell et al. [89] attempted to identify factors which may delay diagnosis of ASD among a community sample of children with ASD. Survey data was collected in Pennsylvania from 969 caregivers of children who had ASD and were younger than 21 years regarding their service experiences. The average age of diagnosis was 3.1 years for children with autistic disorder, 3.9 years for pervasive developmental disorder not otherwise specified, and 7.2 years for Asperger's disorder (a type of ASD). Interestingly, oversensitivity to pain was associated with a 0.6-year increase in the age of diagnosis. The association of oversensitivity to pain with later diagnosis may be because this symptom prompts clinicians to search for other organic causes and not consider developmental issues.

*3.8. Level of Functioning in ASD Group across Case and Experimental Studies.* Of the five case studies only one specifies level of functioning and was mild ASD [17]. The remaining four case studies do not indicate level of functioning [32, 33, 56, 58]. Of the ten experimental studies, two studies include high functioning individuals with ASD [72, 74]. Three studies did not specify level of functioning [70, 79, 88]. One did not specify low or high functioning using clinical guidelines and examined a variety of ASD symptoms to determine a level of functioning but does not report how many are contained within each category [89]. Another study, rather than defining in terms of high and low functioning, describes levels of severity based on scores on the Autism Spectrum Quotient (AQ, [90]) [85]. Two studies used the same data and employed The Childhood Autism Rating Scale (CARS, [91]) to create two groups: severely autistic and mildly-moderately autistic and the majority of the group fell into the severely autistic range [46, 62]. Lastly, another study had 39 patients in the severe ASD group and 39 in the "mild" to "moderate" ASD group, assessing ASD severity using the Autism Diagnostic Interview-Revised (ADI-R, [92]). [41]. Four of the experimental studies did not include a comparison/control group [46, 70, 79, 89].

## 4. Discussion

Five case studies and ten experimental studies were found in the PRISMA search which investigated some aspect of pain in individuals with ASD. All five case studies described individuals with ASD who were exhibiting pain *insensitivity* [17, 32, 33, 56, 58]. The two cases presented by Bursch et al. [33] demonstrate how chronic pain can be the focal symptom and perseverative focus of attention for individuals with an ASD. Once focused on pain, difficulties in shifting attentional focus can serve to increase pain and associated distress. Therefore, implementing a treatment that somehow interrupts the perseveration might reduce or even eliminate the pain that the individual experiences. In fact, this is exactly what Zeltzer and Schlank [93] found. They describe a case in their pain clinic where a child with ASD presented to them yelling repeatedly, "Ow! Ow! Ow!" Two months earlier, the child had sustained a leg injury and he had been shouting ever since. Zeltzer and Schlank suggested that rather than shouting, the child should replace this by squeezing a ball instead. Interestingly, this resulted in a transfer of his expression to the point where he actually reported feeling better because he no longer felt

embarrassed about repeatedly shouting "Ow!". These findings strongly indicate that treating the perseveration can be the most effective way to reduce suffering for some patients [7]. What has also been proposed by numerous researchers is that in children with ASD the anxiety often experienced by this population might actually contribute to their pain experience. This holds especially true for those individuals whose muscles remain tense for extensive durations [93].

Also important for clinical practice is the case study by Mieres et al. [32] which suggests a particular approach is required in assessing the subjective feeling of pain in individuals with ASD. Rather than ask how much pain they are feeling, they suggest instead a new series of questions, the key being "How uncomfortable are you?" (used in addition to the verbal and pictorial pain scale).

Of the ten experimental studies only one found no significant difference in pain sensitivity between patients with ASD and controls. Specifically, no significant differences were found between the pain ratings of youth with ASD or their parents as compared with a sample of typically developing youths [74]. Interestingly, overall, only one of the experimental studies (compared to all five of the case studies) found evidence of underreactivity to pain (suggestive of pain insensitivity) in 40% of their sample [70]. One study [41] found that individuals with ASD do not have a decreased sensitivity for pain and investigated both behavioural reactivity to pain during venepuncture as well as plasma b-endorphin concentrations and heart rate. The additional physiological measures were particularly important since there was an absence of any behavioural pain reactivity in the individuals with ASD during venepuncture despite their higher heart rate and plasma b-endorphin levels—strongly suggesting that the individuals with ASD were not insensitive to pain.

Five studies found evidence of a greater degree of pain sensitivity in individuals with ASD [62, 72, 79, 85, 89]. Interestingly, oversensitivity to pain was associated with a 0.6-year increase in the age of diagnosis [89]. One study [46] investigated the influence of information about the pain experience of children with ASD on observers' judgement of pain intensity in children with ASD and examined the impact of facial activity on observers' judgement of pain intensity in children with ASD. Facial activity was found to have a significant impact on observers' estimates of pain intensity; pain sensitivity information did not [46]. This is in contrast to the view that parents' ratings of pain in their children with ASD may be distorted due to misinformation about pain insensitivity in their children [62]. A possible limitation with this study, in terms of investigating the effect of information of pain sensitivity in individuals with ASD, is that the students in this study had no personal relationship to the individuals they observed and rated in the videos. This might have contributed to the lack of effect of pain information on the judgments made. A different picture might emerge if the same situation was applied to individuals with a personal relationship to the child such as a parent. These results have important implications for the assessment and management of pain in children with ASD [46]. The finding that observers may be able to decode pain information from facial activity [46] is important because children with ASD frequently lack the skills to express their pain verbally and this could put them at risk for substandard health care. The findings of a significant behavioural reaction in response to a painful stimulus in individuals with ASD [62, 72, 79, 85, 89] contradict the widespread belief in the literature of pain insensitivity in individuals with ASD. Some of the findings reported in this review also question the clinical appropriateness of parental global report as an assessment tool for pain in children with ASD [62]. Another study investigated whether P-endorphin plays an important role in infantile autism by measuring the cerebrospinal fluid (CSF) levels of p-endorphin and evaluated the correlation between these levels and ASD symptoms [88]. Findings did not support the opioid hypothesis to explain pain sensitivity in ASD [88].

Another important aspect is whether the five experimental studies that included different levels of functioning or severity of ASD [41, 46, 62, 85, 89] report whether this had any notable effect on the results. For instance, were the findings weaker for individuals who are higher functioning. Two studies did find differences [41, 85] while three did not [46, 62, 89]. Tordjman et al. [41] found that plasma b-endorphin levels were positively associated with ASD severity. Minio-Paluello et al. [85] found that corticospinal inhibition was maximal in the individuals with fewer ASD traits.

*4.1. Expression of Pain in Individuals with ASD.* Numerous anecdotal reports show that caregivers frequently describe unusual, or absent, responses to painful stimuli in their children with ASD. Some caregivers are even able to describe unique behaviours in their child that enable them to know when they are in pain. However, it is crucial to point out here that altered pain expression is not universally observed in ASD. Despite this most experts are in agreement that the pain experience appears different in individuals with ASD [94].

Tordjman et al. [41] argue that their findings indicate that prior reports of reduced pain sensitivity in ASD are related, not to an insensitivity or endogenous analgesia to pain but to a different mode of pain *expression*. This is without doubt the most crucial finding and clearly further investigation to explore this aspect is required. The findings by Tordjman et al. [41] constitute a clear challenge to theories of reduced pain sensitivity in ASD since they found that painful stimuli can produce physical and psychic stress in individuals with ASD and that this stress can be manifested by physiological responses and expressed through autistic behaviours. Tordjman et al. [41] hypothesise that the different mode of pain expression in individuals with ASD may be mediated by (1) verbal communication impairments, (2) deficits in nonverbal communication and body image problems (difficulty locating the painful area), or (3) other cognitive problems such as (a) difficulty in establishing cause-effect relationships between the pain sensation and the stimulus causing the pain, (b) problems discriminating, representing and identifying sensations and emotions which involves abstraction and symbolisation capacities (the perception of pain integrates sensorial, emotional, and cognitive factors [95]), (c) problems of learning socially appropriate responses to pain [41].

The majority of the experimental studies included in the review examine pain reaction to a specific medical

procedure venepuncture. Therefore, the findings cannot be generalised to other contexts and pain situations such as pain during everyday situations and experience of chronic pain in individuals with ASD. It is also important to acknowledge that the experiences of children with ASD occur along a spectrum of severity. Therefore it is highly possible that the experience and expression of pain may differ depending on where the individual lies on this spectrum (Messmer et al. [46]); the level of communicative and language abilities of individuals [94] and the impact of different ASD diagnoses (i.e., Asperger's disorder; PDD-NOS; Rett syndrome) on pain expression and reactivity. This variability again emphasises that interventions and treatments must be tailored to each specific child [94].

Despite the complexity in interpreting the findings from the sparse amount of studies to date which have looked at pain sensitivity in individuals with ASD, what is clear is that there is a need for a pain assessment tool specifically for use in this population [94]. Existing instruments may be inappropriate. To my knowledge, there has only been one study (from a dissertation submitted to the University of Florida for the degree of Doctor of Philosophy) which has attempted to identify whether there are unique pain indicators applicable to a significant amount of children with ASD and whether there are pain indicators identified by caregivers that are completely unique to the one child. Inglese [94] found several objective, observable and measurable indicators which were presumed by the author to be relevant to pain assessment in ASD (i.e., "furrowed brow," "banging his/her head," "injuring oneself," "grimacing," "guarding," and "increased heart rate"), many other identified indicators were subjective and required (a) knowledge of the child's baseline, and (b) monitoring for changes from normal (i.e., "crankiness," "being less active," "rocking unusually," "acting "off", and "irritability"). Inglese [94] suggests then that in the designing of a new instrument specifically for pain assessment in individuals with ASD, there needs to be the inclusion of sections which are objective and quantifiable—these could be used by individual(s) who are unfamiliar to the child being assessed—in addition to sections which are based on caregiver judgments regarding what is typical in their child. In effect encompassing both caregiver information regarding their child's baseline and objective assessment questions which can be conducted by individuals unfamiliar with the child is crucially important in creating a comprehensive pain assessment in this population [94].

*4.2. Limitations.* Sensations are often thought to be logically private, subjective, self-intimating, and the source of incorrigible knowledge for those who have them. Since pain is often thought to be a "subjective" experience, this has lead researchers to use the report as the gold standard for pain experience. Many of the studies identified in the present review investigate pain reactivity using caregiver reports which have obvious limitations such as reporting bias. However, the most notable limitation with this is highlighted by research which suggests that parents of children with ASD perform worse than parents of control children in facial emotion task. For instance, in an emotional labelling task in response to schematic facial patterns representing five basic emotions, parents of children with ASD performed worse than parents of control children (i.e., [96]). The study by Nader et al. [62] (one of the studies reported in this review) is consistent with the difficulties found in parents of children with ASD in correctly interpreting facial emotions. Nader et al. [62] found that some of the caregivers did not interpret their child's pain expression accurately in that children with ASD who had been assessed by their parents as having a lower pain sensitivity and reactivity tended to show greater facial reactions and behavioural distress in response to the venepuncture.

Similarly, there is the issue of asking individuals with ASD to rate pain according to facial expressions of pain (i.e., Faces Pain Scale (FPS)). Numerous researchers maintain that individuals with ASD have difficulty with processing facial expression (i.e., [97]). Individuals with ASD process faces differently and show reduced attention to faces and facial expressions [98]. This reduced interest in faces is likely to impair their face processing skills, so that children with ASD do not become "face experts" like their typically developing peers [99].

The majority of the small number of studies which investigated some aspects of pain specifically in individuals with ASD are limited by their sample size. Seven of the ten experimental studies had sample sizes of ASD groups less than 21. The remaining three had 73, 969, and 208 individuals with ASD. More studies with larger sample sizes examining behavioural reactivity to pain as well as measuring physiological responses are imperative to our understanding of pain experience in individuals with ASD. A further complication in attempting to draw conclusions from the literature to date are the differences across studies in terms of cognitive development of the individuals with ASD (not to mention the wide differences in age). For instance, in one study [41] all patients were cognitively impaired: mean full scale IQ = 42.2, SD = 3.2 (range 40–58) while another study all had IQ of at least 70 [72]. These limitations and differences pose a significant problem when trying to determine whether there is pain insensitivity, greater pain sensitivity or no difference in individuals with ASD.

Lastly, it is also difficult to disentangle from the experimental studies conducted to date as to how much of the observed pain reactions, and so forth were due to the individuals with ASD level of *distress* rather than any pain response. Individuals with ASD might display more distress during the venepuncture procedure compared to controls and this might be completely independent from how painful they find the experience.

*4.3. Future Directions and Clinical Implications.* Further studies are needed to recognise illnesses earlier in the absence of pain or pain perception in children with an ASD and to develop reliable and valid metrics for pain identification for both verbal and nonverbal individuals with ASD [32]. Further research is also needed to explore the concordance between parent report of pain sensitivity and observed reactivity of children with ASD to every day painful incidents. Children with ASD may exhibit typical behavioural reactions to procedural pain in a clinical setting but atypical responses

to everyday pain in their home environment [62]. It is important to understand how different types of pain in different settings are perceived in order to acceptably manage pain in children with ASD. Additionally, more research is needed to understand how observers decode the pain experience of children with ASD and explore the potentially biasing effect of pain sensitivity information on observers' estimates of pain in children with ASD [46]. The study by Mieres et al. [32] also stresses the importance of the way in which clinicians ask patients with ASD about how much pain they are experiencing. They found that asking the individual with ASD how uncomfortable they were on a scale of 1 to 10 was a more accurate representation of the pain they felt than when they were asked directly how much pain they were in on a scale of 1 to 10.

Further research is also need to explore further how children and adults with ASD react to various types (acute versus chronic) or degrees of pain. The need for this research is emphasised by the study reported in this review [41] that a significant number of individuals with ASD reported absent or reduced pain reactivity (41.3% versus 8.7% of controls) but in the same sample the majority (78%) exhibited normal pain reactivity to burning based on caregiver report. This clearly shows that the type and severity of the pain event is important when studying pain in this population.

In a study just published, Wager et al. [100], based on four studies involving a total of 114 participants, developed an fMRI-based measure that predicts pain intensity at the level of the individual person and found that it is possible to use fMRI to assess pain elicited by noxious heat in healthy persons. Given the limitations of the experimental studies to date (for instance the reliability of self-report measures of pain and caregiver report of pain in their child), this would be an more robust and objective way to investigate whether pain experience is any different in individuals with ASD compared to controls. This might also have the potential to show whether there is a discordance between neural signatures of pain and the expression of pain in the individual with ASD.

## 5. Conclusions

There is still relatively little research on the unique problems posed by the expression of pain and sensitivity to painful stimuli in individuals with intellectual and developmental disabilities [101] and particularly in individuals with ASD from childhood to adulthood. Overall, the findings reported here of a significant behavioural reaction in response to a painful stimulus in individuals with ASD contradict the wide spread belief in the literature of pain insensitivity in individuals with ASD. The case studies all reported pain insensitivity in individuals with ASD and provide an example of how impaired sensory perceptions can mask and delay the ability of health care professionals to recognise the need for treatment. However, the majority of the ten experimental studies reviewed here indicate that the idea that individuals with ASD are pain insensitive needs to be challenged. This systematic review highlights the need for a shift away from the widely and long-held belief that children and adults with ASD have a reduced pain sensitivity, do not feel pain as intensely as others, and have an indifference to pain and a high threshold for pain. What was also highlighted by some of the findings of this review is the importance of further study to explore the theory that the pain *expression* in individuals with ASD differs from that of neurotypicals. Recognition of all these findings have important implications for the treatment and recognition of the need for treatment in individuals with ASD.

## Conflict of Interests

The author declares no conflict of interests.

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*Research Article*

# Autism, Processing Speed, and Adaptive Functioning in Preschool Children

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*Objectives*. To study cognitive test profiles with a focus on processing speed in a representative group of preschool children with autism spectrum disorder (ASD) and relate processing speed to adaptive functioning. *Methods*. Cognitive assessments were performed in 190 3.6–6.6-year-old children (164 boys and 26 girls) with ASD, using either Griffiths' developmental scales ($n = 77$) or the Wechsler Preschool and Primary Scale of Intelligence-Third Edition (WPPSI-III) ($n = 113$). Cognitive data were related to adaptive functioning as measured by Vineland Adaptive Behavior Scales (VABS). *Results*. Cognitive profiles were characterized by low verbal skills. Low processing speed quotients (PSQs) were found in 66 (78%) of the 85 children who were able to participate in the processing speed subtests. Except for Socialization, all VABS domains (Communication, Motor Skills, Daily Living Skills, and Adaptive Behavior Composite scores) correlated significantly with PSQ. Multiple regression analysis showed that PSQ predicted 38%, 35%, 34%, and 37% of the variance for Communication, Daily Living Skills, Motor Skills, and total Adaptive Composite scores, respectively. *Conclusion*. Preschool children with ASD had uneven cognitive profiles with low verbal skills, and, relatively, even lower PSQs. Except for Socialization, adaptive functioning was predicted to a considerable degree by PSQ.

## 1. Introduction

Autism spectrum disorders (ASDs) are common disabling conditions with a heterogeneous etiology and clinical presentation as well as a high degree of overlap with other neurodevelopmental disorders.

Diagnosing ASD in young children can be difficult due to the coexistence and overlap with many other developmental disorders, such as developmental coordination disorder, attention-deficit/hyperactivity disorder, speech and language disorders, and/or general developmental delay/impairment, that is, other ESSENCE conditions [1, 2]. Moreover, the full clinical picture often changes during early preschool years and may not have fully appeared at the age of 2-3 years, an age window when different child health screening programs are in use [3, 4]. ASD is linked to a variety of cognitive difficulties affecting the individual and with implications for the child's interaction with his or her family, peers, and in the preschool/school setting.

Intellectual disability (ID) is one of the most common co-occurring disorders in ASD [5, 6] and is an important predictor of outcome [7–10]. In a recent study of preschool children with ASD (Hedvall et al., 2013, submitted), we have reported that a test result in the broad range of Intellectual Disability Developmental Quotient (DQ)/Intellectual Quotient (IQ) <70 at initial preschool assessment was stable at reassessment two years later, whereas a borderline result (IQ/DQ = 70–84) was just as likely to go down, up, or stay in the same range at followup.

Many studies have demonstrated that an uneven profile is characteristic of individuals with ASD with general relative strengths in visual-spatial nonverbal measures and a

concurrent weakness in verbal ability [11–16]. Except for the impact of general intelligence on outcome of ASD, no single cognitive model provides a full explanation of the multiplicity of the clinical presentations in ASD. Two well-known theories are the Theory of Mind hypothesis and the Central Coherence Theory. Theory of Mind is the ability to attribute mental states to self and others and to understand that others have beliefs, desires, and intentions that are different from one's own [17]. Weak central coherence refers to the detailed "peripheral" focused processing style, characteristic of ASD, whereas typically developing children and adults tend to process incoming information for meaning and global understanding [18].

There has also been a growing research interest regarding different executive functions; including planning, working memory, impulse control, and shifting set in individuals with ASD. In a review, Russo and collaborators [19] discussed the importance of understanding executive function in ASD and its relation to general developmental level and in impairments of set shifting/mental flexibility in older groups of children. An early study of executive dysfunction and mental flexibility in preschool children with ASD was conducted by McEvoy et al. [20]. Children with ASD (mean age 5 years) were found to have selective deficits in executive function compared to both developmental delayed children of similar nonverbal mental age and to normally developing children. Pellicano [21] studied the link between theory of mind and executive function in young children with autism and in typically developing children. A significant correlation emerged between theory of mind and executive variables in the autism group. Executive dysfunction may also explain the repetitive behaviors and restricted interests seen in individuals with ASD [22]. Particularly, executive dysfunctions regarding attention, set shifting, and planning have been reported in young children with ASD [23]. Poor mental flexibility is considered to give a more rigid and concrete bound behavior, occasionally transformed into perseverations [24].

Processing speed may be analogous to the operating speed of the central processing unit of a computer [25] and is related to performance of higher-order cognition. Processing speed was found to be weakest relative to other indices using Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) in a group of high-functioning (IQ > 70) children (age 10) with autism [26]. Slow processing speed may give problems with rate of learning, comprehension of new information, and mental fatigue. The study by Mayes and Calhoun [27] indicated that learning, attention, graphomotor and processing speed deficits tended to go together in children with ADHD and high-functioning autism compared to other clinical disorders. Processing speed deficits have been found in hypoactive and inattentive children with Attention Deficit Hyperactivity Disorder (ADHD), using the WISC-IV [28, 29], but have also been demonstrated in the ADHD group in general [30].

Processing speed deficits can be expected to influence many daily activities with demands on completing tasks and responsibilities on time and thus being a cognitive factor of great importance in everyday life. The deficits are in many ways "invisible," and children with ASD and normal IQ, but with processing speed difficulties, may, if this problem is not recognized, fail to carry out tasks that are expected of them without this being an effect of the ASD "per se." Whereas several research studies exist that have established the impact of general IQ on adaptive (daily life) functions in ASD samples [31, 32], little research has examined which *aspect* of a child's IQ it is that has the greatest role in this respect. We have not been able to locate any ASD-related studies that specifically look at associations between processing speed and adaptive functioning across several adaptive domains, except for the association between processing speed and communication, indicating speed to correlate positively with communication abilities [26].

The aim of the present study, therefore, was to analyze developmental and cognitive test data (Griffiths' and WPPSI) [33, 34] in a representative group of preschool children with a clinical diagnosis of ASD, particularly with regards to processing speed, and to relate this result to aspects of daily life functioning, as measured by the VABS [35].

## 2. Methods

*2.1. Procedure.* The sample was drawn from a community representative group of 208 children with clinically diagnosed ASD in the county of Stockholm, previously described in detail by Fernell et al. [6, 36]. The children had had in-depth assessments prior to and at referral to a specialized habilitation center, the Autism Center for Young Children (ACYC), and at a follow-up at the center after 2 years. Of the 208 children, referred to the ACYC, 198 participated in the 2-year follow-up, and of these, 196 participated in a cognitive assessment. The majority, 190 children, were assessed by either of the two research psychologists at the ACYC and therefore included in this study. The remaining 6 children were reassessed by referral team psychologists.

*2.2. Participants.* The 190 children—26 (14%) girls and 164 (86%) boys—were aged between 3.6 and 6.6 years (mean age 5.5, (SD = 0.8) at the time of the study. The distribution of ASD subtypes at the 2-year follow-up, using the DSM-IV criteria (APA, 1994) [37], was 100 (53%) children with autistic disorder (87 boys and 13 girls), 56 (30%) with Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) (50 boys and 6 girls), and 12 (6%) with Asperger syndrome (10 boys and 2 girls). A subgroup of 21 children (11%, 16 boys and 5 girls) had some autistic symptoms but not enough to meet criteria for a full ASD diagnosis at follow-up. One child did not have an assessment with regard to ASD subtype.

Of the 190 children, a total of 87 (46%) had ID, 51 (27%) borderline IQ/DQ, and 52 (27%) an average IQ/DQ [36].

Of the 18 children who did not participate in the cognitive follow-up assessment presented here, 12 children had autistic disorder at referral to the ACYC (8 with ID and 4 with borderline IQ/DQ) and 6 children had atypical autism (2 with average IQ/DQ and 4 with borderline IQ/DQ).

### 2.3. Developmental-Cognitive Tests

*2.3.1. Griffiths' Developmental Scales I and/or II.* For children with a mental age <2.6 years, intelligence/mental age was assessed with the Swedish versions of Griffiths' Developmental Scales [33]. Developmental quotients (DQs) for the total and subscale scores obtained were converted to IQ equivalents in order to obtain a score corresponding to intelligence-quotient points. Results from Griffiths' scale C (Hearing and Speech) and, when available, scale F (Practical Reasoning, for children with mental age >24 months) were converted to Verbal Function, and scale D (Eye and Hand Coordination) and scale E (Performance) were converted to Performance Function. Global Cognitive Function is the average value of verbal function and performance function [38].

*2.3.2. Wechsler Preschool and Primary Scale of Intelligence-Third Edition (WPPSI-III) [34].* WPPSI-III [34] was used for children with a mental age >2.6 years, providing full scale IQ (FSIQ), verbal IQ (VIQ), and performance IQ (PIQ). WPPSI-III generates also Processing Speed Quotient (PSQ) and General Language Composite (GLC). VIQ, PIQ, and FSIQ are referred to as Verbal, Performance, and Global Cognitive Function, respectively.

WPPSI-III version for age span 2.6–3.11 years includes 4 core subtests (Receptive Vocabulary, Information, Block Design, and Object Assembly) and 1 supplemental subtest (Picture Naming). Four composite scores are possible for this age band: VIQ, PIQ, FSIQ, and GLC.

WPPSI-III version for age span 4.0–7.3 includes 7 core subtests (Information, Vocabulary, Word Reasoning, Block Design, Matrix Reasoning, Picture Concepts, and Coding) and 5 supplemental subtest (Similarities, Comprehension, Object Assembly, Picture Completion, and Symbol Search). A total of five composite scores are possible for this age band: VIQ, PIQ, PSQ, FSIQ, and GLC. Receptive Vocabulary and Picture Naming are included in the GLC and Symbol Search and Coding in the PSQ.

### 2.4. Adaptive Functioning Scale

*2.4.1. Vineland Adaptive Behavior Scales (VABS-II).* The VABS-II [35] is an informant-based measure of adaptive behavior that yields a composite score and four domain scores: Communication (receptive, expressive, and written adaptive functions), Daily Living Skills (personal, domestic, and community skills), Socialization (interpersonal relationships, play and leisure time, and coping abilities), and Motor skills (gross and fine motor skills).

*2.5. Statistical Methods.* Statistical analyses were carried out using SPSS version 19 (SPSS, Chicago, IL, USA). Pearson's $r$ was used to investigate the relationship between PSQ and VABS. Those variables that were significantly correlated with the criterion variable (VABS-II domains) were entered as predictors into a multiple regression model using the standard (enter) method. An alpha level of .05 was used for all statistical analyses.

## 3. Results

*3.1. Cognitive and Developmental Test Data.* Intellectual/developmental levels and profiles according to WPPSI-III and the Griffiths' test are presented in Table 1.

Seventy-seven of the 190 children (40%) were assessed with Griffiths' Developmental Scales. For those who were evaluated using Griffiths' developmental scales, the mean verbal function was 33.5 (SD = 15.9), performance function was 46.7 (SD = 16.3), and global function was 41.6 (SD = 14.5) (Table 1).

One hundred and thirteen children (60% of the total sample) were tested with the WPPSI-III, 112 with the version for age span 4.0–7.3 years, and one child with the version for age span 2.6–3.11 years. FSIQ for this group was 84.5 (SD = 14.7), VIQ 84.8 (SD = 16.1), and PIQ 93.6 (SD = 16.7). Mean value for PSQ ($n = 85$) was 76.7 (SD = 12.2) and for GLC ($n = 99$) was 89.9 (SD = 17.1). The differences between PSQ, VIQ, PIQ, and GLC were significant ($P < .000$).

On a group level, the cognitive profile was uneven in both Griffiths' and WPPSI-III with a significantly lower verbal function compared to performance (Griffiths' $P = .01$; WPPSI-III; $P = .01$). No significant difference was found between boys and girls.

*3.2. PSQ.* Twenty-five of 113 children (22%) who were tested with WPPSI-III were not able to participate in the subtests Coding and Symbol Search that together comprise the PSQ. FSIQ in this "non- PSQ" group was 76.3 (SD = 14.9) compared to a mean FSIQ of 86.8 (SD = 13.8, $P = .003$) in the group who were able to perform PSQ subtests. There was also a difference regarding PIQ in the two groups, and mean PIQ was 83.5 (SD = 17.8) in the "non-PSQ" group compared to 96.5 (SD = 15.3, $P = .002$) in the PSQ-group. No difference was found regarding VIQ ($M = 79.6$, SD = 17.4 and $M = 86.3$, SD = 15.4) between the two groups.

PSQ in relation to VABS-II was available for 84 of the 190 children. There were significant positive correlations between PSQ and the Communication domain ($r = .422$, $P = .01$), Motor Skills domain ($r = .414$, $P = .01$), Daily Living Skills (DLS) domain ($r = .377$, $P = .01$), and Adaptive Composite score ($r = .438$, $P = .01$) (Table 2).

*3.2.1. PSQ and Statistical Predictions of VABS.* To examine the role of PSQ as a unique statistical predictor of adaptive functioning, we next performed multiple regression analyses. Four separate analyses were performed using the three VABS subdomain scores that were significantly related to PSQ (i.e., all but socialization) and the total composite score as the dependent variables. PSQ, VIQ, and PIQ were entered simultaneously as independent variables. PSQ predicted 38% of the communication ($\beta = .301$, $P = .005$) scale, 35% of variance for DLS ($\beta = .354$, $P = .004$), 34% for the motor skills domain ($\beta = .341$, $P = .004$), and 37% for the total composite score ($\beta = .373$, $P = .001$). VIQ predicted 24% of motor skills domains ($\beta = .241$, $P = .049$) and 28% of total composite score ($\beta = .277$, $P = .022$), whereas PIQ did not predict any of the VABS scores (all $P$s > .66).

Table 1: Cognitive function measured by WPPSI-III index and subtests results and by Griffiths' Developmental Scales, Adaptive behavior measured by Vineland Adaptive Behavior Scales.

| Index/subtests/development scales | WPPSI-III | | | |
|---|---|---|---|---|
| | *N* | IQ/DQ/scores | Subtest mean | Std. deviation | Range |
| WPPSI verbal IQ (VIQ) | 113 | 84,8 | | 16,1 | 53–133 |
| Information | 112 | | 7,4 | 3,3 | 1–16 |
| Vocabulary | 110 | | 7,4 | 2,9 | 2–16 |
| Word Reasoning | 111 | | 7,2 | 3,1 | 1–15 |
| Comprehension | 63 | | 9,0 | 2,9 | 3–15 |
| Similarities | 67 | | 7,9 | 2,6 | 3–15 |
| WPPSI performance IQ (PIQ) | 113 | 93,6 | | 16,7 | 53–135 |
| Block Design | 112 | | 10,3 | 3,6 | 1–18 |
| Matrix Reasoning | 111 | | 8,8 | 3,5 | 1–16 |
| Picture Concepts | 111 | | 8,2 | 3,4 | 1–17 |
| Picture Completion | 67 | | 9,6 | 3,5 | 2–19 |
| WPPSI Processing speed (PSQ) | 85 | 76,7 | | 12,2 | 49–107 |
| Coding | 110 | | 5,1 | 2,9 | 1–12 |
| Symbol Search | 95 | | 5,9 | 2,6 | 2–14 |
| WPPSI General Language (GLC) | 99 | 89,9 | | 17,1 | 45–128 |
| Receptive Vocabulary | 96 | | 8,2 | 3,1 | 1–15 |
| Picture Naming | 95 | | 8,5 | 3,2 | 2–16 |
| WPPSI full scale IQ (FSIQ) | 113 | 84,5 | | 14,7 | 51–121 |
| Griffiths' verbal functioning | 77 | 33,5 | | 15,9 | 8–72 |
| Griffiths' performance functioning | 77 | 46,7 | | 16,3 | 15–79 |
| Griffiths' global functioning | 77 | 41,6 | | 14,5 | 13–73 |
| VABS Communication | 187 | 71,9 | | 18,9 | 34–120 |
| VABS DLS | 187 | 73,8 | | 16,4 | 38–117 |
| VABS Socialization | 187 | 70,6 | | 14,7 | 46–112 |
| VABS Motor | 187 | 76,4 | | 14,5 | 43–117 |
| VABS total | 187 | 70,5 | | 15,0 | 42–114 |

WPPSI-III index scale and Griffiths' scales mean of 100 and a standard deviation of 15, WPPSI-III subtest scale point range 1–19, mean 10.
VABS: Vineland Adaptive Behavior Scales.
DLS: Daily Living Skills.
IQ: Intellectual Quotient.
DQ: Developmental Quotient.

## 4. Discussion

In accordance with results obtained in previously published studies, the cognitive profiles in our group of preschool children with ASD were characterized by significantly higher performance than verbal skills. This profile was evident both in the higher functioning group tested with WPPSI-III and in those with lower functioning, tested with Griffiths' developmental scales.

Results on the PSQ were significantly depressed compared to both verbal and performance IQ scores. Moreover, results on the two subtests composing PSQ, Coding, and Symbol search were equally low, indicating that these two subtests require cognitive efforts and that the motor function per se is not decisive for the Coding subtest. Analysis of the group that did not accomplish the subtests of the PSQ revealed that this group had a lower mean FSIQ. This finding supports the requirement for cognitive abilities in order to complete the Coding and Symbol search subtests, and, hence, our "PSQ group" can be regarded as a more able ASD group. Processing Speed subtests challenge the child's capacity to work independently according to a given template, and they require graphomotor speed, accuracy, and mental flexibility/set shifting capacity in order to sustain attention to task. Processing speed may be especially important in assessing young children due to its relationship to other cognitive abilities and learning. Clinical developmental research suggests a dynamic interplay between working memory, processing speed, and reasoning. More rapid processing of information enhances the effectiveness of working memory which enhances reasoning ability. Children with processing speed problems might therefore have more difficulties with task that requires working memory and reasoning ability, which both are needed in acquisition of new information [39]. These abilities reflect important executive functions, and our findings, hence, indicate that executive functions may be impaired already at early preschool age. However, demands on executive functions during preschool age are limited,

Table 2: Pearson correlations between WPPSI-III index scores and Vineland Adaptive Behavior Scales Domains.

| | WPPSI-III | | | | | Vineland Adaptive Behavior Scales Domains | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | VIQ | PIQ | PSQ | FSIQ | GLC | Communication | DLS | Socialization | Motoric | Composite |
| VIQ | 1 | ,529** | ,373** | ,869** | ,810** | ,538** | ,223* | ,227* | ,312** | ,376** |
| PIQ | | 1 | ,475** | ,854** | ,435** | ,409** | ,322** | ,237* | ,359** | ,389** |
| PSQ | | | 1 | ,585** | ,278* | ,422** | ,377** | ,206 | ,414** | ,438** |
| FSIQ | | | | 1 | ,713** | ,557** | ,322** | ,251** | ,403** | ,451** |
| GLC | | | | | 1 | ,462** | ,210* | ,231* | ,381** | ,366** |
| Communication | | | | | | 1 | ,832** | ,769** | ,751** | ,921** |
| DLS | | | | | | | 1 | ,822** | ,802** | ,939** |
| Socialization | | | | | | | | 1 | ,712** | ,900** |
| Motoric | | | | | | | | | 1 | ,890** |

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).
VIQ: Verbal IQ.
PIQ: Performance IQ.
PSQ: Processing Speed Quotient.
FSIQ: Full Scale IQ.
GLC: Global Language Composite.
DLS: Daily Living Skills.

and requirements for these abilities will increase significantly when the child starts school.

Salcedo-Marin et al. [40] studied the executive problems of school-aged children with either ASD or ADHD, especially with regards to planning ability. The authors discussed that despite overlapping clinical and cognitive features between the two disorders, children with ASD and with ADHD presented a different pattern in planning function performance. In children with ASD, planning function problems seemed to be mediated by processing speed and motor coordination and not by other executive function problems, including attention, working memory, or response inhibition. Clinical and educational implications of the findings were also discussed.

Our finding that PSQ was significantly correlated to adaptive functions also indicated that processing speed ability will affect everyday functioning. Similar results have been found in a study of school-age children with ASD [26] reporting that processing speed was the greatest area of weakness in the ASD group. The authors found that more than half of the sample scored at least a full standard deviation below the processing speed normative mean score and that processing speed performance also related to autism communication symptoms and adaptive communication abilities.

Our study group had not started school at the time of assessment, but it would probably be of importance that the low PSQ and ensuing implications for school work are conveyed to the child's school teachers. The mediating effect of cognitive processing speed on the ability to achieve the full potential of intellectual functioning at school, that is, the importance of detecting "slow" children, was emphasized by Lundervold and collaborators [29]. In cognitively gifted students with ASD, working memory and processing speed indices were both significantly positively correlated with achievement in math, reading, and written language [41], thus also highlighting the importance of paying attention to this cognitive factor at school.

In our study group, about half the children had ID [36], and they will therefore have the right to receive adapted education in the special schools. However, the rate of ID will decrease in a group of children with ASD at school age when also milder forms of ASD, without ID, have been identified and diagnosed. Among school age children with ASD, the rate of ID can be estimated to be 15%–20% [2]. In our opinion, processing speed results, as markers and predictors for executive and adaptive functions, should be more highlighted in the teaching situation for children with ASD.

Processing speed deficits are common in many ESSENCE conditions, and this underscores the cognitive overlap across many of these disorders and the need for a broad perspective when assessing children with different kinds of developmental disorders/problems.

We have captured cognitive profiles at a specific time point at preschool age, and we can expect that development/maturation may change in some children over time. A limitation of the study was that more than half the group could not participate in the PSQ subtests. The reasons for that were that the WPPSI test could not be used at all in one group and there was also a group that could not participate in the PSQ subtests, although they could complete the other WPPSI subtests. Thus, our results are valid for the more able ASD group. In future research, there is a need for cognitive follow-up studies to examine stability of cognitive profiles and adaptive outcome.

## Ethical Approval

The study was approved by the Ethics Committee in Stockholm.

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*Research Article*

# Self-Directedness and Cooperativeness, Psychosocial Dysfunction and Suffering in ESSENCE

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*Background*. The acronym ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations) highlights that children seeking clinical treatment are often multiply impaired, thus requiring treatment from several specialties. The aim was to map and relate, on a population level, ESSENCE to two salient predictors of health and adaptation to adversities, namely, Self-Directedness and Cooperativeness and also to dysfunction and suffering. *Methods*. Participants were twins ($N$ = 1892) aged 9 or 12 whose parents were interviewed with the Autism-Tics, ADHD and other Comorbidities inventory (A-TAC), and the Junior Temperament and Character Inventory (J-TCI). The A-TAC was first used to discern four ESSENCE-related screening diagnoses: autism spectrum disorders, attention deficit hyperactivity disorder, learning disabilities, and developmental coordination disorder; second, to quantify dysfunction and suffering in important social areas. *Results*. ESSENCE symptoms were continuously and categorically associated with deficiency in Self-Directedness and Cooperativeness and higher ratings of dysfunction and suffering. The impact of ESSENCE symptoms on these measures of mental health was found in a milder form in about 16% of all children and in a severe form in about 2%. *Conclusion*. Therapeutic interventions focusing on Self-Directedness and Cooperativeness might provide a novel method for child psychiatry in its approach to ESSENCE.

## 1. Introduction

During the last decades, the notion of mutually exclusive criteria for psychiatric disorders has been questioned [1]. Not only do mental disorders and symptoms coexist, but also share etiology. Twin studies, for example, have shown that the same etiological factors behind autism spectrums disorders (ASDs) also give rise to attention deficit hyperactivity disorder (ADHD), learning disabilities (LDs), and developmental coordination disorder (DCD) [2]. In addition, specific molecular genetic and chromosomal variants and abnormalities found in family studies of ASDs have been shown to give rise to heterogeneous arrays of clinical symptoms, corresponding to different psychiatric categorical diagnoses (e.g., learning disabilities and/or ADHD) [3, 4]. Further evidence for the lack of clear demarcations between neuropsychiatric disorders as defined in current diagnostic manuals has come from clinical and family studies, the quest for valid biomarkers, and the development of atypical neuroleptics which influence symptoms rather than diagnoses (as reviewed by [5]). Therefore, it has been concluded that coexisting disorders are, indeed, the rule rather than the exception in child psychiatry [6].

Recently, Gillberg [7] coined the acronym ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations) to highlight that children seeking

clinical treatment are often impaired in multiple domains and require treatment from several specialities. The ESSENCE perspective not only acknowledges the possibilities of shared aetiologies behind seemingly different conditions but also puts emphasis on cognitive problems, developmental deficits and treatment opportunities that are similar across diagnostic categories. Hence, advocating broad clinical assessments, and avoidance of compartmentalisation into specific diagnoses and "disease-specific clinics." In addition it highlights the understanding of diagnostic shifts (i.e., language impairments to ASDs, or ADHD to ASDs) [8, 9] and also that children with ESSENCE conditions would benefit from a wide array of treatment possibilities that include, but are not limited to, pediatricians, social workers, language therapists, child neurologists, psychologists, and geneticists.

The named conditions of ESSENCE were initially thought of as discrete categories (a child either had or did not have ASDs or ADHD), but population-based studies have invariably shown that the symptoms thought to identify these conditions are dimensionally distributed in the general population without "zones of rarity." In addition, recent studies have failed to identify any etiological demarcations between autistic-like traits and ASDs [10] or ADHD-related traits and ADHD [11]. The distribution of traits varies; few children have, for example, conduct problems while a majority have had some ADHD problem, at least "to some degree," at some stage of their lives [12].

The named conditions of ESSENCE have theoretical and clinical links with personality disorders in adulthood; Asperger's disorder was initially described as a form of schizoid personality disorder in children [13], conduct disorder is by definition a prelude to antisocial personality disorder [14], anorexia nervosa has been linked to anancastic and alexithymic personalities, and longitudinal studies have shown that ADHD carries an increased risk for antisocial personality disorder, and a growing clinical literature assesses its links with borderline personality disorder [15]. Moreover, even if most ESSENCE conditions have been classified on the DSM-IV Axis I, learning disorders and ASDs have had their place on Axis II alongside with the personality disorders. Personality traits are, for instance, assumed to be normally distributed in populations, and rating scales have been developed and normalized accordingly [16, 17].

To advance our understanding of ESSENCE, the focus of the present study will be on specific developmental cognitive-emotional capacities as measured by the Temperament and Character Inventory's (TCI) [18] scales of Self-directedness and Cooperativeness. These metacognitive strategies to direct behavior are partly learned, language dependent, and serve as principles to guide executive functions [18]. In contrast to executive functions, that are trained to become automatized, Self-directedness and Cooperativeness require metacognition, that is, thinking about thinking, a "theory of mind" in relation to oneself and to others, in order to achieve the simultaneous experiencing of being a person, being with others, understanding what happens in this being, and being able to adjust behavior to constructive strategies. In adult and child psychiatry, these personality dimensions have been salient predictors of health and adaptation to adversities [19–23]. Self-directedness and Cooperativeness have also been inversely linked with ASD and ADHD in a continuous model in the normal population [24]. Self-directedness indicates how responsible, purposeful, and resourceful an individual is when it comes to achieving his or her goals and values and to identify the self as autonomous. Cooperativeness indicates how well adapted the individual is in getting along with others fairly and flexibly, combing intuition with ethical principles and to identify the self as an integral part of groups and society. Low scores have been found in personality disorders, mood disorders, and psychotic disorders. These scales have, therefore, been proposed to form an overall measure of mental health and adaptive skills, with low scores as a general marker of mental health problems [17, 25].

Based on this literature, we expected that children with different combinations of ESSENCE would consistently show low scores in Self-directedness and Cooperativeness, and that the scores would be specifically associated with dysfunctions and/or suffering in important areas (at school or home, in peer groups). If so, Self-directedness and Cooperativeness could be suggested as a dimensional global measure of the impact of the different, mostly—genetic ESSENCE symptom profiles (i.e., ADHD, ASDs, LDs, or DCD). Interventions promoting Self-directedness and Cooperativeness could reasonably be assumed to improve the individual's possibilities to cope with his or her ESSENCE disabilities (e.g., inattention, communication problems, tics, eating problems, opposition, or compulsions). It is, to the best of the authors' knowledge, unknown if different constellations of ESSENCE are associated with Self-directedness and Cooperativeness and if this can be discerned on a population-level, taking the population distribution into account.

The aim of the present study was twofold:

(1) to map, continuously and categorically, ESSENCE in relation to Self-directedness and Cooperativeness and dysfunction and suffering;

(2) to relate ESSENCE to Self-directedness, Cooperativeness and dysfunction and suffering on a population level.

## 2. Methods

*2.1. Subjects.* The participants in this study were recruited from the ongoing Child and Adolescent Twin Study in Sweden (CATSS). Parents of all 9-year-old twins in Sweden born from 1992 and onward (the years 1993–1995 also included 12-year-old twins) were asked to participate in a telephone interview containing the Autism-Tics ADHD and other Comorbidities inventory (A-TAC) [26, 27]. The response rate in CATSS is roughly 80% and currently comprises >22 000 twins. Parents of twins born between 1992 and onwards, where one or both twins in a pair were screened positive in the A-TAC for ADHD, ASDs, conduct disorder, oppositional defiant disorder (OCD), developmental coordination disorder and learning disabilities, plus healthy controls, were invited to participate in a follow-up study (CATSS-questionnaire). CATSS-questionnaire has

answering response frequency of 60% [12] and includes, among other instruments, a parental version of the Junior-Temperament and Character Inventory (J-TCI) [28]. The sample used here consists of 2032 individuals of whom 140 were not eligible due to missing scores on the J-TCI (>5% missing responses), which rendered a final sample of 1892 (boys = 1040, girls = 852; 1121 aged 9 years old, 771 aged 12 years old). For a detailed description of CATSS, please see Anckarsater and colleagues' article [12].

### 2.2. Measures

#### 2.2.1. A-TAC

*ESSENCE.* The A-TAC is a parental telephone interview that was designed to screen for neu-rodevelopmental disorders; it has been validated three times cross-sectionally [26, 27, 29, 30], once longitudinally [11], and once independent of the creators research group [31]. The A-TAC consists of 96 items that are scored "1" for "yes," "0.5" for "yes, to some extent," and "0" for "no." The ASDs-domain in A-TAC consists of three modules: language (6 items), social interaction (6 items), and flexibility (5 items), collapsed these modules give an ASDs-score ranging from 0 to 17. The ADHD-domain consists of two modules: concentration and attention (9 items) and impulsiveness and activity (10 items), which collapsed give an ADHD-score ranging from 0 to 19. The LDs consist of one module comprising three items (score ranging between 0 and 3). The motor control module, corresponding to DCD, consists of one item (score ranging between 0 and 1). In the present study, we used the cut-offs derived by Larson et al. [27]: for ASDs $\geq$ 4,5 (sensitivity .91/specificity .80), for ADHD $\geq$ 6.0 (.91/.73), for LDs $\geq$ 1.0 (.92/.60), and for DCD $\geq$ 0.5 (.63/.68). Distribution, heritability estimates, and Cronbach's $\alpha$ for all scales are given elsewhere in other publications [12, 27].

*Dysfunction and Suffering.* For each module, in which at least one items is scored "0.5" or "1," the parents were asked (1) if the endorsed symptoms have led to dysfunction at school, among peers, or at home, or (2) if the child suffers from the symptoms. These questions are also scored "1" for "yes," 0.5 for "yes, to some extent," and "0" for "no." A scale measuring dysfunction and suffering was created using the answers from the aforementioned seven modules in the A-TAC, and thus, theoretically, the raw score ranged from 0 to 14. Using the means and standard deviations from the full CATSS-sample (i.e., 0.26 $\pm$ 1.15), the scale was standardized by transforming the raw scores into T-scores.

*2.2.2. Junior-Temperament and Character Inventory (J-TCI).* The J-TCI was designed to measure temperament and character during childhood [32] according to the psychobiological model of personality [18]. In the present study, we used the parent-rated version of the J-TCI, which comprises 108 items that are answered using a binary scale ("yes" coded as 1, "no" coded as 0). Here, we focus on the Self-directedness (20 items, e.g., "My child does not blame other people or circumstances for his/her choices") and Cooperativeness (20 items e.g., "My child treats everyone with kindness and respect no matter how unimportant or bad they are") scales. For each scale, the raw score was transformed to T-scores using the means and standard deviations from the Swedish validation of the parent version of the J-TCI [28] (for Self-directedness: 16.8 $\pm$ 2.7; for Cooperativeness: 16.8 $\pm$ 2.5). Moreover, as the sum of Self-directedness and Cooperativeness is commonly used as a measure of character maturity [33], we also summarized the raw scores into a single scale (SD + CO). Using the means and standard deviations of the SD + CO composite (33.6 $\pm$ 4.4) from the Swedish validation of the J-TCI [28], the sum was then transformed to T-scores. In T-scores, 50 represents the mean and a difference of 10 from the mean indicates a difference of one standard deviation. With regard to Self-directedness and Cooperativeness, immaturity is measured as 2 standard deviations below the mean, that is, a T-score of 30 [33].

### 2.3. Analyses

*2.3.1. Continuous.* The mean T-score of SD + CO, Self-directedness, and Cooperativeness were calculated for each A-TAC score. The distributions of autistic traits, ADHD-traits, LD-traits, and DCD-traits were converted into population percentiles based on the results from the baseline CATSS-study, $n$ = 17 220 [12]. The mean T-scores for the SD + CO composite were then calculated for each population percentile, in order to describe the impact of ESSENCE traits on a population level. Similarly, T-scores of dysfunction and suffering were calculated for each A-TAC score and each population percentile.

*2.3.2. Categorical.* Using the four categorical screening diagnoses, ten different categories of coexisting conditions that always included ADHD or ASDs were created taking all different constellations of coexisting conditions into account (i.e, ADHD + ASDs + DCD + LDs or ASDs + DCD, etc.). In addition, four "pure" categories were created: ASDs, ADHD, LD, or DCD only). All categories were mutually exclusive; that is, it was not possible to belong to more than one category. Mean T-scores for Self-directedness, Cooperativeness, SD + CO, and dysfunction and suffering were then calculated for all of the 14 categories.

## 3. Results

*3.1. Continuous Measures of ESSENCE Conditions.* For each increasing A-TAC scale step (i.e., one more endorsed symptom question on ADHD, ASDs, LDs, or DCD), the mean SD + CO score decreased and the number of reported dysfunctions and sufferings increased (Tables 1 and 2). This pattern was similar for all four types of ESSENCE A-TAC scores (see Tables S1 and S2 of the Supplementary Material available online on http://dx.doi.org/10.1155/2013/416981 for results regarding Self-directedness and Cooperativeness).

As compared to the ASDs score, a higher ADHD score was required to affect Self-directedness and Cooperativeness

and to cause dysfunction and/or suffering (at 7 or more points in the ADHD score; mean SD + CO was lowered by more than one standard deviation, while the corresponding effect was noted at 3 points on the ASDs score). The number of reported areas of dysfunction and/or suffering increased at about the same scores.

*3.2. Analysis of ESSENCE Groups/Categories.* The mean T-scores in Self-directedness, Cooperativeness, SD + CO, and dysfunction and suffering are reported for all diagnostic groups in Table 3. In Figure 1, we have plotted the mean T-scores of SD + CO and dysfunction and suffering. The presence of any ESSENCE condition was related to a decrease in Self-directedness and Cooperativeness, including DCD (i.e., motor discoordination) that is often overlooked in psychiatry. The diagnostic combinations that included ASDs resulted in Self-directedness and Cooperativeness scores at least two standard deviations below the mean. A trend could also be discerned showing that the higher the number of concomitant conditions, the greater the decrease in Self-directedness and Cooperativeness. For instance, the combination of ASDs + ADHD+ DCD + MR displayed a mean T-score of 21 while ADHD + LDs and ASDs + MR had mean scores of 37 and 32, respectively, while higher mean SD + CO T-scores could be seen in groups without any concomitant conditions (ASDs = 34; ADHD = 38; LDs = 41; DCD = 46). Again, a decrease in Self-directedness and/or Cooperativeness was accompanied by reports of dysfunction and suffering.

*3.3. Deficits in Self-Directedness and Cooperativeness and Dysfunction and Suffering in relation to the Population Distribution of ESSENCE.* In a subsequent step, to avoid the effects of scoring ESSENCE problems by symptom scales that contain different numbers of items and are ordinal data, the different A-TAC symptom scores were transformed into population percentiles. Mean T-scores of SD + CO and dysfunction and suffering were plotted against these population percentiles (see Figure 2). A consistent pattern of population impact across the ESSENCE conditions (DCD with is limited distribution only vaguely reflected the pattern) ensued. Going from the average towards the extreme end of the population distribution, dysfunction and suffering were first noticeable at about the 82–84th percentile of ESSENCE symptom scores, where also the SD + CO score had decreased by about one standard deviation. At about the 98 percentile in ADHD, ASDs, and LDs, a surge in dysfunction and suffering was mirrored by a rapid decrease in mean SD + CO (Figure 2). At the 99th percentile, SD + CO was 2 standard deviations below the mean, mirroring high ratings of dysfunction and suffering. The seemingly different impact of each scaling step in the A-TAC algorithms thus disappears when transformed into percentiles.

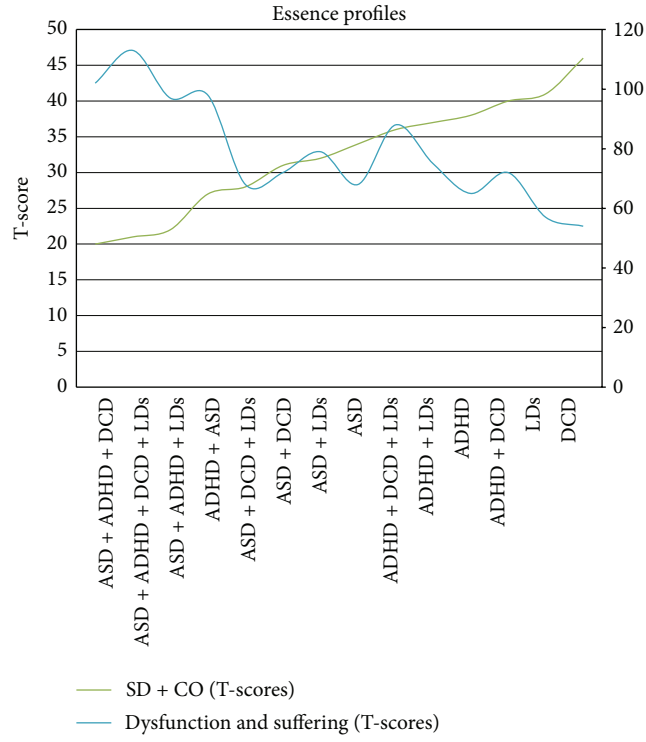


Figure 1: The graph shows means in SD + CO and dysfunction and suffering (T-scores) as a function of ESSENCE profiles. SD + CO: left-axis scale; dysfunction and suffering: right-axis scale.

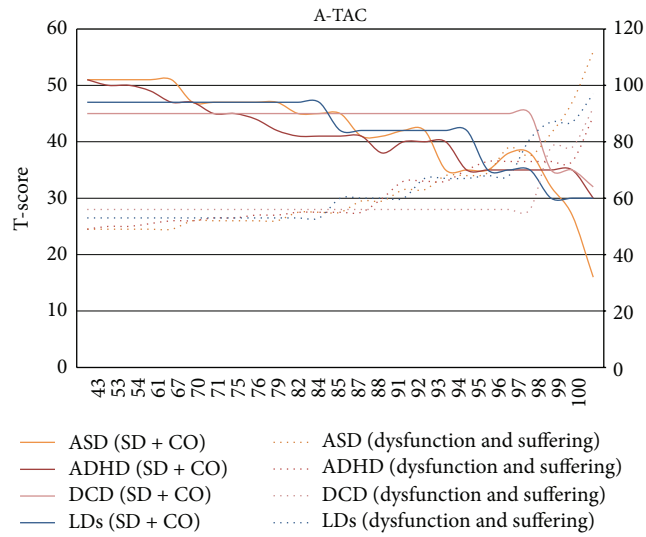


Figure 2: The graph shows means in SD + CO and dysfunction and suffering (T-scores) as a function of the population percentile. SD + CO: left-axis scale; dysfunction and suffering: right-axis scale.

## 4. Discussion

In this paper, we forward the knowledge of the field by showing that (1) the number of symptoms of ESSENCE is continuously associated with both deficient development of Self-directedness and Cooperativeness and psychosocial dysfunction and suffering on a population level in children aged 9 or 12. (2) Combinations of ESSENCE, especially those including ASDs, were associated with particularly low scores in Self-directedness and Cooperativeness and with higher

Table 1: Number of individuals (*N*), means (*M;* bold typed), and standard deviations (sd) in SD + CO (T-scores) for each gate score in the A-TAC modules: ASDs, ADHD, LDs, and DCD.

| A-TAC score | | 0 | 0.5 | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 | 3.5 | 4.0 | 4.5 | 5.0 | 5.5 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | 9.0 | 9.5 | 10.0 | 10.5 | 11.0 | 11.5 | 12.0 | ≥12.5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *N* | 657 | 291 | 215 | 141 | 121 | 75 | 69 | 57 | 35 | 33 | 22 | 24 | 9 | 19 | 18 | 10 | 11 | 83* | | | | | | | | |
| ASDs | *M* | **50.7** | **47.0** | **44.7** | **41.3** | **42.3** | **34.8** | **35.1** | **38.4** | **37.6** | **31.8** | **32.3** | **29.9** | **30.2** | **22.2** | **21.2** | **28.9** | **30.5** | **16.0** | | | | | | | | |
| | Sd | 9.6 | 11.4 | 13.2 | 15.1 | 12.4 | 13.7 | 14.1 | 15.1 | 11.3 | 16.8 | 20.4 | 17.1 | 16.2 | 13.6 | 18.2 | 16.5 | 13.5 | 16.2 | | | | | | | | |
| | *N* | 504 | 164 | 139 | 98 | 80 | 80 | 57 | 56 | 56 | 46 | 51 | 46 | 39 | 37 | 33 | 29 | 32 | 25 | 27 | 20 | 24 | 27 | 24 | 23 | 16 | 154 |
| ADHD | *M* | **51.3** | **49.5** | **49.1** | **46.9** | **45.1** | **44.3** | **41.8** | **41.5** | **41.3** | **40.7** | **35.8** | **41.0** | **39.1** | **35.1** | **33.9** | **37.9** | **32.7** | **37.5** | **39.7** | **34.2** | **31.9** | **34.8** | **31.1** | **29.6** | **26.1** | **26.1** |
| | Sd | 9.5 | 11.3 | 9.7 | 10.9 | 12.2 | 14.0 | 13.0 | 15.6 | 13.6 | 13.7 | 17.4 | 12.4 | 13.9 | 14.1 | 15.2 | 14.2 | 13.7 | 15.1 | 14.6 | 15.5 | 15.7 | 17.2 | 15.6 | 16.9 | 16.2 | 18.6 |
| | *N* | 1180 | 203 | 157 | 106 | 102 | 55 | 88 | | | | | | | | | | | | | | | | | | | |
| LDs | *M* | **46.6** | **42.0** | **41.6** | **35.5** | **35.2** | **29.7** | **29.6** | | | | | | | | | | | | | | | | | | | |
| | Sd | 13.0 | 15.3 | 15.4 | 16.7 | 18.2 | 18.3 | 16.5 | | | | | | | | | | | | | | | | | | | |
| | *N* | 1591 | 211 | 89 | | | | | | | | | | | | | | | | | | | | | | | |
| DCD | *M* | **44.9** | **34.7** | **31.7** | | | | | | | | | | | | | | | | | | | | | | | |
| | Sd | 13.9 | 17.6 | 20.4 | | | | | | | | | | | | | | | | | | | | | | | |

* ≥8.5.

Table 2: Number of individuals (*N*), means (*M*; bold typed), and standard deviations (sd) in dysfunction and suffering (T-scores) for each gate score in the A-TAC modules: ASDS, ADHD, LDs, and DCD.

| A-TAC score | | 0 | 0.5 | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 | 3.5 | 4.0 | 4.5 | 5.0 | 5.5 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | 9.0 | 9.5 | 10.0 | 10.5 | 11.0 | 11.5 | 12.0 | ≥12.5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ASDs | *N* | 657 | 291 | 215 | 141 | 121 | 75 | 69 | 57 | 35 | 33 | 22 | 24 | 9 | 19 | 18 | 10 | 11 | 83* | | | | | | | | |
| | *M* | **48.9** | **51.9** | **54.8** | **59.5** | **63.3** | **67.9** | **68.9** | **77.9** | **74.9** | **78.7** | **89.2** | **87.8** | **81.1** | **103.3** | **100.2** | **80.8** | **103.5** | **112.3** | | | | | | | | |
| | Sd | 4.0 | 8.5 | 11.5 | 14.0 | 16.1 | 18.7 | 19.3 | 18.9 | 20.9 | 20.0 | 23.4 | 26.6 | 24.5 | 26.5 | 23.7 | 20.2 | 21.7 | 30.4 | | | | | | | | |
| ADHD | *N* | 504 | 164 | 139 | 98 | 80 | 80 | 57 | 56 | 56 | 46 | 51 | 46 | 39 | 37 | 33 | 29 | 32 | 25 | 27 | 20 | 24 | 27 | 24 | 23 | 16 | 154 |
| | *M* | **48.8** | **49.7** | **51.0** | **52.1** | **52.8** | **54.0** | **53.9** | **55.3** | **59.0** | **60.3** | **59.9** | **63.0** | **70.5** | **66.8** | **73.7** | **67.2** | **78.4** | **74.3** | **74.8** | **78.6** | **80.3** | **75.9** | **92.1** | **87.1** | **92.6** | **99.4** |
| | Sd | 3.7 | 5.1 | 7.3 | 9.3 | 8.0 | 11.2 | 9.9 | 12.1 | 13.6 | 15.2 | 15.3 | 16.6 | 21.4 | 21.8 | 21.9 | 21.4 | 24.5 | 19.8 | 21.7 | 21.2 | 28.2 | 21.3 | 28.1 | 19.8 | 25.3 | 28.8 |
| LDs | *N* | 1180 | 203 | 157 | 106 | 102 | 55 | 88 | | | | | | | | | | | | | | | | | | | |
| | *M* | **53.5** | **60.2** | **66.6** | **67.9** | **80.7** | **86.6** | **96.5** | | | | | | | | | | | | | | | | | | | |
| | Sd | 13.2 | 18.7 | 24.5 | 20.6 | 27.1 | 28.3 | 29.5 | | | | | | | | | | | | | | | | | | | |
| DCD | *N* | 1591 | 211 | 89 | | | | | | | | | | | | | | | | | | | | | | | |
| | *M* | **56.5** | **78.0** | **91.8** | | | | | | | | | | | | | | | | | | | | | | | |
| | Sd | 16.1 | 28.9 | 35.0 | | | | | | | | | | | | | | | | | | | | | | | |

* ≥8.5.

Table 3: Number of individuals and mean (T-scores) in Self-directedness, Cooperativeness, SD + CO, and dysfunction and suffering across ESSENCE profiles.

| ESSENCE profile | *N* | Self-directedness | Cooperativeness | SD + CO | Dysfunction and suffering |
|---|---|---|---|---|---|
| ASDs + ADHD + DCD | 25 | 23 | 26 | 20 | 102 |
| ASDs + ADHD + DCD + LDs | 79 | 23 | 28 | 21 | 113 |
| ASDs + ADHD + LDs | 50 | 24 | 29 | 22 | 97 |
| ADHD + ASDs | 28 | 33 | 28 | 27 | 98 |
| ASDs + DCD + LDs | 9 | 28 | 35 | 28 | 68 |
| ASDs + DCD | 9 | 39 | 29 | 31 | 72 |
| ASDs + LDs | 9 | 30 | 41 | 32 | 79 |
| ASDs | 20 | 37 | 35 | 34 | 68 |
| ADHD + DCD + LDs | 44 | 33 | 44 | 36 | 88 |
| ADHD + LDs | 105 | 34 | 44 | 37 | 75 |
| ADHD | 151 | 39 | 41 | 38 | 65 |
| ADHD + DCD | 28 | 40 | 43 | 40 | 72 |
| LDs | 181 | 43 | 48 | 41 | 57 |
| DCD | 75 | 46 | 47 | 46 | 54 |

rating scores of dysfunction and suffering. (3) The impact of symptoms of ESSENCE on deficient Self-directedness and Cooperativeness and psychosocial dysfunction and suffering was found in a milder form in about 16% of all children and a severe form in about 2%, which corresponds to an underlying normal distribution of overall mental health.

Based on the findings presented here, the following conclusions may be drawn. First, not only in adults [25, 33, 34] and adolescents [35–41] but also in childhood, the Self-directedness and Cooperativeness scales measure an intrinsic aspect of global mental health. At least, low-to-very low scores identify something shared by individuals who (also) exhibit symptoms of mental disorders and associated functional deficits and/or suffering. It may be argued that low Self-directedness and Cooperativeness is merely an epiphenomenon, a "marker" of the neuropsychiatric dysfunctions, and that lacking sense of responsibility, self-control, and social skills such as tolerance to others, empathy, and the ability to be helpful and showing compassion is part of the definitions of ADHD and ASDs. The clear association to the dysfunction and suffering scale here, however, speaks against this stance. How successful a person is in influencing his or her own behavior and in interacting with others depends on sophisticated metacognition (i.e., thinking about thinking, taking different perspectives, and evaluating possible consequences of actions on others and on oneself) based on intuition and other emotions, mental strength and education-given knowledgeable insights, goals, and respect. Deficiencies in these processes, expressed as undercontrolled behavior patterns with destructive consequences, may be seen as "endophenotypes" of the ESSENCE conditions. This is supported by recent results [24], where cross-twin cross-trait correlations indicate commonalities in the etiology in ADHD, ASDs, and Self-directedness and Cooperativeness. A viable approach for future twin studies would be to disentangle the etiological association between Self-directedness and Cooperativeness and ESSENCE. The results presented here indicate that goal setting, effortful control, respect for the own person and for others (all descriptions of high Self-directedness and Cooperativeness) are important in order to avoid developing the full picture of psychosocial dysfunction and suffering associated with severe forms of ESSENCE.

Second, the results seem to indicate worse trajectories for those that are impaired in multiple ESSENCE domains, which further highlights the need for broad assessments. Further studies should investigate whether the number of conditions is an independent risk factor even when the total score is taken into account.

Third, the continuous population association results further advance the notion that there is no qualitative demarcation between traits and disorders [10, 30]. The mirroring of the SD + CO to dysfunction and suffering suggests that ESSENCE traits, or a third factor associated to both ESSENCE and SD + CO, give rise to mental health vulnerability in a considerable group of developing individuals, while the impact is severe on a small group of individuals; that is, if problems are prolonged, they may be more prone to develop deleterious disorders like schizophrenia.

*4.1. Clinical Implications.* The main focus of interventions for ESSENCE has been directed towards the core-symptoms of the disorders per se (e.g., pharmacotherapy for inattention/hyperactivity, special education for learning problems, and sociocommunicative training for ASDs). However, there is now evidence from children [24], adolescents [42], and adults [20] to state that Self-directedness and Cooperativeness are intrinsic to ADHD and ASDs, and conversely, that behavior problems referred to as personality disorders, deviant personality traits, destructive behavior patterns, or merely poor education, on the population level and in many individual cases, have antecedents in the form of childhood neuropsychiatric problems as included in the ESSENCE definition.

Recent population-based longitudinal studies show increases in Self-directedness and Cooperativeness (which

is an indicator of increasing responsibility and relatedness) with age (from 20 to 45) [43]. Prospective studies show that parental care giving and home environment are more strongly associated with offspring's Self-directedness and Cooperativeness than with offspring's temperament later in adulthood [44]. Moreover, the possibility to treat deficiency in Self-directedness and Cooperativeness in relation to ESSENCE in the developing years is supported by a recent adolescent study, where the possibility to develop a sense of responsibility (i.e., self-directed behavior) and cooperation even when constrained by genetic and environmental adversity was assessed [42]. Monozygotic cotwins of probands reporting severe personality problems (i.e., extremely low in Self-directedness and Cooperativeness) were found to vary widely into the normal range. This pattern was also found among monozygotic co-twins to probands who had a parent-rated DSM-IV disruptive behaviour disorder (i.e., attention-deficit/hyperactivity disorder, oppositional defiant disorder, or conduct disorder). In other words, Self-directedness and Cooperativeness are to some degree malleable even under genetic and environmental adversity. Thus, the identification of Self-directedness and Cooperativeness as a core deficit in ESSENCE might be a promising starting point to focus on for professionals in the treatment of children impaired within multiple domains. The success of such collective effort might end in the alleviation of dysfunctions and self-related suffering.

According to Cloninger [45], therapeutic interventions focusing on the development of positive emotions and different constructs of Self-directedness and Cooperativeness (e.g., sense of responsibility and purpose, helpfulness, and empathy) have been shown to enhance well-being and provide alleviation for problems and disabilities in the general population, as well as in most, if not all, mental disorders [33, 45–50]. When compared with cognitive behavioral therapy or psychotropic medications alone, these interventions show improvements in Self-directedness and Cooperativeness and in treatment adherence among individuals with mental disorders [45]. The question whether Self-directedness and Cooperativeness can be increased among children with ESSENCE, however, remains to be formally tested in controlled trials, before personality disorders and their spectra of associated mental health problems are established in early adulthood. It is plausible to suggest that the adolescent years provide a window of opportunities for improving an individual's Self-directedness and Cooperativeness. Indeed, neuroimaging research suggests that cognitive and behavioral changes occurring during adolescence might be understood from the perspective of increased "executive functioning" (e.g., attention, response inhibition, regulation of emotion, organization, and long-range planning; for a review, see [51]).

*4.2. Limitations.* The findings in this paper should be viewed in the light of some limitations. (1) The scores for dysfunctions and suffering have not been formally validated. In support of the assumption that these questions provide valid information on children, it may be argued that they are concrete questions asked after describing every possible diagnostic symptom of the condition, and that they have convergence with the symptom scores and the scores presented here. (2) The finding that the presence of multiple ESSENCE domains was associated with a more severe impairment might have been an artifact from the rating process, as broader problems in several modules gave more opportunities to answer dysfunction and suffering questions. However, the concomitant decrease in SD + CO would speak against the notion of this as merely an artifact. In addition, it is unusual that individuals with ASDs do not report one single ADHD symptom [52], and since only one fully or partially endorsed question in any of the A-TAC modules would have led to the questions of dysfunction and suffering, it seems unreasonable that this would explain a large part of the observed effect. (3) The low sensitivity and specificity of the DCD-cutoff warrants caution when interpreting the results, at the same time it was associated (±0.5 standard deviations) with a decreased SD + CO and an increase in dysfunction and suffering.

## 5. Conclusion

Self-directness and Cooperativeness are related to a number of problems included in the ESSENCE and to dysfunction and suffering in individuals screening positive for ASDs, ADHD, LDs, and DCD. These associations can also be discerned on a population level. Based on symptom scores, it would seem that ASDs have a stronger influence, compared to that of ADHD, on Self-directedness and Cooperativeness, but this effect disappeared when the population distribution was accounted for. The results from the present study would indicate that developmental deficits in Self-directedness and Cooperativeness affect a group of about 16% of all children moderately and 2% of all children severely.

Medicalization of problems ("it was the ADHD that smashed the window" or "it's a disease, nothing he/she can help") may contribute to the development of even lower Self-directedness and Cooperativeness and thereby even more severe mental health problems. Therapeutic interventions focusing on Self-directedness and Cooperativeness might provide a novel method for child psychiatry in its approach to ESSENCE and also provide constructive ways to acknowledge the reality of neurocognitive problems.

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*Clinical Study*

# A Feasibility Randomised Controlled Trial of the New Orleans Intervention for Infant Mental Health: A Study Protocol

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Child maltreatment is associated with life-long social, physical, and mental health problems. Intervening early to provide maltreated children with safe, nurturing care can improve outcomes. The need for prompt decisions about permanent placement (i.e., regarding adoption or return home) is internationally recognised. However, a recent Glasgow audit showed that many maltreated children "revolve" between birth families and foster carers. This paper describes the protocol of the first exploratory randomised controlled trial of a mental health intervention aimed at improving placement permanency decisions for maltreated children. This trial compares an infant's mental health intervention with the new enhanced service as usual for maltreated children entering care in Glasgow. As both are new services, the trial is being conducted from a position of equipoise. The outcome assessment covers various fields of a child's neurodevelopment to identify problems in any ESSENCE domain. The feasibility, reliability, and developmental appropriateness of all outcome measures are examined. Additionally, the potential for linkage with routinely collected data on health and social care and, in the future, education is explored. The results will inform a definitive randomised controlled trial that could potentially lead to long lasting benefits for the Scottish population and which may be applicable to other areas of the world. This trial is registered with ClinicalTrials.gov (NC01485510).

## 1. Background

Child maltreatment is known to be associated with significant problems in later life affecting both physical [1] and mental health [2–4]. Intervening early can improve outcomes when children's social and emotional development is at risk [5], and recovery from the effects of maltreatment is possible if children are provided with safe and nurturing care early, ideally in the first year of life [6–8]. Failure to do so puts children at risk of disrupted attachments and poor emotional well-being [9]. There is a growing international research and policy consensus on the need for prompt decisions about permanent placement (i.e., regarding adoption or return home) so that children can experience secure care as early as possible [9–14]. However, a recent audit of services in Glasgow revealed that children frequently "revolve" between maltreating birth parents and various temporary foster placements [10]. Moreover, there are no infant mental health services focusing on maltreated infants in Scotland.

There have been attempts to develop interventions to improve the mental health of maltreated infants [6, 7], but only one evaluated programme was identified, the Tulane Infant Team in New Orleans, Louisiana [8]. This is still in operation and aims to improve the permanency decision-making process using a comprehensive mental health intervention. Permanency decisions involve placing a child in the care of one family until the child reaches the age of independence. The Tulane Infant Team offers a tailored intervention to every family with a child coming into care. It assesses the quality of child's relationships and the degree of change over the course of the intervention. It makes considered recommendations to inform the legal system about the best placement outcome for each child. The aim of the Tulane Infant Team is to rehabilitate children back to their birth parents, and when this cannot be achieved safely or quickly enough, to free the children for adoption. An evaluation based on analysis of routine data was conducted four years prior to and four years after the introduction of this intervention to New Orleans [8]. This suggested that more children were adopted following its introduction; however, for those returned to birth families, there was a significant reduction in repeated maltreatment both for that child and subsequent siblings. The limitation of the study was a consecutive cohort design, and the lack of randomisation means that factors other than the intervention may be contributing to the positive effects.

Deciding which are the most appropriate outcome measures for this population is challenging. Gillberg [11] described the high levels of coexistence between symptoms of different disorders in early childhood, which he defined as ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations). This demonstrates the need for a diverse and thorough assessment across the various fields described by Gillberg [11], including general development, language, social interrelatedness, mood, and behaviour.

The overall aim of this exploratory randomised controlled trial (RCT) is to evaluate the feasibility and to inform the design of a definitive RCT evaluating a Scottish adaptation of the New Orleans intervention for maltreated children. The specific research questions are as follows:

(1) what are the size and nature of any effects of the Glasgow version of the New Orleans model, the Glasgow Infant and Family Team (GIFT), on the mental health of maltreated preschool children?

(2) is a definitive multicentre RCT of GIFT feasible, acceptable, and necessary?

(3) what would be the required size of a definitive RCT of GIFT?

(4) what would be the optimal outcome measures for a definitive RCT of GIFT?

(5) what are the beliefs, attitudes, and experiences of those managing and delivering GIFT and an enhanced usual service, the Family Assessment and Contact Service (FACS)?

(6) is GIFT likely to be cost-effective in Glasgow and, if so, what design parameters are required for a definitive RCT?

## 2. Methods/Design

*2.1. Study Design and Setting.* This study is an RCT comparing two arms: GIFT (the intervention arm) and FACS (enhanced version of services as usual arm). Outcome measures from all participants are being collected one month after a child comes into care and then again one year later.

The study is set in the city of Glasgow, Scotland's largest and most ethnically diverse city with an estimated population of 588,470 of which almost 6% represent an ethnic minority (http://www.glasgow.gov.uk/index.aspx?articleid=3969). Children represent 16% of the Glasgow population; over one-third live in areas in the most deprived decile within Scotland, whilst only 3% live in areas in the least deprived decile within Scotland.

*2.2. Participants.* All parents (or recognised parental guardians) with a child aged between 6 and 60 months who come into a period of care due to child protection concerns are invited to take part in the study. Children are excluded from the study if

(1) they have a profound learning disability (as assessment outcome measures would not be appropriate),

(2) and/or their primary caregiver is unavailable to take part in the intervention (such as long-term imprisonment, death, or being uncontactable by services or research team for 3 months or more).

*2.3. Recruitment and Randomisation.* Recruitment is taking place over 17 months from December 2011 to April 2013. An estimated 153 eligible children are expected to enter care due to maltreatment during this period, that is, 9 children per month. Consent from parents and foster carers to be approached by the research team to discuss the study is obtained

by the social worker who gives the potential participants an information leaflet and a digital video disc explaining the study, its intent, and what participation would entail. Thereafter, informed consent from those agreeing to be contacted is obtained by the study's recruitment officer.

An anticipated consent rate of 65% will include approximately 100 families in the study, with 50 children in each trial arm (Figure 1). The families are randomly allocated to GIFT or FACS by the Robertson Centre for Biostatistics. Children from the same birth family, regardless of placement, are assigned the same study arm to reduce contamination (as birth parents are the primary target of the intervention). Randomisation is also stratified by child's age (<2 and ≥2 years). The trial arm allocation is concealed from the researchers who carry out the baseline and follow-up assessments, and the first research assessment is carried out prior to randomisation.

*2.4. Care as Usual: Family Assessment and Contact Service (FACS).* FACS comprises a team of social workers, which undertakes an assessment of the child and the family in order to make a decision about the child's future care. It examines family functioning and makes recommendations regarding placement outcomes for children. It is able to refer family members onto additional services (e.g., drug rehabilitation). Although FACS is an established service in Glasgow, it was previously a specialised team assessing only small numbers of children. As the delivery of early assessment services in Scotland was known to be highly heterogeneous, FACS will offer a new level of consistency and therefore is considered to be "enhanced services as usual". Any child whose parent or foster carer does not consent to participate in the research study will therefore receive the service from FACS.

*2.5. The Trial Intervention: Glasgow Infant and Family Team (GIFT).* GIFT is a structured intervention with the primary goal of rehabilitating the child back with their primary caregiver, when it is safe to do so. The team is multidisciplinary incorporating social workers, psychologists, a psychotherapist, and a psychiatrist. Like FACS, GIFT makes an assessment of the children in the context of their relationships with their caregivers. Whilst both teams assess relationships with the birth parents, GIFT also always assesses the relationships with foster carers. GIFT arranges referrals onto other services as described in FACS. GIFT also offers an intensive relationship focussed intervention to every birth family, which is anticipated to take between 6 and 9 months. This intervention is aimed at improving the relationship between the child and his/her birth family and according to the outcome, GIFT recommends whether the children should return home or be adopted. The intention is that all foster carers who care for children coming to the GIFT intervention should be jointly registered as potential adopters so that, if rehabilitation home is not feasible, the child does not have to experience another change of placement before achieving permanency. However, it is likely that this will take time to achieve and that not all carers will be dually registered within the recruitment period.

*2.6. Outcome Measures.* Baseline assessment based on the outcome measures is administered at a minimum of one month after the child is received into care. One month is allowed to let the carer get to know the child as well as to allow for the child to settle into the carer's home. Follow up assessment of the outcome measures is then repeated one year later. At baseline, the assessment is completed for all children with their foster carers. At follow up, the assessment is completed with the child's primary caregiver at that time who may be the birth parent, adoptive parent, or the foster carer—who may be the same or different from the foster carer at baseline.

*2.7. Primary Outcome Measure.* Infant mental health is measured using the Infant-Toddler Social and Emotional Assessment (ITSEA) [12, 13]. This 166-item questionnaire is well validated and is completed by the parent or carer [14]. It covers a wide range of social and emotional behaviours in infants, across four domains: externalising, internalising, dysregulation, and competence. It has been used successfully in previous interventions research with maltreated children showing medium to large effect sizes and good longitudinal stability [15].

*2.8. Secondary Outcome Measures.* A cognitive assessment of the child is undertaken. Children under 2.5 years are assessed with the Bayley Scales of Infant Development [16], while children 2.5 years and over are assessed using the Wechsler Preschool and Primary Scale of Intelligence (WPPSI IV) [17]. The parent or carer also completes the Parent Evaluation of Development Status (PEDS) [18] which assesses cognitive milestones including language, the Disturbances of Attachment Interview (DAI) [19] which identifies symptoms of attachment disorders, the Parent-Infant Relationship Global Assessment of Functioning (PIR-GAS) [20] which assesses global relationship functioning following observation of both play and meal time activities, and the Paediatric Quality of Life Inventory (PedsQL) [21] which assesses health-related quality of life. The Development and Well-being Assessment (DAWBA) [22] is completed by carers with a child aged two and above and is used to generate International Classification of Diseases (ICD) and Diagnostic and Statistical Manual of Mental Disorders (DSM) codes. The Waiting Room Observation (WRO) [23], a structured observation for symptoms of attachment disorders, is also completed by the researcher when the child and carer first arrive at the clinic. In addition, the Strange Situation Procedure (SSP) [24], the gold standard measure of infant/toddler attachment patterns, is completed at the follow-up time only.

In addition, the "This Is My Baby" (TIMB) [25] interview, which assesses the degree of commitment to the child by the foster carer is included as it may be investigated as a potential moderator between maltreatment and outcome.

In this exploratory trial, the feasibility, reliability, and developmental appropriateness of each measure will be examined in order to select the best measures for a definitive trial. In addition, the potential for linkage of data with routinely collected data on health and social care and, in the future, education and legal services will be explored.

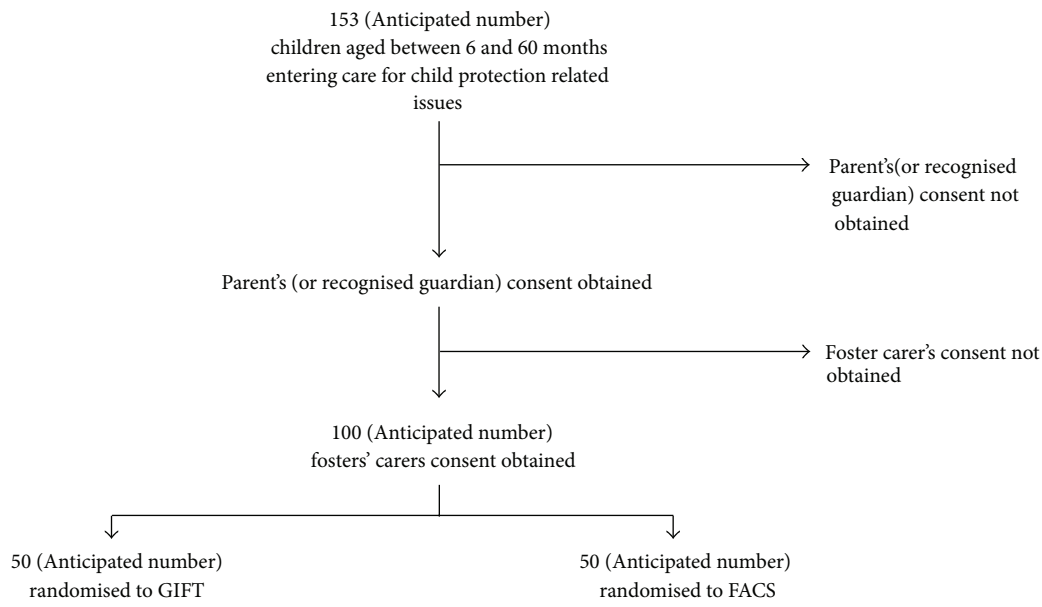


Figure 1: Anticipated number of eligible children recruited and randomised in the trial between December 2011 and April 2013.

*2.9. Data and Statistical Analysis.* The study will be analysed using the intention-to-treat analysis. To make preliminary assessment of the efficacy of GIFT, changes in scores on the ITSEA competence scale will be compared between the GIFT and FACS groups, adjusting for important baseline variables. To assess feasibility, the percentage consenting and the retention rate will be estimated: whether these are related to social circumstances or the type of intervention will be investigated using routine data where possible.

*2.10. Treatment Fidelity.* A fidelity monitoring model will be tailored to the specific needs of this complex intervention. This aims to capture five key components of fidelity [26] encompassing adherence to the prescribed intervention (staff supervision, training, and participant attendance), exposure (volume of trial intervention received per family), quality of delivery (monitoring assessment and treatment reports, focus group data), responsiveness of families (attendance and case studies), and program differentiation (identifying distinctive features and challenges). The purpose of the model is to ensure that the key components of the intervention are maintained throughout the study, to identify challenges and areas of improvement, and to generate data with which to compare evaluation results with the performance of the intervention.

*2.11. Health Economics.* An economic model will be built and populated with data from the trial to explore the potential cost-effectiveness of GIFT in comparison to FACS, using the ITSEA measure of child's mental health. Child's quality of life will also be measured within trial using the PedsQL for infants and toddlers. Measurement of quality of life is an important input for the economic component of this study and will enable assessment of any short-term change in quality of life for children between baseline and 1 year, and also between the trial arms. The model will be analysed probabilistically in order to characterize uncertainty in the model parameters and estimate confidence limits around the cost and effectiveness outcomes. The economic model will be used to help design the definitive trial proposal.

*2.12. Qualitative Process Evaluation.* Qualitative mapping and modelling work will accompany the exploratory trial in order to track the ways in which FACS and GIFT evolve and impact as services, capturing and exploring issues as they arise throughout the trial and feeding into service development. Qualitative work in the first part of the trial focuses on the implementation and delivery of services from the perspectives of social workers, foster carers, and the GIFT and FACS teams. The main data collection method for this purpose is focus group discussions, which will be repeated throughout the trial in order to track changes and developments over time. The trial consent process is also a focus in this first phase with data being collected from birth parents and foster carers who consent to the study, as well as the professionals responsible for the consent procedure. The second phase of the study, although still tracking the development of issues already gleaned in the first phase, will adopt case study methodology to focus more specifically on the impact of GIFT and FACS on a selection of children and families involved in the trial. This narrower focus will allow an in-depth investigation into the process of experience from the perspectives of the birth family, foster carers, social workers, and health professionals surrounding specific children enrolled in the trial. Case studies will be selected on the basis of a criterion matrix to allow exploration of the experience of receiving both services and different outcomes regarding permanency decisions. Key to this stage of the research is also the gathering of qualitative data from the Children's Hearing

System (a panel of specifically trained lay people who, in Scotland, are involved in most child's welfare decisions) in order to explore perspectives about the reports from the service and their impact on decision making.

The study was approved by the West of Scotland NHS Research Ethics Committee 5 and NHS Greater Glasgow and Clyde (Research and Development Committee). In addition, the research team attended Good Clinical Practice Training and also a study-specific session on obtaining informed consent from very vulnerable families. The protocol was registered before recruitment began on http://www.clinicaltrials.gov/.

## 3. Discussion

Both FACS and GIFT are new services and, during the mapping and modelling phase of this study, it was clear that opinion was divided as to which was likely to provide the best service for maltreated children. We are therefore in a position of equipoise.

The results from the study will provide us with the necessary findings in order to conduct a definitive RCT evaluating the New Orleans intervention for maltreated children. We aim to identify the feasibility of recruiting birth and foster families and the retention of these families to both the research and the interventions. We will assess not only the appropriateness of each measure but the assessments ability to capture problems in any ESSENCE domain. We will also explore the outcomes of the interventions. We will use fidelity monitoring to ascertain and optimise adherence to the GIFT model and to document the delivery of the control intervention. Health economic techniques will be used to assess the implications of such a model in terms of both the costs and outcomes, the results of which will feed into the development and design of a definitive RCT. In addition, we will explore qualitatively the perspectives of those implementing, delivering, and receiving the interventions as part of investigating the feasibility of implementing the model of intervention. In time, we will also examine the impact of the trial on the wider systems through routine data follow up.

Both GIFT and FACS aim to identify care arrangements which will ensure that the future care of any child who has experienced maltreatment is safe and nurturing. This could potentially lead to a long lasting benefit for the Scottish population as a whole, as well as a reduction in costs to society. Should the GIFT intervention be beneficial to infant's mental health and cost-effective in comparison to FACS, it would be important to consider whether a GIFT intervention could be of benefit in other areas of the UK to improve the life chances of maltreated children and address key policy goals such as improvement of school readiness and community safety.

*3.1. Limitations.* The GIFT team only has the capacity for a caseload of 50–60 children in one year. This limited capacity means that children removed from parents due to maltreatment but then placed in kinship care, being looked after by family members, are not included. This accounts for a large number of children who are removed from birth parents due to maltreatment. Children in kinship care may be included in future trials.

An additional limitation is that some children will change placement between baseline and follow up, meaning that there will be different respondents. If one intervention proves better at achieving permanent placements than the other, then the number of placement moves is likely to vary between the arms of the trial, thereby introducing bias. This creates a challenge in interpreting results, but the child's primary caregiver at the time is likely to be the best person to report on the child's health and development.

Children are allocated randomly into GIFT or FACS, and while birth siblings will all be allocated to the same intervention, this will not be possible for nonsiblings placed in the same foster care home. If both birth families and foster families were allocated to the same intervention then this would lead to significant clustering effects; that is, potentially large groups of children (e.g., a large birth sibship spread across several foster homes and all the associated foster sibships) could require randomisation together creating imbalances. Consequently, some foster carers may have children in their care going through both the GIFT and FACS assessments which has the potential to introduce contamination.

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*Research Article*

# Coexisting Disorders and Problems in Preschool Children with Autism Spectrum Disorders

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*Objectives*. To analyze cooccurring disorders and problems in a representative group of 198 preschool children with autism spectrum disorders (ASD) who had had interventions at a specialized habilitation center. *Methods*. Parents and children were seen by a research team. Data were based on parental interviews, pediatric assessments, and tests of the child. Information on autistic symptoms, general cognitive function, speech and language, motor function, epilepsy, vision, hearing, activity level, behavior, and sleep was collected. *Results*. Three ASD categories were used: (1) autistic disorder (AD), (2) autistic-like condition (ALC) or Asperger syndrome, and (3) one group with autistic symptoms/traits but not entirely all its criteria met for ASD. Children with autism had a mean of 3.2 coexisting disorders or problems, the ALC/Asperger group had a mean of 1.6, and children with autistic traits had a mean of 1.6. The most common disorder/problems in the total group pertained to language problems (78%), intellectual disability (ID) (49%), below average motor function (37%), and severe hyperactivity/ADHD (33%). *Conclusions*. The results accord with the concept of early symptomatic syndromes eliciting neurodevelopmental clinical examination (ESSENCE), and highlight the need of considering ASD in a broad perspective taking also other cooccurring developmental disorders into account.

## 1. Introduction

Autism spectrum disorders (ASDs) constitute complex and heterogeneous developmental disorders, and besides the core symptoms, children with ASD display many accompanying deficits and behavioral problems. Cooccurring disorders, such as intellectual disability, attention deficit hyperactivity disorder (ADHD), language impairment, epilepsy, and various types of behavioral disorders/problems, are common and will affect daily life. To provide adequate support and intervention for the child and the family, the child's total developmental profile as well as coexisting medical disorders needs to be considered.

Increased awareness in the society of ASD, screening at child health centers (CHCs) [1, 2], and improved habilitation and intervention services have contributed to the increased prevalence rates of ASD reported now and ASD is now diagnosed in children at younger ages than previously [3].

To establish a definite diagnosis at early ages, imply some uncertainties, especially in the milder variants of the spectrum. A change of the symptom/developmental profile may occur during the child's preschool age. Among several coexisting symptoms, some may become more manifest, and some may turn out to become less prominent. The importance of having a broad view in the assessment of young children with developmental deviations has been emphasized by Gillberg [4], who has developed the concept of early symptomatic syndromes eliciting neurodevelopmental clinical examinations (ESSENCE). This concept highlights that many disorders such as attention deficit/hyperactivity disorder

(ADHD), oppositional defiant disorder (ODD), tic disorders, developmental coordination disorder (DCD), language disorder, and intellectual disability (ID) may coexist in children in different combinations, and all these mentioned disorders may coexist with ASD. Many of these disorders are also accompanied by different types of behavioral problems—tantrums, sleeping problems, feeding problems, and sensory hyper- or hyposensitivities.

In young children, the dominating disorder or problem may not be clear, and there is a definite need to follow these children's developmental trajectory over time.

The importance of having such broad view was illustrated by Levy and collaborators [5] who examined cooccurring non-ASD diagnoses and symptoms in a population-based cohort of 8-year-olds with ASD, identified from 2,568 children in a multisite surveillance program. The cooccurrence of at least one other developmental diagnosis was 83%, and at least one other psychiatric diagnosis was found in 10%.

We have previously presented data from a representative group of about 200 children with ASD referred for intervention at a specialized habilitation center for young children with autism. Data on these children were collected at referral to the center and after two years during which the child had received intervention, mainly based on applied behavior analyses (ABAs) of varying intensities [6, 7].

The aim of this study was to give a comprehensive picture of these preschool children's coexisting conditions identified at the two-year follow-up and to relate these to the types of ASD.

## 2. Methods

*2.1. Participants.* The total group consisted of 198 children, 29 (15%) girls, aged from 4.5 to 6.5 years, who had received intervention for 2 years at a specialized habilitation center for young children with ASD in Stockholm. Details regarding the recruitment process are described in the previous paper [6] and data regarding the group at follow-up, after two years, in a following paper [7]. Of the 198 children, 119 (60%) had two Swedish born parents. All parents of children enrolled in the study communicated in Swedish or English. The children were assessed by our research team, consisting of two neuropediatricians, one pediatrician, and one child psychiatrist, two speech and language pathologists, and two psychologists [7].

Of the 198 children, 106 children were considered to meet criteria for autistic disorder (AD), 58 had autistic-like condition (ALC), 13 had Asperger syndrome, and 21 were considered not to meet full criteria for ASD at follow-up but had autistic traits. Four of these 21 children had an intellectual disability (ID). In the follow-up assessment, a DISCO interview was performed to ascertain the child's type of ASD, and all ASD diagnoses were based on DSM-IV criteria [7].

The group was considered to be relatively representative of ASD except for the most severely disabled children with ASD, such as those with very severe epilepsy or severe syndromes and a few other children who had their follow-up at ordinary habilitation centers, and therefore they are not included in our study [6].

*2.2. Data Collection.* A clinical interview with at least one of the parents had been carried out by one of the four physicians in the team. During the same visit, a clinical observation and physical developmental examination of the child were performed. The clinical interview followed a structured questionnaire and included a detailed developmental history and information about the child's current clinical symptoms. Moreover, the children were tested by a psychologist. Children without ID were also evaluated by an experienced speech and language pathologist.

*2.2.1. Intellectual Function.* Each child was invited to a cognitive assessment by an experienced psychologist with Griffiths' developmental scales [8] and/or WPPSI-III [9]. Intellectual disability (ID) was defined as a total IQ < 70.

*2.2.2. Language.* Within the project, all children without ID ($n = 101$) were invited to an assessment of receptive and expressive language carried out by a speech and language pathologist using the following tests: (1) Reynell developmental language scales III [10], (2) SPIQ [11], (3) Illinois test of psycholinguistic abilities (ITPA) [12] and (4) Processability test (grammar screening) [13]. A child was classified as having a language problem if the performance was below a set criterion in two or several of the tests. In addition, all children with ID were considered to have a language problem.

*2.2.3. Motor Function.* Motor function was estimated according to the motor skills domain score of the Vineland Adaptive Behavior Scales (VABS) [14]. A motor function problem was considered to be present if this score was below 70, that is, corresponding to below—2SD from the mean of 100.

*2.2.4. Epilepsy.* Epilepsy was documented when the child had a diagnosis of epilepsy confirmed in a following medical assessment [15].

*2.2.5. Vision and Hearing.* Visual impairments were recorded when parents reported that the child had a diagnosis of visual impairment, verified by an ophthalmological examination. A hearing impairment was recorded when this was confirmed by a hearing test. Vision and hearing tests are included in the 4-year health assessment at child health centers. Children who cannot cooperate or fail in these assessments or when there is a suspicion of visual or hearing problem before this age are referred for ophthalmological and/or a hearing examination.

*2.2.6. Activity Regulation and Behavioral Problems.* Parents were asked if the child had behavioral disorders or problems, including severe hyperactivity or diagnosed ADHD, severe hypoactivity, and problems with severe outbursts or severe sleeping problems. Activity regulation was also observed and noticed by the examining physician.

*2.3. Data Analyses.* A between-subjects ANOVA followed by post hoc tests (Fisher LSD) was used to examine if the mean number of coexisting problems differed significantly between ASD groups. An alpha level of .05 was used.

*2.4. Ethics.* The study was approved by the Ethics Committee in Stockholm.

## 3. Results

Of the 198 children, 181 (91%) had at least one coexisting disorder or problem, Figure 1. A between-subjects ANOVA showed that the mean number of coexisting problems differed significantly between ASD groups, $F1,184 = 35.94$, $P < .001$, $\eta 2_{\text{partial}} = .28$.

In the group of 106 children with AD, the mean number of coexisting disorders or problems was 3.2 (SD 1.4) (range 0–6), in the 71 children with ALC/Asperger syndrome, the mean number was 1.6 (SD 1.3) (range 0–5), and in the 21 children with autistic traits but not a full ASD diagnosis, the mean number of coexisting disorders or problems was 1.6 (SD 1.2) (range 0–4), Figure 2.

Post hoc test (Fisher LSD) revealed that the difference between the autism group and the ALC/Asperger group as well as the difference between the autism group and the Autistic traits group were significant ($P < .001$ for both comparisons). The difference between the ALC/Asperger group and the autistic traits group was not significant ($P > .1$).

*3.1. Language.* The most common recorded problem was related to receptive and expressive language. Of the 101 children without ID, parents of 94 children accepted to let their children participate in a language assessment. Of these, 94, 53 (56%) had a definite problem; that is, they fell below a set criterion in two or more of the language tests. The remaining 41 children either failed on one test only or passed all language tests.

When the children with ID ($n = 95$) and the children without ID who exhibited a definite language problem according to the assessment ($n = 53$) were included and the 7 children without ID who could not be assessed by a speech and language pathologist were excluded from the 196 children who had a DQ/IQ assessment, the rate of language problems was 78% (148/189).

*3.2. Intellectual Disability.* Of the 196 who had a cognitive test in the project, 95 (49%) received full DQ/IQ below 70. ID was more common in the group with AD, 80/105 children (75%), compared to the group with ALC/Asperger syndrome, 10/71 children (14%), and autistic traits, 4/21 children (19%).

*3.3. Motor Function.* More than a third of the children who had Vineland interview data (71/194; 37%) had a motor skills function below −2SD corresponding to a Vineland domain score below 70. Of these 71 children, 51 (72%) also had ID.

*3.4. Activity Regulation.* Severe hyperactivity or diagnosed ADHD was recorded in 63/198 children (32%) and severe hypoactivity in 6 children (3%). Of the 63 children with severe hyperactivity, 31 (49%) also had ID, and 39 (62%) also had AD.

*3.5. Tantrums.* Severe problems with tantrums were reported for 28/198 children (14%).

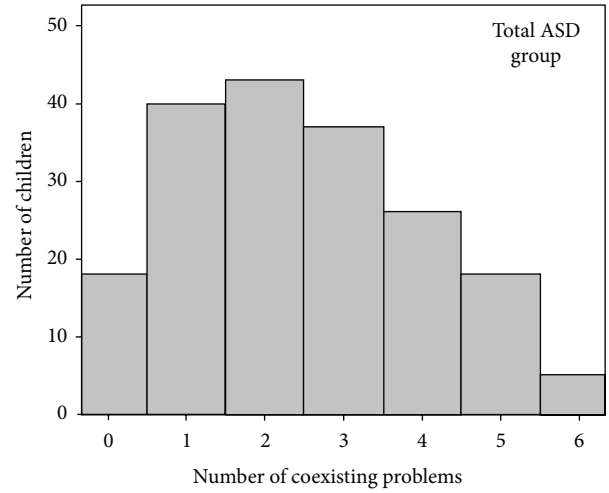


Figure 1: Numbers of coexisting problems/disorders in the total group of children with ASD ($n = 198$).

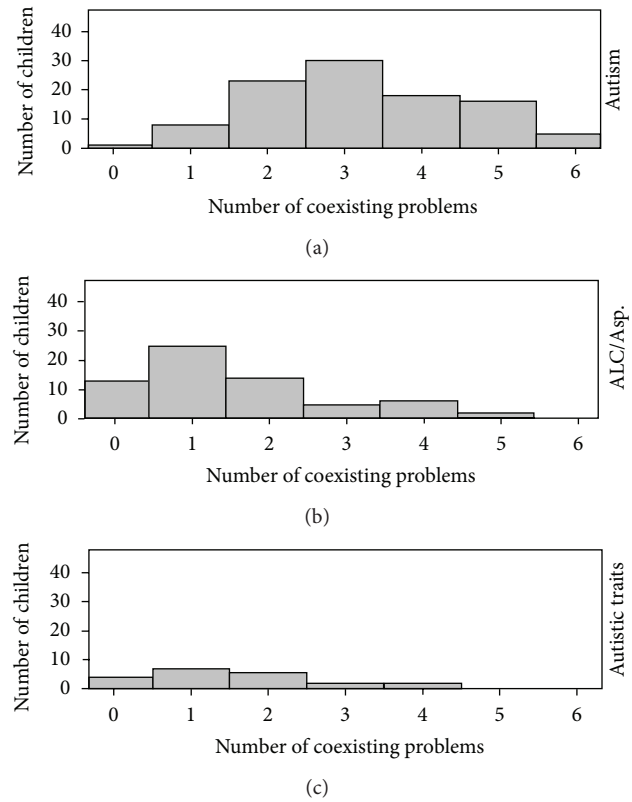


Figure 2: Numbers of coexisting problems/disorders in the three different ASD groups.

*3.6. Sleeping Problems.* Severe sleeping problems were reported for 24/198 children (12%).

*3.7. Vision and Hearing.* Any kind of visual impairment or strabismus was reported in 21/198 children (11%). Of these 21 children, 10 (48%) had ID. A hearing impairment was recorded in only one child (0.5%).

*3.8. Epilepsy.* At this time, 17 children (9%) had diagnosed epilepsy. Of these 17, 12 (71%) also had ID.

## 4. Discussion

Coexisting disorders and problems, in areas of many developmental and cognitive domains, including language, intellectual disability, and behavior, and with regard to motor function and epilepsy, were very common in this group of young children with ASD. When different subgroups of ASD were considered, children with AD had significantly more coexisting disorders compared to the group with autistic like condition/Asperger syndrome or those with autistic traits. The same finding with significant differences between diagnostic groups was also reported by Horowitz and collaborators [16] in their study of cooccurring psychiatric symptoms in toddlers with ASD.

The most common coexisting disorder in our study group was language problems occurring in 78% of the total group. The children comprised, on the one hand, the 95 children who due to their general cognitive impairment, ID, were considered to have a definite language problem, and on the other hand, the 53 out of the 94 children without ID (56%) who had been assessed by a speech and language pathologist and had been found to exhibit language problems. Language and/or communicative impairments or problems of different types and severities are part of the autism spectrum and vary highly according to the general intelligence of the child with ASD and according to the type and severity of the ASD per se. The previous, mentioned concept of ESSENCE highlights relationships between language delay/disorder and other developmental disorders [4]. In many children with autism, language delay is the presenting symptom that will entail further developmental evaluation. The importance of considering language delay in a wider developmental perspective was demonstrated by Miniscalco and collaborators [17] who followed children with marked language problems, as identified at the child health screening at the age of 2.5 years. At the age 7 years, 72% of the children were found to have a major neuropsychiatric or learning disorder.

Almost half of the preschool children had ID in combination with ASD. In the group with AD, the rate of ID was 80/106 (75%) which is in accordance with O'Brien and Pearson [18] who found that autism is more common among individuals with ID and increases with lower levels of IQ.

Low motor skills function was found in about a third in this study group. Motor function in children with ASD relates to the wide aetiological panorama of ASD and to the general cognitive function. In our group, 72% of those with low motor function also had ID. In our previous study, we found that age at unsupported walking in this group of children with ASD differed significantly from Swedish norms [6]. There was a clear correlation between late onset of walking and ID, present in almost all children who started to walk after the age of 18 months.

Autism and attention deficit disorder cooccur to a considerable degree. Both disorders are relatively common with ADHD showing a prevalence of 5% [19] and ASD a prevalence of about 1% [20] in the general population. Comorbidity of ADHD in ASD patients has been found to be around 30% as estimated in an epidemiologically based study [21]. The authors underlined the necessity of always evaluating cooccurring psychiatric disorders in children with ASD since these may provide targets for intervention. Evidence for overlapping genetic influences on autistic and ADHD behaviors was reported by a UK study based on a community twin sample [22]. There was a substantial overlap between ASD and ADHD; 41% of children who met criteria for ASD had suspected ADHD, and 22% with suspected ADHD met criteria for ASD. The findings support the idea that there are some common genetic influences operating across autistic traits and ADHD behaviors throughout normal variation as well as at the extreme. As pointed out in the paper by Frazier and collaborators [23], the importance of considering stimulant medication also in children with PDD/ASD and ADHD to improve adaptive behavior must be considered for this patient group.

Common challenging behaviors in children with autism are aggression, property destruction, disruptions/tantrums, impulsivity, self-injurious behaviors, and stereotypies [24]. These behaviors are the targets of many intervention programs of today for children with autism. The relatively low rate of behavioral problems/tantrums in our study group may be due to the early interventions that had been provided in this group. The applied behavior analysis (ABA) programs incorporate methods to modify and improve problem behavior [25]. The importance of the concept of an "autism-friendly environment" has been emphasized by Billstedt and collaborators [26] and conveys important considerations.

In our group, 12% of the children exhibited severe sleeping problems, mainly with insomnia. In a Norwegian study, sleep problems in children with autism were reported to be more than ten times higher compared to controls. The authors also found that the sleep problems were more persistent over time, implying a need for increased awareness of these problems in children with autism [27].

In our group of preschool children, epilepsy was found in 9%, and the rate can be expected to rise over time. The prevalence of epilepsy in samples of children with ASD varies according to the age group studied, etiology of ASD, and cooccurring ID. In our group, 71% of the children with epilepsy also had ID [15]. In the study by Bolton and collaborators [28], seizures in the majority of children with autism began after 10 years of age.

## 5. Limitations

In this study, only definite disorders or severe problems were considered. There were additional children with parental reports of some or minor problems, that is, those with borderline intellectual function and those with signs of hyperactivity but not definitely deviant from developmental age. There were also children who failed in one of the speech and language tests, but this was not considered to be a definite problem. However, in some children the problems may be more overt over the coming years. We did not have resources to examine all children with ID with regard to specific language problems. Another limitation is that we

considered that all children with ID would have a language problem due to their general cognitive impairment. Other limitations are due to the lack of formal testing for ADHD and motor performance. Data on tantrums and sleeping problems were only collected through parental interview and not from parental diaries.

## 6. Conclusion

Our study of a representative group of preschool children with ASD demonstrates that most children had additional disorders or developmental problems. There were also children in this study group with minor developmental deviations which may turn out to become more significant over time. Cooccurring ID was strongly related to the presence of many other comorbidities, such as motor skills problems, hyperactivity, epilepsy, and visual problems.

The interplay of many disorders and problems cooccurring with ASD illustrates the validity of the concept of ESSENCE. About 90% of the children in our cohort of children with ASD, consisting of about 200 young children, exhibited other problems than the ASD per se. Thus, coexisting conditions should always be looked for in the assessment procedure.

## Conflict of Interests

The authors have no conflict of interests.

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*Research Article*

# Reactive Attachment Disorder in the General Population: A Hidden ESSENCE Disorder

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Reactive attachment disorder (RAD) is a severe disorder of social functioning. Previous research has shown that children with RAD may have poor cognitive and language abilities; however, findings mainly come from biased, institutionalised samples. This paper describes the characteristics of all children who were given a suspected or likely diagnosis of reactive attachment disorder in an epidemiological study of approximately 1,600 children investigating the prevalence of RAD in the general population. We found that children with RAD are more likely to have multiple comorbidities with other disorders, lower IQs than population norms, more disorganised attachment, more problem behaviours, and poorer social skills than would be found in the general population and therefore have a complex presentation than can be described as ESSENCE. We discuss the clinical and educational implications.

## 1. Introduction

Reactive attachment disorder (RAD) is a severe disorder of social functioning. It has two subtypes: inhibited type, where the child will display wary, watchful, and hypervigilant behaviours and disinhibited type, where the child displays indiscriminately friendly behaviours, engages socially with strangers, and shows no need to remain near the safety of their primary caregiver [1]. It is thought that RAD is a result of severe maltreatment in early childhood, and there is research indicating that adopted children will be more likely diagnosed as having RAD than children raised by a biological parent [2].

In addition to the core features described above, there are numerous symptoms associated with RAD for example, Stinehart et al. [1] describe some potential early symptoms including failure to gain weight or feeding difficulties developing into unusual eating habits, lack of empathy, or impulse control which could lead to criminal behaviours and cruelty to animals as the child grows older. Both DSM and ICD state that core symptoms of indiscriminate friendliness or emotional withdrawal/hypervigilance need to be present before age 5. We would therefore describe RAD as having early symptomatic symptoms eliciting neurodevelopmental examination (ESSENCE).

There have been many studies which have examined cognitive and developmental characteristics of children with this disorder. Minnis et al. [3] compared children who had been referred by a clinician as they were suspected to have RAD with a general population comparison group. They found that children with RAD had significantly higher problem scores on both parent and teacher reports in the Strengths and Difficulties Questionnaire (SDQ) which covers symptoms of conduct problems, emotional problems (anxiety and depression), hyperactivity, and peer relations. They also had a lower receptive vocabulary than the comparison group, on the British Picture Vocabulary Scale (BPVS). A further study with these children showed that children with RAD

demonstrate significant problems in social relatedness and pragmatic language skills with a degree of severity equivalent to children in an ASD comparison group [4].

Kocovska et al. [5] looked at the characteristics of adopted children with a history of severe maltreatment, who were indiscriminately friendly. They found that these children had a lower IQ than a comparison group, were more likely to have language problems and to have several comorbid psychiatric disorders.

Some of the key research in this area comes from the Bucharest Intervention Studies. Zeanah et al. [6] have published widely on their randomised controlled trial of foster placement as an alternative to institutionalisation in abandoned infants and toddlers in Romania. They have found high levels of Reactive Attachment Disorder symptoms in the sample and associations between RAD and lower cognitive ability [7]. In addition, their results show adverse effects of poor institutional care on later language development [8], and found attachment security as an important mediator of the relationship between the quality of early caregiving and later psychopathology [9].

These important studies have shown that children with RAD may experience additional problems affecting both development and future outcomes. Gillberg [10] discussed the coexistence of disorders, concluding that the sharing of symptoms across disorders is the rule rather than the exception and argued that numerous childhood disorders such as autism spectrum disorder, attention deficit hyperactivity disorder, and reactive attachment disorder all share symptoms in the early stages which should be treated by a multidisciplinary team of specialists. RAD has not traditionally been considered to be a neurodevelopmental disorder, as it is thought to be caused by maltreatment, but it may be that maltreatment in early life can set in train developmental trajectories that are shared by other ESSENCE disorders.

Because all of the previous research has been conducted in clinical or otherwise select samples, such as children from institutions, we were keen to explore the difficulties which children with RAD encounter while living in the general population. Minnis and colleagues [11] conducted the first epidemiological study focussing on the prevalence of RAD in the general population and found a prevalence of 1.4%. With such a high prevalence of RAD in the general population, it is imperative to understand the additional needs of these children. This study describes the characteristics of the children identified as having RAD in this sample. We were interested to explore whether children with RAD in the general population also have complex, overlapping problems i.e. are they an example of children with ESSENCE?

## 2. Method

*2.1. Design and Participants.* This study was part of a population-based study investigating the prevalence of Reactive Attachment Disorder (RAD) in 6–8 years old children from a sector of a UK city characterised by high levels of deprivation. For a detailed description of the methodology, see [11]. The prevalence paper predicted 23 RAD cases, made up of 13 children who were given a definite diagnosis of RAD and an additional 10 cases that would have been expected to have been diagnosed with RAD using an imputation dataset.

This current paper describes the characteristics of the 13 children who were given a definite diagnosis of RAD and an additional 9 with a suspected or likely diagnosis of Reactive Attachment Disorder after screening of the total population of 1600 children. Of this sample ($n = 22$), fourteen completed the whole procedure; however, the remaining 8 children did not complete the cognitive or attachment measures. One family had moved away, one was uncontactable, and six opted out including three who felt the child's difficulties were too extreme to cope with the assessment, or they were already seeing enough professionals that they did not want to place additional burden on the child.

*2.2. Measures*

*2.2.1. Strengths and Difficulties Questionnaire (SDQ).* The SDQ is a brief behavioural screening questionnaire for 3–16 years olds [12]. It contains 25 items, covering 5 subscales: emotional symptoms; conducts problems; hyperactivity/inattention; peer relationship problems; and prosocial behaviour. It can be completed by the children themselves, the caregiver, or the teacher. In this study, both the parent/carer and the teacher completed the SDQ.

*2.2.2. Relationship Problems Questionnaire (RPQ).* The RPQ is a 10-item parent and teacher-report screening instrument for RAD symptoms [13]. In a large general population twin sample, the RPQ had good internal consistency (Cronbach's alpha .85), and factor analysis identified that 6 items describe inhibited RAD behaviours and 4 items describe disinhibited RAD behaviours [13].

*2.2.3. Waiting Room Observation (WRO).* The waiting room observation is a structured observation of child behaviour with strangers in an unfamiliar waiting room setting [14]. It has been shown to discriminate between children with RAD and those without [14] as it identifies key relationship behaviours, for example, over friendliness with strangers.

*2.2.4. Development and Well-Being Assessment (DAWBA).* The DAWBA is a screening questionnaire for a number of psychiatric diagnoses including emotional, behaviour, and hyperactivity disorders used with parents of children aged 2–17 years [15]. The DAWBA can be completed either using a paper format or, as in this study, using a computerised format. The parent is asked a number of closed questions, for example, "does he ever worry?" which, depending on the answer, may lead to a section being skipped or to more questions, for example, about how often the child worries. The DAWBA has been shown to be a valid measure of child psychopathology [15] and has been used in nationwide surveys of child and adolescent mental health [16].

*2.2.5. The Child and Adolescent Psychiatric Assessment, Reactive Attachment Disorder Module (CAPA-RAD).* The CAPA-RAD is a 28-item semistructured parent-report interview, which assesses RAD symptoms and is a module of the Child and Adolescent Psychiatric Assessment, a well validated semistructured parent-report interview for child psychopathology used in large epidemiological studies (CAPA) [17]. The CAPA-RAD has good interrater reliability with good discrimination [3].

*2.2.6. Social Skills Improvement System (SSIS).* The SSIS assesses social skills, problem behaviours, and academic competence and has been shown to have good reliability and validity [18]. In this 140-item questionnaire, the child's caregiver rates the frequency that their child displays various behaviours.

*2.2.7. Manchester Child Attachment Story Task (MCAST).* The Manchester Child Attachment Story Task (MCAST) is a doll-play story stem technique measuring attachment patterns in middle childhood [19]. It includes four stories with attachment related themes using a dolls house, designed for use with school aged children. The child's story is videotaped and subjected to structured coding based on the SSP and Adult Attachment Interview (AAI) codes to provide an attachment classification [19]. It has good interrater reliability, stability of attachment patterns over time, and concurrent validity with well-validated measures of attachment [20].

*2.2.8. Wechsler Intelligence Scale for Children (WISC IV).* The WISC is a scale of intelligence producing both a cognitive score (IQ) as well as scaled scores by age [21]. It can be used with children aged between 6 years and 16 years. It covers 4 domains: verbal comprehension; perceptual reasoning; working memory, and processing speed, with a full-scale IQ produced when these are combined. Extensive reliability and validity evidence was provided by Wechsler [21] and by Prifitera, Saklofske, and Weiss [22].

*2.3. Procedure.* Our results describe the characteristics of a group of children identified in an epidemiology study examining the prevalence of RAD. That study involved a 3-stage approach with 1,600 participants. The procedure of that study is described in detail in Minnis et al. [11]. In brief, the first stage involved parents and teachers both completing the SDQ and the RPQ. The second stage involved the parents completing the DAWBA, the CAPA-RAD, and the SSIS, while the third stage involved the child being assessed using the MCAST and the WISC-IV. All the data was reviewed, and where criteria for RAD was met, a diagnosis was made. This paper describes the characteristics of those children with a suspected or likely diagnosis of RAD.

*2.3.1. RAD Diagnoses.* RAD diagnoses were made, based on DSM IV criteria, by HM and the research team, following review of the CAPA-RAD, the teacher RPQ, the Observational Checklist, 10 comorbid diagnoses (from the DAWBA), and videotaped interaction between the child and researcher (who was a stranger to the child at the assessment visit). In previous research, this has been shown to be highly sensitive and specific in discriminating children with RAD from typically developing children [3]. The child was given a "borderline/suspected" diagnosis when the diagnosis was not absolutely clear or when we were unable to see the child in school and were relying simply on interview and questionnaire data. Both DSM IV and ICD-10 suggest that RAD should only be diagnosed in the presence of a history of "pathogenic care." It was decided that it would be upsetting for participants, and it would reduce response rates if we asked parents from the general population direct questions about abuse and neglect of their child, although this was explored to some extent in the posttraumatic stress disorder section of the DAWBA.

## 3. Results

We describe the characteristics of all 22 children with RAD behaviours. We gave 13 a definite diagnosis with the remaining 9 given a suspected or borderline diagnosis.

*3.1. Demographics.* We found that, of the 22 children with RAD behaviours, 13 (59.1%) were male and 9 (40.1%) were female. Ten (45%) of the children were thought to be living with birth parents, while 9 (41%) were known to be in foster care, and a further 3 (14%) were known to be in kinship care, living with a relative.

*3.2. Social Skills.* Ten of the children (45.5%) were below average in the SSIS, as compared to American norms (UK norms are unavailable for the SSIS), while only 1 child scored above average in this measure.

*3.3. Attachment.* Attachment patterns of 14 of the children were classified using the MCAST and compared to general population norms. Of the 14 children included, 8 (57.1%) were given a secure attachment and 6 (42.9%) insecure. This is illustrated below and compared to the distribution which would be expected in a normative sample (Figure 1).

*3.4. Problem Behaviours.* The SDQ gives the total difficulties score which can characterise a child's risk of developing problems. Figure 2 shows the risk level of problem behaviours in the RAD sample, as reported by parents, and compares it with the risk level of the entire school sample from which this data was from, which is in line with the UK norms.

*3.5. Cognitive Ability.* The WISC showed that the children in this sample were below average (100) in every aspect of this test of intellectual functioning (Table 1).

*3.6. Psychiatric Diagnoses.* The DAWBA is a screening tool for a number of psychiatric diagnoses based on ICD-10 and DSM IV criteria. The results showed that 11 (52%) had a likely diagnosis of attention deficit hyperactivity disorder (ADHD); 6 (29%) oppositional defiant disorder; 6 (29%) conduct

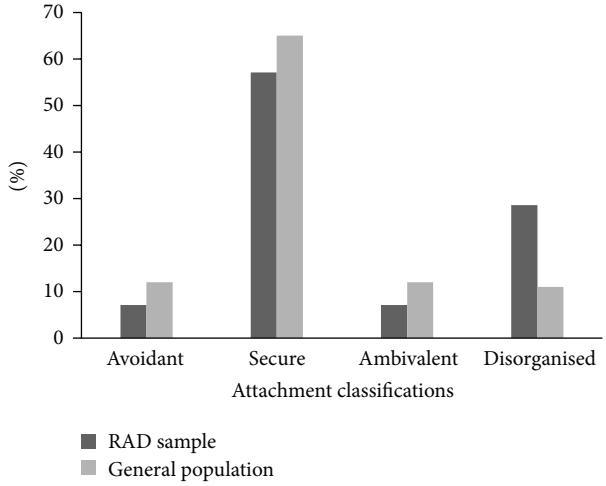


Figure 1: MCAST classifications in sample of RAD cases compared to the general population.

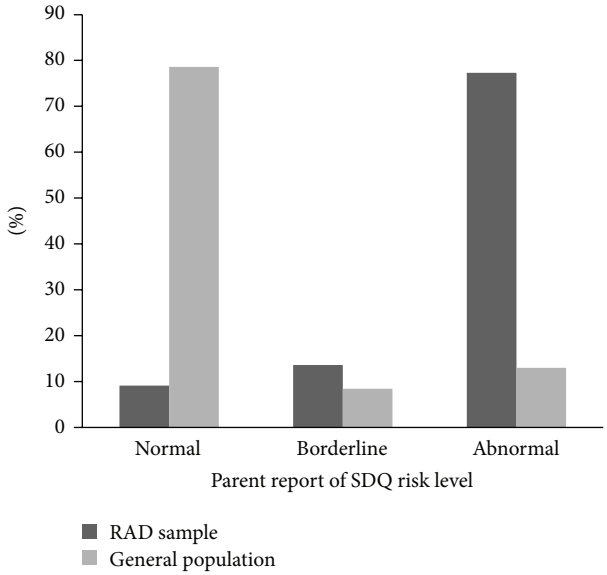


Figure 2: SDQ risk level for problem behaviours in sample of RAD cases compared to the general population.

Table 1: Average scores in the WISC in our sample of children with RAD ($n = 14$).

| | Mean (SD) | Range |
|---|---|---|
| Verbal IQ | 82 (14.3) | 63–119 |
| Perceptual reasoning | 83.7 (11.9) | 65–104 |
| Working memory | 82.9 (11.5) | 62–104 |
| Processing speed | 87.1 (10.5) | 68–106 |
| Full-scale IQ | 79.36 (12.0) | 56–106 |

disorder; 4 (19%) posttraumatic stress disorder (PTSD); 3 (14%) an autism spectrum disorder (ASD); 3 (14.3%) a specific phobia; and 1 (5%) a tic disorder. Overall, over 85% of the children identified as having RAD in this sample had another diagnosis predicted by the DAWBA.

All but one of the children with a definite diagnosis of RAD had histories of definite or suspected maltreatment documented during the DAWBA interviews with parents or carers, and all but two of those with a borderline/suspected diagnosis of RAD had such a history. In the others, a history of maltreatment was impossible to determine but may well have been present; we made a child protection referral regarding one child on whom there was no clear previous history of maltreatment.

## 4. Discussion

We described the characteristics of 22 children with a suspected, borderline, or definite diagnosis of RAD. We found that they have a high level of comorbidity with other disorders, had lower IQs than population norms, had a higher level of disorganised attachment than has been found in general population studies, more problem behaviours, and had lower social skills than would be found in the general population. These findings are in line with previous research about children coming from institutions. This study shows that those children in the general population with RAD also have these additional problems, providing further evidence that a multidisciplinary approach is needed when working with these children, in line with the research on ESSENCE.

We found that over half of our sample had a secure attachment; this offers support to the growing body of research showing that RAD and insecure attachment are not the same thing [3]. We did, however, also find that there was a higher rate of disorganised attachment than would be found in the general population. This is not surprising as research has previously shown that those with a history of maltreatment have a greater chance of having a disorganised attachment in later development.

### 4.1. Implications of Results

*4.1.1. Clinical Implications.* The results of this study demonstrate that reactive attachment disorders are present in the general population. Previous research has shown that this may be as a result of both environmental factors and genetics [13]. Children who begin their lives with compromised/disrupted attachment are at significant risk for subsequent developmental difficulties including low self-esteem, lack of emotional regulation, difficulty with peer/social relationships, lack of empathy, and behavioural difficulties, any number and combination of which may see the child present to specialist children's services.

This has implications for the assessment, intervention, and education of this group of children when they present with difficulties. Aspects of the RAD presentation such as indiscriminate friendliness (a core feature of disinhibited reactive attachment disorder) may be overlooked in a child who presents from the general population. This has potential implications for targeting the most appropriate and effective intervention for the child. Such presenting difficulties should

not be underestimated when there is a suggestion of a history of pathogenic care.

This study also demonstrates the high levels of comorbidity with other disorders including ADHD. There are potential implications from a formulation and intervention perspective if there is a lack of awareness of RAD presenting within the general population group leading to exclusive treatment of the "comorbid" disorder coupled with a lack of recognition of the child's difficulties in forming and maintaining relationships.

*4.1.2. In the Classroom.* Most teachers in recent years have become more aware of the diverse needs of children in the classroom, and ongoing professional development will include training in attachment issues, autism, ADHD, and other social/emotional difficulties [23, 24]. The problem for the class teacher may be that children who have RAD may not be easily identifiable and are therefore not considered to be in an "at risk" group. So, while the teacher may have some kind of classification system to help support the children with specific conditions such as autism or ADHD, there is a need to raise awareness that there are some children who may well suffer from more than one psychiatric condition or educational difficulty. Support plans need to be flexible and individually tailored for each child with a difficulty.

Within a class situation, misbehaviour can escalate to exclusion for a child. For children who have been traumatised or abused, it is particularly important that they feel a part of the class and the wider school community with inclusion being even more vital for neglected or abused children [25]. Success for these children is essential for their emotional wellbeing, and training on good techniques to support vulnerable children has to involve all school staff members, not just teachers [26].

This study used the WISC to measure the cognitive ability of the children in this sample. Despite being a measure of general intelligence, there are components which are indicative of school taught material. We suspect that, due to both early maltreatment and behaviour issues, children with RAD may have been more likely to miss out on educational opportunities. This suggests that with proper learning support, cognitive scores could improve for the children in our sample.

*4.2. Limitations.* The findings here describe the characteristics of only a small sample of children; however, they are the first children with RAD to be described from a total population. In addition, these children were compared to population norms as opposed to a matched control group.

## 5. Conclusions

Our findings demonstrate that, even when identified through population screening, children with RAD have a complex presentation that fits well within the ESSENCE group of disorders. The logical conclusion to be drawn from this is that children presenting with RAD symptoms will require a detailed holistic assessment looking for comorbid disorders, cognitive, and language problems.

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*Review Article*

# Maltreatment-Associated Psychiatric Problems: An Example of Environmentally Triggered ESSENCE?

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This paper presents a new concept—maltreatment associated psychiatric problems (MAPP)—a syndrome of overlapping complex neurodevelopmental problems in children who have experienced abuse or neglect in early life. Children with MAPP are a hidden population in the community and, in clinical settings, their problems can seem overwhelming. Individual disorders associated with maltreatment are discussed as well as the overlap between these disorders and their shared environmental and genetic predisposing factors. Because of the complex and overlapping nature of MAPP, with symptoms emerging in early life, I argue that it should be considered an example of ESSENCE. Children presenting with likely MAPP should receive a comprehensive assessment, probing for symptoms of all of the ESSENCE disorders and leading to the use of evidence-based treatments where these are available.

## 1. Maltreatment and Mental Health

Maltreated children are at significantly greater risk of developing psychiatric disorders compared to the general population [1] and these can have profoundly negative consequences across the lifespan: as a group and compared with the general population, maltreated children have significantly poorer educational [2] and employment [3] outcomes, are more likely to become homeless [4] or go to prison [5], and have poorer relationship and family functioning once they reach adulthood [6].

Much of the existing research literature has come from studies of children reared in institutions and there is now no doubt that emotional neglect in early life places children at risk of a wide range of problems including reactive attachment disorder (RAD) (characterised by indiscriminate friendliness and/or hypervigilance and emotional withdrawal); attention-deficit hyperactivity disorder (ADHD) (characterised by poor concentration, impulsivity, and overactivity); posttraumatic stress disorder (characterised by flashbacks, nightmares, and avoidance of reminders of traumatic events); depression and anxiety [7–9]. Similar findings have emerged from longitudinal studies of children maltreated within a family context [10]. Coupled with these psychiatric problems, maltreated children may also have cognitive problems [11], language problems [12] and motor problems [1].

## 2. What Are the Maltreatment-Associated Psychiatric Problems?

*2.1. Reactive Attachment Disorder.* The only disorder in the psychiatric classifications systems that is specifically associated with maltreatment is reactive attachment disorder (RAD). RAD is a serious disorder of social functioning associated with maltreatment with two subtypes: inhibited (wary, watchful behaviour) and disinhibited (overfriendly behaviour). The disinhibited form is known to be associated with significant psychiatric morbidity [13] and can persist despite changes in caregiving context [14]. Inhibited RAD is thought to be very rare beyond the specific context of maltreatment [14] but we have recently shown that the disinhibited form is far from being rare and has a prevalence of around 1.4% in a deprived population [15]—similar to or even higher than the population prevalence of ASD [16]. We have also found that children with RAD often have complex neurodevelopmental problems [17] and that, even after living for several years in loving adoptive families, these

children can still have problems that are a major burden for themselves, their families, and their peers [18].

*2.2. Attention-Deficit Hyperactivity Disorder (ADHD).* Although ADHD is fairly common in the general population with prevalence estimates of around 6-7% in children and 5% in adults [19], it is even more prevalent in maltreated [20] or postinstitutionalised populations [7]. Adoption in stable nurturing families does not necessarily ameliorate the problems: the rates of ADHD medication are almost 5 times higher for boys who were adopted internationally in Sweden compared to the general population [21]. This is something of a conundrum because ADHD is one of the best-researched disorders when it comes to genetics and is known to have a high heritability in the general population of around 70–90% [22]. In a recent review, however, Thapar and colleagues emphasise the close associations between genetic and environmental factors (e.g., a genetic predisposition in the mother to smoking may confound the environmental effects of smoking in the antenatal period on the development of ADHD) and suggest that, despite the strong evidence for heritability in ADHD, severe early adversity/privation has a strong enough evidence base to be considered a causal risk factor for ADHD [22].

*2.3. Posttraumatic Stress Disorder.* Unsurprisingly, posttraumatic stress disorder (PTSD) is common in populations of children who have been maltreated [23]. It is, however, less clear whether PTSD is distinct from inhibited reactive attachment disorder and the complexity of the presentation of trauma symptoms in abused and neglected children has prompted some to suggest that the term developmental trauma disorder may be more appropriate [24].

*2.4. Conduct Disorder and Oppositional-Defiant Disorder [25].* It is well known that harsh parenting and early maltreatment are strongly associated with conduct disorder [26] but a history of maltreatment is also present in nearly half of children presenting to clinics with oppositional defiant disorder (ODD) [25]. Interestingly, children who were reared in Romanian orphanages and adopted to the UK do not appear to be at a higher risk of conduct disorder and ODD compared to family-reared comparison children [8], therefore there appears to be some—so far poorly understood—specificity as regards particular types of early adversity and particular developmental outcomes.

*2.5. Anxiety and Depression.* There is some debate as to whether or not anxiety and depression are particularly associated with maltreatment. Retrospective clinic-based studies have suggested that there is evidence of an association between childhood physical and sexual abuse and later anxiety disorders [27] and in the Bucharest Early Intervention Study, children who grew up in institutions were almost three times as likely to be diagnosed with an anxiety disorder at followup compared to children who grew up in families [7]. However, children adopted from Romania to the UK were not more likely, at age 6, to have anxiety or depression [8]. Interestingly, however, by adolescence higher than expected rates of anxiety and depression had emerged in the sample of Romanian children adopted to the UK and risk was influenced by both genetic factors (5HTT genotype) and environmental factors (stress during adolescence) [28].

## 3. What Is the Overlap?

In a detailed diagnostic study of 165 consecutive outpatients, Ford and colleagues found that where a diagnosis of comorbid ADHD/ODD was made, 73% of these children had a history of maltreatment compared to 26% of those with a diagnosis of ADHD alone and 48% of those with a diagnosis of ODD alone [25]. This has led us to suspect that comorbidity may be the rule, rather than the exception, in MAPP. In our own clinical research group, we have been struck by the neurodevelopmental complexity of the problems displayed by the subgroup of maltreated children who have psychiatric disorders. For example, in a study of adopted maltreated children with indiscriminate friendliness, there was a very high degree of psychiatric comorbidity with many children suffering from reactive attachment disorder, ADHD, and conduct and anxiety disorders, despite their having spent an average of 4 years with their adoptive parents [18]. This was not simply a feature of a selected clinical population: in a total population sample of around 1600 children, all children with a diagnosis of RAD also had other diagnoses including over half also suffering from ADHD and nearly a third suffering from conduct disorder [15].

## 4. Why Do Trajectories Differ So Much?

One of the great conundrums in the maltreatment field is why some children develop complex neurodevelopmental problems in the context of abuse and neglect yet others do not, despite having apparently suffered the same degree of early adversity. In the seminal studies by Rutter and colleagues, in which they followed up a random sample of the children adopted from Ceausescu's Romanian orphanages, despite more than two years of exposure to extreme neglect, between a fifth and a quarter were "free of any measurable dysfunction" at age 6 [8]. This perhaps implies that there are protective genetic factors that render some children resilient even to very adverse environmental circumstances. We showed, in a general population twin study, that despite being apparently caused by maltreatment, there is a substantial heritable component to the aetiology of RAD [29]. Various other groups have investigated the molecular basis of the "differential susceptibility hypothesis"—in which heritable characteristics render some children more at risk of developing psychiatric disorder in the context of maltreatment than others. For example, meta-analysis of several studies has now shown that the association between maltreatment and mental health problems is significantly stronger in the group of boys who have a genotype conferring low versus high monoamine oxidase A activity [29, 30], and a polymorphism at the dopamine D4 (DRD4) receptor renders some children at significantly higher risk of developing disruptive

behavioural disorders in the context of insensitive parenting than others [31]. The molecular genetic research, however, also suggests a logic in regarding maltreatment-associated problems as overlapping ESSENCE disorders: for example, Thapar stated in her review of the aetiology of ADHD that "the genetic risks implicated in ADHD generally tend to have small effect sizes or be rare and often increase risk of many other types of psychopathology." Little is known about *how* genes interact with the environment to produce differing outcomes, but one area of intense research scrutiny is the hypothalamic-pituitary axis. We have conducted a recent systematic review of stress responses in the context of maltreatment that demonstrated a wide range of effects on the stress response system of maltreatment depending on the sample [32] and differences in a child's ability to regulate stress hormones in response to adversity may potentiate the effects of maltreatment on development.

## 5. Is There a Specific MAPP Phenotype?

Various groups, including our own, have found that the subgroup of maltreated children who have psychiatric problems tend to have overlapping complex difficulties that are often associated with language and other cognitive problems [7, 8, 18]. In addition, there tends to be a core problem with forming and maintaining close intimate relationships. This is undoubtedly true of children who have RAD, but a recent systematic review conducted by our group showed that problems with facial emotion recognition were common in a wide range of child psychiatric disorders [33]. Such difficulties in recognising the basic emotions crucial to successful social interaction are likely to be disabling for children with MAPP. A recent review of the literature on the brain effects of early maltreatment has suggested that a dysfunction in limbic brain circuits might impede the child's ability to respond to emotional faces appropriately leading to a particularly disabling mixture of attentional problems and problems with relationships [34].

## 6. What Are the Long-Term Outcomes of MAPP?

There are many unanswered questions about how MAPP might develop across the lifecourse but we do know that early adversity is associated with both physical and mental health problems [35, 36]. Maltreatment is now recognised as an important risk factor for both personality disorder [37] and schizophrenia [38] but we do not know what proportion of children with MAPP are at risk of these adult psychiatric disorders nor the extent to which MAPP is a necessary mediator between maltreatment and adult mental health problems. There is, however, a recognised developmental route from early harsh parenting through conduct disorder and on to various later health problems; for example, delinquent adolescents have 9 times the *all-cause* mortality compared to their nondelinquent peers [39]. The longitudinal course of MAPP will be an important focus for future study.

## 7. A Hidden Population

The one aspect of MAPP that mitigates against it being described as an ESSENCE group of problems is that of referral to services. A core feature of the ESSENCE concept is that these are early symptomatic syndromes recognised by parents and/or professionals that result in referral to services and some sort of neurodevelopmental clinical examination. Sadly, for children who are experiencing neglect, their problems may be neither recognised nor resulting in referral to services. An additional problem may be that, even when referred, the complexity of their difficulties is so overwhelming that they defy description by parents and paralyse clinicians. Our recent study of adopted children with complex neurodevelopmental problems [18] lends some support to this notion: despite very burdensome problems, many of which have evidence-based treatments available, only a small proportion of children were in touch with child and adolescent mental health services (CAMHS). Those parents who had had contact with CAMHS sometimes reported tense and frustrating interactions with clinicians who did not seem to know where to start in teasing apart the array of difficulties being presented to them. This group of children was, however, advantaged by living with assertive adoptive parents compared to children with RAD living in birth families. In our recent study of RAD prevalence in a deprived population, several home visits were sometimes required to achieve a face-to-face assessment of a child, even when parents had opted into the study [15]. This level of assertive outreach would be well beyond the capacity of CAMHS services as currently structured, certainly in the UK and probably in many other countries. This has led us to conclude that there may be a hidden population of children with complex neurodevelopmental problems being denied the interventions that could radically change their developmental trajectories for the better. Because this is potentially such an important group, whose problems need to be addressed as early as possible in order to avoid extremely negative outcomes, new models of assertive outreach and preventative and intervention services need to be developed if we are to reduce the burden to these children, their families, and to society as a whole.

## 8. Future Directions

A focus on children with MAPP as a group may allow more coherent and pragmatic longitudinal studies, ideally starting in the antenatal period, to follow this very vulnerable group closely in the early years and to track trajectories through life. More research needs to be conducted into how to identify these children early enough for preventative and therapeutic interventions to significantly alter trajectories for the better. It is very likely that existing evidence-based treatments, for example, pharmaceutical treatment for ADHD, will be effective in this group, but treatment trials will need to focus on recruiting and retaining children with MAPP if we are to be confident of this. There also needs to be a focus on developing preventative interventions and, again, this research will require very assertive techniques to recruit

and retain samples. Key underexplored areas include the role of antenatal stress and toxins, parent-infant interaction in the early months and years of life, molecular genetics and epigenetics of MAPP as a whole and mechanisms at the level of brain structure and function. While the research evidence accrues regarding mechanisms, we must also be investigating new ways of reaching these children at the service level in order to deliver the services they need. Once engaged in services, a detailed diagnostic assessment covering all of the ESSENCE disorders is essential so that the right interventions can be put in place.

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*Research Article*

# Eating Problems and Overlap with ADHD and Autism Spectrum Disorders in a Nationwide Twin Study of 9- and 12-Year-Old Children

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*Aim*. To establish the prevalence of restrictive eating problems, the overlap and association with attention-deficit/hyperactivity disorder (ADHD), and autism spectrum disorders (ASD) and to estimate the heritability of eating problems in a general population sample of twins aged 9 and 12. *Methods*. Parents of all Swedish 9- and 12-year-old twin pairs born between 1993 and 1998 ($n$ = 12,366) were interviewed regarding symptoms of ADHD, ASD, and eating problems (EAT-P). Intraclass correlations and structural equation modelling were used for evaluating the influence of genetic and environmental factors. Cross-twin, cross-trait correlations were used to indicate a possible overlap between conditions. *Results*. The prevalence of eating problems was 0.6% in the study population and was significantly higher in children with ADHD and/or ASD. Among children with eating problems, 40% were screened positive for ADHD and/or ASD. Social interaction problems were strongly associated with EAT-P in girls, and impulsivity and activity problems with EAT-P in boys. The cross-twin, cross-trait correlations suggested low correlations between EAT-P and ADHD or EAT-P and ASD. Genetic effects accounted for 44% of the variation in liability for eating problems. *Conclusions*. In the group with eating problems, there was a clear overrepresentation of individuals with ADHD and/or ASD symptoms.

## 1. Introduction

In typically developing younger children, the prevalence of the clinical eating disorders is low [1, 2], with one large-scale study reporting a prevalence of 0.15% for DSM-IV eating disorders in 11- to 12-year olds [3]. However, some degree of milder eating problems is relatively common, affecting from 20 to 40 percent of children [1]. Selective eating or picky or faddy eating is a transient problem in over 10% of all toddlers [2]. A recent surveillance study [4] based on close to 2500 Canadian paediatricians' reports on "any disordered eating behavior sufficient to cause a disruption, weight gain, or actual loss of weight" found 161 children from 5 to 12 years of age. The highest incidence, 9.4 cases per 100 000 person-years, was found in girls aged from 10 to 12 years (1.3 for boys).

Dieting as a general, non-specific risk factor increases the risk of developing an eating disorder by about five times [5]. It has been suggested that subclinical variants of eating disorders start at an earlier age now than was the case in the twentieth century and that the prevalence of early dieting/restrictive eating is increasing [6]. While eating problems in childhood may be a risk factor for the development of eating disorders in adolescence and young adulthood [7–9], a comprehensive review on risk factors for eating disorders stressed a need for larger-scale studies [10].

Children with early symptomatic neuropsychiatric disorders have been found to have high frequencies of feeding/eating problems [11, 12] compared to children without such disorders, but there have been few, if any, large-scale studies in the general population investigating this problem [1].

As far as we are aware, there are few studies on heritability in prepubertal eating problems/eating disorders. In one study of over 5000 twins aged from 8 to 11 years, parent-reported food neophobia was highly heritable explaining 78% of the variance while 22% was explained by nonshared environmental factors [13].

The present paper assesses the rate of eating problems in a large young cohort of twins from the general population. Results are broken down by gender, genetic background factors, and by validated screening diagnoses of ADHD and ASD. In addition, we examined which facets of ADHD and ASD that had the strongest associations with eating problems.

## 2. Methods

*2.1. Subjects.* The Child and Adolescent Twin Study in Sweden (CATSS) is an ongoing longitudinal twin study targeting all twins born in Sweden since July 1, 1992. Since 2004, parents of twins are interviewed regarding their children's somatic and mental health and social environments in connection with the children's 9th or 12th birthdays (CATSS-9/12), with an overall response rate of 80% of all families contacted [14].

Parental information on 12,496 children from the birth cohorts between 1993 and 1998 of CATSS was used for analysis. In the present study, 130 individuals were excluded because they had known severe brain damage or known chromosomal aberrations, leaving data on 12,366 individuals (6331 boys and 5996 girls). In a further 62 cases there were missing items on key variables. Therefore in analyses including all key variables 12,304 children (3023 boys and 2852 girls aged 9 and 3296 boys and 3133 girls aged 12) were included.

*2.2. Measures*

*2.2.1. The A-TAC Inventory.* All twins participating in the study were screened for possible neurodevelopmental problems using a specially developed inventory, the Autism-Tics, ADHD, and other Comorbidities (A-TAC) inventory, including a previously used algorithm for eating problems and validated algorithms for ADHD and ASD [15].

The A-TAC inventory includes questions to investigate child psychiatric problems based on criteria stated in the *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition [16]. The A-TAC was designed for use in large-scale epidemiological research as an easy-to-administer, dimensional, and comprehensive parental interview that can be carried out by lay interviewers over the phone [15, 17]. The instrument is freely available as additional web material to the second validation study [15]. Items are organized into modules (e.g., Concentration/Attention and Impulsiveness/Activity form the ADHD domain, and Language, Social interaction, and Flexibility form the ASD domain). Modules are assessed without diagnostic hierarchies or exclusion criteria.

*2.2.2. Questions and Scoring.* In two validation studies [15, 17] lower cutoffs for screening purpose and higher cutoffs for use as clinical proxies have been defined for both the ADHD and the ASD scales. In the present study we have used the lower cutoffs for identifying children screening positive for ADHD (scores ≥6; sensitivity, 0.98; specificity, 0.81) and/or ASD (scores ≥4.5; sensitivity, 0.96; specificity, 0.88) [15].

Modules used in the present study were Concentration and Attention, Impulsiveness and Activity, Language, Social interaction, Flexibility, and Feeding/Eating. Each module starts with a reminder that the questions refer to a lifetime perspective, in comparison to peers, and that the questions addressing specific symptoms or characteristics may be answered by the response categories "no" (score 0), "yes, to some extent" (score 0.5), and "yes" (score 1.0). As alternatives, "do not know" or "do not wish to answer" are given, both of which are coded as "missing."

The Eating module screens for restrictive eating problems. Eating problems "(EAT-P)" was defined here as scoring ≥1.5 on the collapsed score for the two key questions of the Eating module [15]. These questions are (1) has s/he ever failed to gain enough weight for more than a year? (2) Has s/he seemed fearful of gaining weight or growing fat?

*2.3. Statistical Analyses*

*2.3.1. Association Analyses.* To investigate the association between the different facets of ADHD: (1) Concentration/Attention and (2) Hyperactivity/Impulsiveness, and ASD: (1) Language, (2) Social interaction, and (3) Flexibility- and EAT-P we used a binary logistic regression response model with data on 12,366 children. To account for the dependency within twin pairs a generalized estimation equation (GEE) model was fitted to the data. All variables were inserted as continuous covariates, except age. In a first step all factors were assessed in a univariate model, and, in a second step, a multivariate model was created that only included significant associations from the univariate model.

*2.3.2. Twin Statistics.* Twin methodology is based on the comparison of monozygotic and dizygotic twin pairs. Monozygotic twins share all their genes, while dizygotic twins, on average, share 50% of their segregating alleles. This makes it possible to disentangle genetic from environmental components of a trait or condition. In twin methodology, etiological factors are partitioned into genetic (A) factors, shared environmental (C) factors (factors that make the twins more similar), and nonshared environmental factors (E) (factors that make twins dissimilar). Intraclass correlations and standard continuous univariate heritability models were calculated in Mx [18]. We did not attempt to reduce the models since that can lead to biases in the observed estimates [19]. Cross-twin, cross-trait correlations (the continuous score of trait 1 in twin 1 is correlated with the continuous score of trait 2 in twin 2) were calculated using the PROC CORR procedure in SAS 9.3. Cross-twin, cross-trait correlations are used to indicate if common genetic and environmental effects over two traits existed. If the correlation is higher for monozygotic

Table 1: Prevalence of EAT-P.

| Groups | Total study group[a] *n* (boys + girls) | EAT-P *n* (boys + girls) | % within the group (boys + girls) |
|---|---|---|---|
| ADHD only | 903 (601 + 302) | 12 (8 + 4) | 1.33 (1.33 + 1.32) |
| ASD only | 89 (61 + 28) | 1 (1 + 0) | 1.12 (1.64 + 0.00) |
| ADHD + ASD | 288 (216 + 72) | 16 (9 + 7) | 5.56 (4.17 + 9.72) |
| Comparison (no ADHD, no ASD) | 11024 (5441 + 5583) | 43 (12 + 31) | 0.39 (0.22 + 0.56) |
| Study population (boys + girls) | 12304[a] (6319 + 5985) | 72 (30 + 42) | 0.59 (0.47 + 0.70) |

[a]Excluding 62 individuals for whom items were missing on the response variables yielded 12,304 individuals for prevalence analyses.
EAT-P: eating problems; ADHD: attention deficit hyperactivity disorder; ASD: autism spectrum disorder.

twins than for dizygotic twins, then common genetic effects influencing both traits are implicated. As the cross-twin cross traits correlations were quite similar for monozygotic and dizygotic twins, we did not go on to attempt bivariate model fitting.

Zygosity was determined in over 90% of the twins with a panel of 48 single nucleotide polymorphisms or, for those twins where DNA samples were missing, with the help of validated algorithms [20].

## 3. Results

*3.1. Prevalence of EAT-P, ADHD, and ASD.* Of the 12,304 children included in the present study, 903 were screened positive for ADHD only (scoring ≥6.0 in the ADHD and <4.5 in the ASD blocks), 89 were screen positive for ASD only (scoring ≥4.5 in the ASD and <6 in the ADHD blocks), and 288 children were screened positive for both ASD and ADHD. The rest of the children ($n$ = 11,024) constituted the comparison group.

The prevalence of EAT-P was low ($n$ = 72; 0.6%) of the total population of 12,304 children aged 9 and 12, with a close-to-equal distribution between ages, and a predominance of girls (30 boys and 42 girls). In the comparison group of 11,024 children with no ADHD/ASD, there were 43 children with EAT-P (0.4%; boys 0.2%, girls 0.6%) (Table 1). In the group of children with ADHD and/or ASD ($n$ = 1280) there were 29 children with EAT-P (2%; boys 2%, girls 3%). The prevalence of EAT-P was significantly higher in the group of children with ADHD and/or ASD compared to the group of children with no ADHD and no ASD ($P < 0.001$). The highest prevalence of EAT-P was seen in children scoring positive for both ADHD and ASD (5.6%; boys 4.2%, girls 9.7%).

*3.2. Prevalence of ADHD and ASD in Children with and without EAT-P.* Forty percent of all children who were reported to have EAT-P and 10% of those without EAT-P were screen positive for ADHD and/or ASD, as shown in Figure 1.

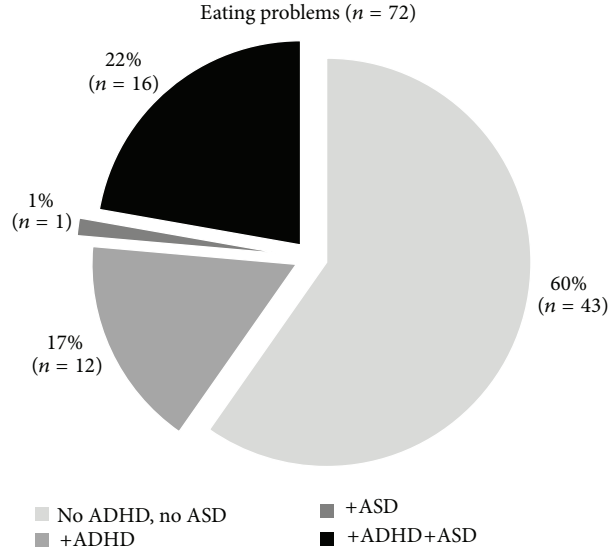


Figure 1: Prevalence of ADHD and/or ASD in the children with EAT-P. EAT-P: eating problems; ADHD: attention deficit hyperactivity disorder; ASD: autism spectrum disorder.

*3.3. Associations with Subdomains of ADHD and ASD.* Table 2 summarizes the association in measures of odds ratios (ORs) between EAT-P and age and between modules of ADHD and ASD, separately for both genders. Both ADHD modules (Concentration/Attention, and Impulsiveness/Activity) and all three ASD modules (Language, Social interaction, and Flexibility) were significantly associated with EAT-P in both genders in the univariate models. For example, for each new Concentration/Attention symptom the risk of eating problems increased with 36% in boys and with 33% in girls (OR = 1.36/1.33; CI = 1.21–1.53/1.16–1.52, resp.). When fitting all the significant variables of EAT-P into a multivariate model, only three variables were significantly associated with EAT-P. These were Social interaction problems (OR = 1.95, $P < 0.005$) for girls, and for boys Impulsiveness/Activity

Table 2: Measuring associations between EAT-P and subdomains of ADHD and ASD, for boys and girls separately by GEE models.

| Factors/covariates | Crude measures | | | | Univariate model | | Multivariate model[a] | |
|---|---|---|---|---|---|---|---|---|
| | *n* | Min–max | *M* | SD | OR | 95% CI | OR | 95% CI |
| | Boys | | | | EAT-P (Prevalence 0.5%) | | | |
| Age 9 | 3029 | — | — | — | 0.40* | 0.18–0.89 | 0.37* | 0.16–0.84 |
| Age 12 (reference group) | 3302 | — | — | — | 1 | — | 1 | — |
| Concentration/attention problems | 6325 | 0–9 | 1.26 | 1.90 | 1.36*** | 1.21–1.53 | 0.98 | 0.76–1.26 |
| Impulsiveness/activity problems | 6326 | 0–10 | 1.09 | 1.78 | 1.46*** | 1.34–1.60 | 1.41*** | 1.18–1.69 |
| Language problems | 6326 | 0–6 | 0.31 | 0.67 | 1.97*** | 1.67–2.33 | 1.33 | 0.85–2.08 |
| Social interaction problems | 6318 | 0–6 | 0.30 | 0.69 | 1.76*** | 1.48–2.09 | 0.70 | 0.44–1.12 |
| Flexibility problems | 6329 | 0–5 | 0.31 | 0.68 | 2.07*** | 1.68–2.55 | 1.42 | 0.86–2.37 |
| | Girls | | | | EAT-P (prevalence 0.7%) | | | |
| Age 9 | 2858 | — | — | — | 0.65 | 0.34–1.28 | | — |
| Age 12 (reference group) | 3138 | — | — | — | 1 | — | | — |
| Concentration/attention problems | 5992 | 0–9 | 0.74 | 1.43 | 1.33*** | 1.16–1.52 | 0.94 | 0.74–1.18 |
| Impulsiveness/activity problems | 5988 | 0–10 | 0.70 | 1.37 | 1.41*** | 1.26–1.58 | 1.18 | 0.94–1.47 |
| Language problems | 5993 | 0–6 | 0.19 | 0.47 | 2.32*** | 1.82–2.97 | 1.27 | 0.77–2.11 |
| Social interaction problems | 5976 | 0–6 | 0.20 | 0.50 | 2.45*** | 2.02–2.98 | 1.95** | 1.22–3.10 |
| Flexibility problems | 5995 | 0–5 | 0.17 | 0.46 | 2.10*** | 1.57–2.81 | 0.89 | 0.52–1.51 |

$N$ = 12,366, boys $n$ = 6331, Girls $n$ = 5996; EAT-P: eating problems; [a]with significant variables of the univariate models; *$P < 0.05$; **$P = 0.005$; ***$P < 0.001$.

problems (OR = 1.41, $P < 0.001$), and age 9 years compared to 12 years (OR = 0.37, $P < 0.05$).

*3.4. Heritability.* Intraclass correlations were at least twice as strong in monozygotic pairs as in dizygotic same-sex pairs, both generally and in each gender separately (Table 3). Genetic effects (heritability) accounted for 44% of the variance in EAT-P. There was no indication of shared environmental effects. The remaining variance was due to nonshared environmental effects. The phenotypic correlations did not exceed 0.23, and the cross twin, cross trait correlations suggested low correlations (<0.20) between EAT-P and ADHD or EAT-P and ASD, which did not differ substantially between monozygotic and dizygotic twins.

## 4. Discussion

EAT-P in the present study was defined by parent-reported weight stop/loss combined with fear of gaining weight in the child, and the main findings were as follows.

(i) The prevalence of EAT-P was low (under one per cent) in these cohorts of 9- and 12-year olds.

(ii) The prevalence of EAT-P was significantly higher in children who also screened positive for ADHD and/or ASD, with the highest prevalence of EAT-P, almost ten percent, reported for girls who screened positive for both ADHD and ASD.

(iii) Social interaction problems were strongly associated with EAT-P in girls, and impulsivity and activity problems were strongly associated with EAT-P in boys.

(iv) In childhood, eating problems seemed to be in equal parts accounted for by genetic and nonshared environmental background factors.

Based on earlier published reports, the low prevalence of restrictive eating in the age cohorts in the present study was to be expected [2, 5]. However, as far as we are aware there have been few studies on the general population of 9 to 12-year olds. Furthermore, few existing reports have looked specifically at the critical prepubertal years, critical if the purpose is to examine early onset of restrictive eating [21]. The expected overrepresentation of girls could be expected from all previous epidemiological studies. In boys there was a significant increase in EAT-P with age. However, earlier literature also gives the expectation of an increasing prevalence of restrictive eating in 12-year old girls compared to 9-year olds [22] which was not substantiated in this study.

The prevalence of EAT-P, at least as defined in this study, was relatively low compared to other developmental problems [15]. Similar to some previous studies [23, 24], in the present study children screening positive for ADHD and/or ASD had an increased risk of eating problems causing weight loss. In the children with such eating problems there was a clear overrepresentation of individuals with ADHD and/or ASD. Concerning this finding there are few studies except a study in UK of a nonclinical sample of 132 schoolchildren with similar results [25]. Eating disorders are now considered to be neurodevelopmental disorders [26], and a link with childhood obsessive-compulsive personality traits [27], and even with ASD, has been suggested [28, 29]. The neurodevelopmental disorders should be considered in children with eating disorders, especially in girls where mild forms of ADHD and ASD tend to be overlooked [30].

Table 3: Intraclass correlations, heritability estimates, and cross-twin cross-trait correlations for the collapsed sample and by gender.

| EAT-P | Intraclass correlations (95% CI:s) | | Heritability estimates (95% CI:s) | | | Cross-twin, cross-trait correlations (95% CI:s) | | | | Phenotypic correlations (95% CI:s) | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | ADHD | | ASD | | | |
| | MZ | DZ ss | A | C | E | MZ | DZ ss | MZ | DZ ss | ADHD | ASD |
| ALL | 0.42 (0.39–0.45) | 0.18 (0.15–0.21) | 0.44 (0.40–0.48) | 0.00 (0.00–0.02) | 0.56 (0.53–0.60) | 0.16 (0.11–0.21) | 0.13 (0.09–0.17) | 0.15 (0.10–0.19) | 0.11 (0.07–0.15) | 0.15 (0.13–0.18) | 0.20 (0.18–0.22) |
| Boys | 0.34 (0.30–0.38) | 0.10 (0.06–0.14) | 0.32 (0.25–0.38) | 0.00 (0.00–0.05) | 0.68 (0.62–0.73) | 0.19 (0.12–0.25) | 0.15 (0.09–0.21) | 0.17 (0.10–0.24) | 0.14 (0.08–0.20) | 0.18 (0.15–0.21) | 0.23 (0.20–0.26) |
| Girls | 0.48 (45–0.52) | 0.23 (0.18–0.27) | 0.53 (0.43–0.52) | 0.00 (0.00–0.04) | 0.47 (0.43–0.52) | 0.16 (0.09–0.22) | 0.14 (0.08–0.20) | 0.17 (0.10–0.23) | 0.09 (0.02–0.15) | 0.16 (0.12–0.19) | 0.18 (0.15–0.21) |

EAT-P: eating problems, MZ: monozygotic, DZ-ss: dizygotic same sex, CI:s: confidence intervals.
A: genetic factors, C: shared environmental factors, and E: nonshared environmental factors.
Pairs where information was eligible from both twins were included in the analyses, giving a total of 1620 MZ boys, 1694; DZ girls, 2310 DZ-ss boys 2310, and 1944 DZ-ss girls.

Gender specific differences could be seen concerning neurodevelopmental problems associated with EAT-P. Hyperactivity and impaired social interaction showed strong and significant association to EAT-P for both genders. As far as we know it is a new finding for prepubertal eating symptoms, but it would seem to be in agreement with earlier literature on adolescent onset eating disorders [31–33]. However, in the multivariate analysis, the strongest association of EAT-P for girls was problems with social interaction, and in boys the strongest association was with hyperactivity and impulsivity. These gender differences seem to be in agreement with some reports of excessive exercise as more common in male than in female eating disorders [34].

Eating problems in 9 to 12-year olds appear, similar to later in adolescence [29, 35], to have an equally large genetic and non-shared environmental background. However, the scant literature of boys and men with eating problems/eating disorders does not allow any comparing with earlier findings. The very similar cross-twin cross-trait correlations together with the low phenotypic correlation suggested that the small part of variance that is shared between the conditions is mainly due to shared environmental factors. Future studies should investigate if this association is similar above the diagnostic threshold. A review [22] stressed the complexity of influences on eating behaviours and weight as parents provide both the genetic predispositions and the environment (the food and the attitudes to food) in which these predispositions are expressed. Maternal food intake strongly correlates with child food intake [30]. The clinical implications of the interplay between environmental and genetic risk factors for eating disorders have been comprehensively described in a recent review [36].

The strengths and limitations of the study should be taken into account in interpreting findings. The population-based nature of the study sample is an important strength. An obvious limitation is that the information regarding symptoms and behaviour consisted of parent ratings in a telephone interview. The A-TAC inventory has a proven excellent ability to distinguish children with neurodevelopmental problems from children with no such problems [14], but it has not been validated for the assessment of eating problems which suggests that the results should be interpreted with caution. The focus of this study is on restrictive eating, and questions on bingeing and obesity have not been included in the analyses in the present study. The study was cross-sectional and could not say anything about causality.

The clinical implication of this study is that neurodevelopmental disorders should be considered in children with disordered eating, and, conversely, that eating problems/disorders should be considered in children with ADHD and/or ASD. Interventions must be matched to the patient, and only if neurodevelopmental aspects are considered in each individual case, one can expect results.

## Ethical Approval

The CATSS-9/12 study has ethical approval from the Karolinska Institute Ethical Review Board: Dnr 03-672 and 2010/507-31/1.

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*Research Article*

# Mental Health Services Use Predicted by Number of Mental Health Problems and Gender in a Total Population Study

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We examined the relationship between service use and the number of problem areas as reported by parents and teachers on questionnaires among children aged 7–9 years old in the Bergen Child Study, a total population study including more than 9000 children. A problem area was counted as present if the child scored above the 95th percentile on parent and/or teacher questionnaire. A total number of 13 problem areas were included. Odd ratios (ORs) for contact with child and adolescent mental health services (CAMH), school psychology services (SPS), health visiting nurse/physician, and school support were calculated with gender as covariate. The number of symptom areas was highly predictive of service use, showing a dose-response relationship for all services. Children scoring on ≥4 problem areas had a more than hundredfold risk of being in contact with CAMH services compared to children without problems. The mean number of problem areas for children in CAMH and SPS was 6.1 and 4.4 respectively, strongly supporting the ESSENCE model predicting multisymptomatology in children in specialized services. Even after controlling for number of problem areas, boys were twice as likely as girls to be in contact with CAMH, replicating previous findings of female gender being a strong barrier to mental health services.

## 1. Introduction

Already in 1979, when elaborating on taxonomy and classification, in view of the coming DSM-III manual, Woods declared that "Substantially supplanting this nineteenth century definition of disease as structural lesion or abnormality is the notion of disease as construct rather than material that exists in the ostensive finger-pointing sense. Diseases of all sorts are constructs that are found useful at different points in time for organizing subject matter" [1]. From hindsight, he might have been a bit too optimistic, as we still in the 21st century tend to overlook this fundamental dogma.

Both in clinical and population studies, psychiatric comorbidity is generally prevalent [2–5] and underresearched, especially regarding treatment, as many trials exclude individuals with certain kinds of comorbidity [6, 7]. Gillberg argued that the very concept of comorbidity prevents clinicians and researchers from providing our patients with the care they need [8]. Comorbidity implies that something exists separated from something else and that there are clear boundaries between one morbus and another morbus. To cite Woods once again, the problem with the word "comorbidity" is that "the data that we see are to an appreciable extent determined by the categories that we apply to them" [1]. Thus the very word comorbidity leads us to believe that the two "comorbid" disorders exist as separate, distinct entities. The symptoms described within the diagnostic criteria for autism and attention deficit hyperactivity disorder (ADHD) are a fragrant example. According to the diagnostic criteria, these disorders are mutually exclusive [9], although recent research (ignoring the diagnostic criteria) points to tight links both genetically and clinically between the two disorders

[10–12]. If this is not taken into consideration by clinicians, valuable time and effort may have been wasted and the needs of children neglected. This example demonstrates the dire consequences of believing that diagnoses exist in the absolute sense and in one *exact form* and that diagnostic manuals are idealized but faithful representations of reality.

The large National Comorbidity Surveys carried out in 1990–1992 and 2001–2003 in the US both highlight the high comorbidity rates found in psychiatric disorders and the strong relationship between the presence of comorbidity and severity of the illness [2, 3, 13]. Both found that although half of the entire population was likely to experience at least one psychiatric disorder in their lifetime, only 21% of life-time psychiatric disorders occurred in people who reported only one life-time disorder. In the 1990–1992 study, a sixth part of the population had three or more life-time psychiatric disorders, and nine out of 10 *severe* psychiatric disorders occurred in this group [2]. In spite of their obvious problems, only one-third of them had received any professional treatment in the last year. The same pattern emerged in the 2001–2003 study, where 7% of the population was characterized by having high rates of comorbid psychiatric disorders accounting for 44% of the serious cases [13].

Genetic work including both genome-wide scans, twin studies, and specific genetic deletions/mutations have shown a large overlap between both bipolar disorder, schizophrenia, ADHD, learning disabilities, and autism, indicating that the same genes are involved in these disorders [14–17], but perhaps through varying mechanisms. It should not come as a surprise then that the symptomatology itself may be largely overlapping, and that "specific" disorders perhaps ultimately only exist in an idealized stereotype form.

In 2010, Gillberg proposed an alternative concept: Early Symptomatic Syndromes Eliciting Neurodevelopmental Examinations (ESSENCE) [8]. Although parents and children usually present with one major concern, the concept calls for us as professionals to know that a difficulty seldom appears on its own. Gillberg claims that the clinical practice of only addressing the presenting problem may be of limited use if the child is struggling in various domains, and that the presenting concern should be viewed more as a warning signal, a cue for the professional to look across domains for more problems. This broader concept may have a cost for the child and his/her family, and the clinician as well as for the society. It is therefore important to investigate the evidence for ESSENCE, as well as the practical and economic consequences of working according to this model rather than following the traditional model of narrowly defined disorders. At the individual clinical level, a narrow approach may be easier to handle in the short-term, but the broader approach may be more beneficial in the long-term and at a societal level. Both approaches may be efficient, depending on where in the school/health services you meet a child. According to Gillberg and the ESSENCE model, we should expect that the children with multiple problems are primarily found among those referred to specialist services [8].

Several studies have demonstrated an unequal access to services for girls, where girls are less frequently brought to services, receive their diagnosis later in life, and have unmet needs [5, 18–20]. The reasons for this bias are not well understood, but several studies using case vignettes demonstrate that both parents and teachers seem to rate interventions as less useful for problems exhibited by girls [21, 22]. This prejudice seems to exist also within the health services. One study showed that girls with inattentive type of ADHD, although as likely to be in contact with services as boys, received treatment for their comorbid internalizing disorder rather than for their ADHD [23], and further other studies have shown the reduced likelihood for ADHD diagnosis and treatment for girls, even after adjusting for ADHD symptom severity [20, 24]. Several studies have questioned the frequently cited disruptive behavior hypothesis that boys are more likely to be referred because they show more disruptive behavior, finding that, in vignettes, girls with disruptive behavior were *more* likely to be referred, whereas there was no difference for boys [21]. This study also found parents and teachers beliefs about the efficacy of ADHD treatment to be the mediator explaining the gender bias in seeking health services, and the strongest effect was due to rating teaching assistance as more effective for boys than for girls [21]. Derks et al. (2007) found that although clinically girls and boys with ADHD had the same symptomatology and comorbidity, teacher ratings of boys with ADHD were likely to be higher on inattentive symptoms and aggressive behavior, and the authors speculated that this might contribute to the lower treatment rate for girls [19].

Most of the studies on comorbidity have included clinical samples and are therefore probably affected by participation bias, characteristics of the clinic performing the study, and assessment methods. Population-based studies are thus called for to characterize children at various levels of health services. To that end, the present study examined the rate of reported multiple problems in children at various levels of health/school services in a large total population sample of children the 7–9 years of age. We ask whether, children referred to specialist services show symptom profiles mainly indicating specific symptomatology or a broad range of problems. We further ask whether there is a relationship between the level of service use of the child and the number of problem areas reported, and whether sex impacts on contact with health/educational services after controlling for number of problem areas.

## 2. Materials and Methods

The first wave of the longitudinal Bergen Child Study (BCS) assessed a broad range of mental health problems in a total population of school children aged 7–9 years old ($N = 9430$) through teacher and parent questionnaires [25, 26]. The teacher questionnaires ($N = 9152$) covered 97% of the population, whereas the parental questionnaires ($N = 6295$) covered 67% of the same sample. In the present study, "unidentified children" were defined as children with only (anonymous) teacher reports and no parental report and identifying consent ($N = 2857$), whereas children with parental questionnaire were labeled as "identified children" ($N = 6295$). The main instruments of the questionnaire

Table 1: Problem areas and actual percentages of children scoring above the 95th percentile on parental and teacher questionnaires.

| Problem area | Parent questionnaire | Teacher questionnaire | Either informant* |
|---|---|---|---|
| SDQ emotion | 5.9% | 5.7% | 9.7% |
| SDQ peer problems | 7.3% | 4.1% | 8.9% |
| Hyperactivity | 6.4% | 5.8% | 9.2% |
| Inattention | 6.5% | 6.0% | 9.1% |
| Oppositional behaviour | 7.0% | 5.3% | 8.4% |
| ASSQ | 5.9% | 5.2% | 8.4% |
| Language problems | 6.4% | 6.0% | 8.6% |
| Tics | 9.8% | 6.4% | 13.5% |
| Obsessions/compulsions | 10.2% | 3.5% | 12.5% |
| Hypoactivity | — | 9.3% | 7.7%* |
| Selective mutism | — | 4.1% | 4.0%* |
| Eating problems | 4.7% | — | 4.7% |
| Sleep problems | 8.5% | — | 8.5% |

*This column only represents identified children with questionnaires from both informants ($N = 6295$), whereas the teacher questionnaire column represent the total population ($N = 9152$), which is the cause of differing percentages of hypoactivity and selective mutism in these two columns.

were the Strength and Difficulties Questionnaire (SDQ), the Autism Spectrum Screening Questionnaire (ASSQ), and the DSM-IV criteria for ADHD and ODD. In addition, there were 5 items targeting obsessive compulsive problems (OCD), 5 items targeting tics, and 5 items targeting language difficulties. All items were scored on a three-point Likert scale (not true, somewhat true, definitely true). There were slight differences between the informants' questionnaires in that parental questionnaires included 5 items on eating disorders and one item targeting sleep problems, while the teacher version included two items on hypoactivity and one item asking for selective mutism. Both informants were asked whether the child, to their knowledge, had been referred to child and adolescent mental health services (CAMH), to school psychology services (SPS), or a health visiting nurse/physician for any of the problems reported in the questionnaire. Response options were "yes," "no," or "I don't know." In the present study, a child was defined as referred to a service if either the parent and/or the teacher reported "yes" regarding that service.

The problem areas included were the emotional and the peer problem scale of the SDQ, attention, hyperactivity, and oppositional behavior from the DSM-IV criteria, tics, obsessive compulsive disorder (OCD), language difficulties (LD), eating problems (parent only), sleeping problems (parent only), selective mutism (teacher only), and hypoactivity (teacher only) (Table 1). A problem area was defined as present if parent and/or teacher reported a score above the 95th percentile of the whole population sample, except for selective mutism and sleeping problems, where a report of partly true or definitely true was counted as problem present. This procedure corresponded to the 91th percentile for sleeping problems and the 96th percentile for selective mutism. For eating problems, a score of one corresponded to the 96th percentile. For teacher defined OCD, a score ≥2 was used, corresponding to the 96th percentile, as a score of one effectively resulted in a cutoff at the 89th percentile (see Table 1). Each problem area was only counted once (i.e., not twice if reported by both informants).

*2.1. Statistical Analyses.* Descriptive statistics were used to calculate the frequency of children within each of the problem areas. Logistical regressions analyses were computed separately for identified (teacher and parent reports) and unidentified (teacher reports) children. The number of problem areas, categorically defined, and gender were used as predictor variables and contact with services as outcome variable.

## 3. Results

*3.1. Characteristics of Children in Contact with Services.* Tables 2 to 4 describe the overall number of children and percentages referred to child and adolescent mental health services (CAMH), school psychology services (SPS), nurse/physician, or having any kind of school support. Table 2 reports results for children where both parental and teacher information is available, whereas Table 3 reports results for unidentified children with only teacher information. As can be seen, many children had some kind of support in school. This service includes all the commonly used interventions in schools, for example, extra reading assistance and increased supervision during meals; still the majority of these children (66%) scored above the 95th percentiles on 2 or more areas. As expected, children in contact with CAMH services were reported to have very high symptom levels, with 73% of children scoring above the 95th on at least four problem areas, with six areas as both mean and median number.

As many problem areas were included, the number of problem areas in children without service contacts were included for comparison. In this group, very few scored high on any area, and only 3.7% scored above the 95th percentile on ≥4 areas (Table 2).

Table 2: Identified children, percent of referred children with ≥2 and ≥4 problem areas according to parent and/or teacher, mean and median number of problem areas above 95th percentile ($N = 6295$).

| Service | Number of children | % Children with ≥2 problems | % Children with ≥4 problems | Mean number of problems | Median number of problems |
|---|---|---|---|---|---|
| CAMH | $N = 153$ | 91% | 73% | 6.1 | 6 |
| SPS | $N = 533$ | 79% | 54% | 4.4 | 4 |
| Physician/nurse | $N = 760$ | 69% | 43% | 3.7 | 3 |
| School support | $N = 829$ | 66% | 40% | 3.5 | 3 |
| No services | $N = 4945$ | 15.2% | 3.7% | 0.7 | 0 |

Table 3: Unidentified children, percent of referred children scoring above 95th percentile ≥2 and ≥4 problem areas, mean and median number of problem areas above 95th percentile. Information based on teacher information only (lacking sleep and eating problems) ($N = 2857$).

| Service | Number of children | % Children with ≥2 problems | % Children with ≥4 problems | Mean number of problems | Median number of problems |
|---|---|---|---|---|---|
| CAMH | $N = 64$ | 80% | 59% | 4.4 | 4 |
| SPS | $N = 267$ | 72% | 49% | 3.6 | 3 |
| Physician/nurse | $N = 247$ | 66% | 38% | 3.1 | 3 |
| School support | $N = 528$ | 53% | 31% | 2.5 | 2 |
| No services | $N = 2223$ | 8.6% | 2.2% | 0.4 | 0 |

Table 4: Identified children, percent of referred children above 95th percentile on ≥2 and ≥4 problem areas, mean and median number of problem areas above 95th percentile. Based on teacher information only (lacking sleep and eating problems) ($N = 6295$).

| Service | Number of children | % Children with ≥2 problems | % Children with ≥4 problems | Mean number of problems | Median number of problems |
|---|---|---|---|---|---|
| CAMH | $N = 101$ | 81% | 62% | 4.4 | 5 |
| SPS | $N = 398$ | 64% | 38% | 3.1 | 2.5* |
| Physician/nurse | $N = 327$ | 56% | 36% | 2.8 | 2 |
| School support | $N = 690$ | 46% | 23% | 2.1 | 1 |
| No services | $N = 5420$ | 5.8% | 1.0% | 0.3 | 0 |

*Out of 398 children, exactly 199 had ≤2 symptoms and 199 had ≥3 symptoms therefore the median is exactly between 2 and 3 symptoms.

Having anonymous teacher questionnaires for the 30% children without parental consent (unidentified children) in the BCS provided us with the possibility of examining the effect of nonresponse. We compared problem areas in relation to service use using only teacher information in the identified group as well (Table 4), to enable comparison between the identified sample and the unidentified sample. As expected, in the identified group, the number of children reported to be in contact with health services and the number of problem areas they suffer from are lower when only teacher information is used. Unidentified children have higher problem levels and higher rates of referral to services when compared to identified children when based on teacher reports only.

*3.2. Predicting Contact with Services.* Table 5 shows the odds ratios (OR) for being in contact with child and adolescent mental health services (CAMH), school psychology services (SPS), and health visiting nurse/physician and for having any kind of support in school according to number of problem areas. The relationship between service contact and number of problem areas was very strong for all services, following a dose-response relationship. Having four or more problem areas increased the OR of being in contact with CAMH by 147 times (identified children).

With the exception of contact with health visiting nurse/physician among unidentified children, male gender was a significant predictor for all service contact. Even when controlling for number of symptoms, boys were 1.8 times more likely to be in contact with CAMH services for identified children (OR 1.8, 95% CI 1.2–2.6) and more than twice as likely in the group of unidentified children with OR 2.4 (95% CI 1.2–4.9).

## 4. Discussion

The symptom load in children in contact with specialized services (CAMH) was high, with children scoring above the 95th percentile on six different areas as a mean. Primary education services, such as any kind of assistance in school, targeted a larger percentage of the population, and children in touch with these services also had a lower symptom load. This supports the notion that children who are referred to specialist services should be assessed broadly, as they are

Table 5: Logistic regression analyses showing odds ratios (OR) for services with number of symptoms and gender as predictors, for identified and unidentified children separately.

| Predictor | Identified children | | | Unidentified children | | |
|---|---|---|---|---|---|---|
| | Not ref. *N* | Ref. *N* | OR (95% CI) | Not ref. *N* | Ref. *N* | OR (95% CI) |
| Child and adolescent mental health | | | | | | |
| 0 symptoms | 3592 | 5 | 1 (ref) | 1885 | 9 | 1 (ref) |
| 1 symptom | 1180 | 10 | 6.0 (2.0–17.5) | 402 | 3 | **1.5 (0.4–5.4) n.s.** |
| 2 symptoms | 516 | 12 | 15.6 (5.5–44.5) | 199 | 6 | 5.4 (1.9–15.5) |
| 3 symptoms | 281 | 14 | 32.6 (11.6–91.2) | 103 | 8 | 14.3 (5.4–38.2) |
| ≥4 symptoms | 494 | 112 | 147.2 (59.7–363.0) | 199 | 38 | 30.0 (14.1–64.2) |
| Girls | 3117 | 42 | 1 (ref) | 1291 | 10 | 1 (ref) |
| Boys | 3023 | 115 | 1.8 (1.2–2.6)* | 1435 | 52 | 2.4 (1.2–4.9)** |
| School psychology service | | | | | | |
| 0 symptoms | 3537 | 61 | 1 (ref) | 1856 | 38 | 1 (ref) |
| 1 symptom | 1132 | 59 | 3.0 (2.0–4.2) | 372 | 33 | 4.0 (2.5–6.6) |
| 2 symptoms | 466 | 62 | 7.1 (4.9–10.3) | 172 | 33 | 8.8 (5.4–14.6) |
| 3 symptoms | 230 | 65 | 14.8 (10.1–21.5) | 83 | 28 | 13.9 (8.0–24.3) |
| ≥4 symptoms | 322 | 286 | 47.2 (34.9–63.8) | 102 | 135 | 57.4 (37.7–87.6) |
| Girls | 3010 | 147 | 1 (ref) | 1237 | 64 | 1 (ref.) |
| Boys | 2745 | 393 | 2.2 (1.8–2.7) | 1293 | 194 | 1.6 (1.1–2.2)* |
| Health visiting nurse/physician | | | | | | |
| 0 symptoms | 3484 | 114 | 1 (ref) | 1851 | 43 | 1 (ref) |
| 1 symptom | 1056 | 134 | 3.9 (3.0–5.0) | 368 | 37 | 4.3 (2.8–6.8) |
| 2 symptoms | 423 | 105 | 7.4 (5.6–9.9) | 170 | 35 | 8.8 (5.5–14.2) |
| 3 symptoms | 205 | 90 | 13.0 (9.5–17.8) | 78 | 33 | 18.2 (11.0–30.2) |
| ≥4 symptoms | 289 | 317 | 32.4 (25.3–41.5) | 138 | 99 | 30.9 (20.8–46.0) |
| Girls | 2858 | 299 | 1 (ref) | 1229 | 72 | 1 (ref) |
| Boys | 2664 | 474 | 1.2 (1.0–1.4)** | 1318 | 169 | **1.3 (0.9–1.7) n.s.** |
| School support | | | | | | |
| 0 symptoms | 3438 | 159 | 1 (ref) | 1749 | 145 | 1 (ref) |
| 1 symptom | 1059 | 131 | 2.6 (2.1–3.3) | 310 | 95 | 3.6 (2.7–4.7) |
| 2 symptoms | 410 | 118 | 5.9 (4.5–7.6) | 135 | 70 | 5.9 (4.2–8.3) |
| 3 symptoms | 205 | 90 | 8.8 (6.5–11.8) | 61 | 50 | 8.6 (5.6–13.1) |
| ≥4 symptoms | 275 | 331 | 24.0 (19.2–30.2) | 69 | 168 | 26.2 (18.7–36.6) |
| Girls | 2885 | 272 | 1 (ref) | 1142 | 159 | 1 (ref) |
| Boys | 2569 | 569 | 1.8 (1.5–2.2) | 1133 | 354 | 1.5 (1.2–1.9) |

*$P < 0.01$, **$P < 0.05$; nonsignificant values are marked with n.s. and shown in bold. All other values are statistically significant at $P < 0.001$.

likely to suffer from symptoms from more than one specific problem area. It also supports the idea that this is true mainly for specialized services, as many children at lower levels of services actually do suffer from problems from one or two domains only.

To assess the relative risk of being in contact with various services, logistic regression analyses were performed with number of problem areas as predictor. Gender was entered as well and turned out to be a significant predictor for both CAMH and SPS also after having controlled for symptoms, with boys much more likely to have been in contact with these services than girls. This pattern was even stronger among unidentified children, maybe due to the fact that they only had teachers as informants. Publications from BCS have previously shown that teachers seem to have a stronger gender bias than parents in their ratings of the children [26, 27], and Derks et al. (2007) also found teacher scores to be lower for girls than for boys [19]. The present analyses indicate that the gender bias is even more far reaching, in that even when the symptoms have been consciously registered by the teacher, contact with services is less likely to be available for girls. Kopp et al. (2010) found that girls, in spite of having very disabling symptoms and high levels of comorbid problems, were brought late to services and had a much higher than expected age at diagnosis of ASD and ADHD [5]. The results are all the more alarming as we used the 95th percentile of the total population, whereas gender specific norms are lower for girls for most problem areas in this age group (http://www.sdqinfo.com/UKNorm.html) [28]. This means that compared to their own kind, they are likely to be even more deviant than the boys referred to same specialist services. Ohan and Visser (2009) found

the same pattern. The gender bias in their study was driven by the low chances of referral of girls with only ADHD; whereas boys with ADHD only were likely to be referred, girls needed the additional presence of disruptive behavior to be referred [21]. In a population-based study, Sawyer et al. (2004) also found comorbid conditions predictive of service use in ADHD, but only for girls [29]. In two American studies, parents of girls with ADHD reported higher stigma-related barriers to seek help than parents of boys [24] and girls were less likely to receive services in spite of scoring higher on ADHD symptoms [20]. In other words, girls are required to be more impaired before referral is likely. This bias was true for both parents and teachers alike, and the reason for this difference was explained by parental and teacher assumptions that treatment, particularly teaching assistance, would be more efficacious/needy for boys [21].

A minor note concerns the difference between identified and unidentified children. We know from previous studies on the BCS sample that unidentified children have higher symptom scores on all areas [25–27, 30]. Still, they are less in contact with services and the children in contact with services demonstrate lower amount of problem areas, if compared with all the available information from both parents and teacher questionnaires. However, when comparing identified and unidentified children on teacher reports only, it is clear that the difference is explained by the lack of parental reports on these children, not due to their having less problems. The teacher is less likely to be informed about the child's health seeking behavior, and we see that the difference in percentage in contact with school psychology services (which the teachers are generally informed about) is less pronounced. Comparing the findings based on one informant versus two informants in the identified children, we see that the number of problem areas is drastically lower, indicating the importance of including several informants, as one informant may not have access to the entire range of behaviours and difficulties the child is exhibiting.

The present study did not investigate the differential contribution of specific symptoms to the service contact. The aim of the study was rather to investigate whether children in contact with specialist services suffer from many different symptom areas rather than from one or two specific problems. A total of 13 symptom areas was included for identified children, and one might argue that, having so many symptom areas, chances are high for any child to score above the 95th percentile. However, of children not referred to any services, only 15.2% had problems on more than one symptom area, and only 3.7% scored above the cutoff on three symptom areas. For children in contact with CAMH more than 90% had at least 2 problem areas, and 73% scored above the 95th percentile on four or more problem areas. The symptom areas covered a wide range of problems, but many common problems among children referred to CAMH, were still not included, such as enuresis, clumsiness, and conduct disorders. It is therefore not unlikely that the present study actually underestimates the width of problems children in CAMH services suffer from.

When it comes to the gender bias, the disruptive behavior hypothesis has been put forward as explaining why girls are less likely to be referred to school and health services than boys, indicating that we should have analyzed whether differences in specific problem areas contributed to the gender bias. However, several studies have found parental and teachers beliefs about treatment efficacy for girls and boys to be central to explaining the referral bias to CAMH rather than symptoms within the child [20–22, 24], and this bias is further enhanced by the health services, in being less likely to diagnose ADHD and provide adequate treatment for girls [20, 23, 24]. Furthermore, only one problem area targeted the internalizing domain (SDQ-emotional problems) (stereo) typically associated with female symptomatology, making it rather unlikely that this alone would explain the gender differences.

One limitation is only having access to questionnaire ratings. The questions regarding contact with services did not specify when the contact was and the nature of the contact. The main strength is the total population sample included, with teacher questionnaires covering 97% of the population, eliminating the effects of selection bias. Thus, we trust the main conclusion of the study; that as a rule, children in contact with specialized educational and health services are reported to have symptoms suggesting a wide range of mental health problems. These services need to adopt a broad assessment approach in order to adequately meet the needs of these children. Even though one area may cause the referral and be the main problem at one point, the child and its family are unlikely to benefit from specific interventions targeting that single problem if several others occur in conjunction.

## 5. Conclusion

The ESSENCE model was supported in the present study of a total population of children 7–9 years of age, as almost all children in contact with CAMH suffered from many problems rather than single and specific problems as measured by parent and teacher questionnaires. High scores within several areas were also highly predictive of being in contact with specialized services. A sad finding was that girls were much less likely to be in touch with services, even after controlling for number of symptoms. This indicates that not only are girls struggling unseen, but even worse they are struggling unaided even when being seen.

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*Research Article*

# Mental Health in Children with Cerebral Palsy: Does Screening Capture the Complexity?

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*Introduction*. Children with cerebral palsy (CP), one of the most common childhood neurological disorders, often have associated medical and psychological symptoms. This study assesses mental health problems compared to population controls and the ability of a mental health screening tool to predict psychiatric disorders and to capture the complexity of coexisting symptoms. *Methods*. Children with CP ($N = 47$) were assessed according to DSM-IV criteria using a psychiatric diagnostic instrument (Kiddie-SADS) and a mental health screening questionnaire (SDQ). Participants from the Bergen Child Study, a large epidemiological study, served as controls. *Results*. Children with CP had significantly higher means on all problem scores including impact scores. Two in three children scored above 90th percentile cutoff on Total Difficulties Score (TDS), and 57% met criteria for a psychiatric disorder, yielding a sensitivity of 0.85 and a specificity of 0.55. Mental health problems coexisted across symptom scales, and peer problems were highly prevalent in all groups of psychiatric disorders. *Conclusion*. A high prevalence of mental health problems and cooccurrence of symptoms were found in children with CP compared to controls. Screening with SDQ detects mental health problems, but does not predict specific disorders in children with CP. ADHD is common, but difficult to diagnose due to complexity of symptoms. Mental health services integrated in regular followup of children with CP are recommended due to high prevalence and considerable overlap of mental health symptoms.

## 1. Introduction

*1.1. Cerebral Palsy (CP).* CP is one of the most common neurodevelopmental conditions in childhood, affecting 2-3/1000 [1, 2]. While motor impairment is the diagnostic basis, the disorder often presents with associated symptoms and a wide range of related impairments such as epilepsy, pain, and cognitive and communicative impairments. Mental health problems as another main associated symptom, have recently gained awareness, as assessed by screening questionnaires [3–6] and by diagnostic interviews [7]. Using a diagnostic interview, one in two children with CP met criteria for a psychiatric disorder, of which attention deficit hyperactivity disorder (ADHD/ADD) was the most common. Additionally, one in five children had more than one diagnosis, and the presence of psychiatric disorders was not significantly determined by type and severity of the CP condition [7]. The complex symptom presentation is in accordance with the Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examination (ESSENCE) model that emphasizes the coexistence of symptoms in multiple domains in neurodevelopmental disorders [8]. Further, there is growing evidence that many children with neurodevelopmental disorders are more prone to psychiatric disorders in adulthood, some of which can be screened for and treated in childhood [9, 10]. While there is growing awareness about the complexity of the CP condition, most of the health services are provided in specialized paediatric clinics with motor impairments as the main focus. To detect mental health problems in children with CP, screening questionnaires may be useful. However,

little is known regarding the ability of these questionnaires to disentangle the complexity of mental health problems in children with CP.

*1.2. Mental Health Screening.* Questionnaires such as the Child Behaviour Checklist (CBCL) [11] and the Strengths and Difficulties Questionnaire (SDQ) [12, 13] have both been used to describe the prevalence of mental health symptoms in children with CP [3, 4]. An Icelandic study using CBCL and comparing 36 preschool children having CP with a randomly selected sample of preschool children found that 40–50% of children with CP suffered substantially from behavioural and emotional problems as reported by parents, demonstrating the early coexistence of these symptoms as suggested by the ESSENCE model [4, 8]. A high prevalence of diverse mental health problems have also been found in other studies including school age children when using the SDQ [3, 14, 15]. Children with CP scoring above abnormal range were found in one of four children in a European multicentre study, and in a recent Canadian study [3, 15], and an even higher number in a study including children with CP hemiplegia only, a subtype generally less severely affected [14]. All three studies has used British comparison norms. Peer problems were found to affect more than one third of children with CP in these studies. Likewise, hyperactivity problems were found in one of four children, conduct problems in one of six children, and emotional problems ranging from 17% to 32%. These findings indicate a high prevalence of mental health problems in children with CP and a considerable coexistence of problems.

*1.3. The Strengths and Difficulties Questionnaire.* The SDQ is a short 25-item screening tool to detect mental health problems and prosocial behaviour in children. In combination with the impact scores, which depict the impairment from mental health problems in response to family, social, and school situations, it has shown accuracy in detecting psychiatric disorders, and has been thoroughly validated both in general populations, and in populations of children suffering from chronic illnesses [12, 13]. Psychometric properties of the Total Difficulties Score (TSD) of the SDQ compared to the Development and Well-being Assessment (DAWBA) has shown a sensitivity level of 0.63 in the general British childhood population, up to 0.87 in at-risk populations, likewise specificity has shown values from 0.47 in an at-risk populations, to 0.95 in a general British childhood population [12, 16, 17]. To our knowledge, none of the previously used questionnaires have yet been validated against a diagnostic interview in a population of young children with CP, despite knowledge that there is a considerable overlap of mental health symptoms in addition to a complexity of somatic symptoms which may affect the psychometric properties of the screening tool.

*1.4. Using the ESSENCE Model as a Framework.* We wanted to assess mental health problems in children with CP compared to population-based controls and to assess frequency and coexistence of symptoms. Secondly, we wanted to assess the ability of a mental health screening instrument (SDQ) to sufficiently detect prevalence and coexistence of mental health problems in children with CP, comparing SDQ findings to results from a diagnostic psychiatric interview (the Kiddie-SADS).

## 2. Methods

*2.1. Population.* A cohort of children with cerebral palsy (CP) in the three western counties of Norway born 2001–2003 were invited to participate in the study. Cerebral palsy (CP) was stated for 101 children prior to the study. Three of the children had however subsequently been rediagnosed and given a different neurological diagnosis and were therefore excluded from the study. Of the 98 children invited, 67 (68%) participated and were examined regarding psychiatric disorder. For 11 children however, diagnosing a psychiatric disorder using a diagnostic interview was inappropriate due to severe disability, and these children were omitted from the study. The remaining 56 children were included in the present study. The population has been described in detail in an earlier study [7].

The Bergen Child Study (BCS) served as control group [18]. This study is a large longitudinal population-based study involving all children (9155) in the two Norwegian municipalities Bergen and Sund with matching parent SDQ obtained from 6297 children. It has been described in detail elsewhere [19], and we will only give a brief description here. The whole population was assessed for mental health problems using the Strengths and Difficulties Questionnaire (SDQ) as well as answering a question about chronic illness or disability. Data collected when the children were 7–9 years old were used as comparisons for the present study.

*2.2. Classification, Functional Levels, and Medical Information.* Cerebral palsy was classified according to ICD-10 criteria with the following subgroups: spastic bilateral and unilateral, dyskinetic, atactic, or not further classified. Functional level was classified by the Gross Motor Function Classification System (GMFCS) and Manual Ability Classification System (MACS) which distinguishes five levels (I–V), with level V being the most severe [20, 21]. The cognitive level was recorded through information in the medical record, or through the educational system, and was verified by parents during the interview if results from updated cognitive tests were not available. The population is described in detail in a previous study [7].

*2.3. Mental Health: SDQ.* The Strengths and Difficulties Questionnaire (SDQ) consists of 25 items, of which four record problem domains, each including five items, and one prosocial domain (scale) including five items. Each item can be answered with "not true," "somewhat true," or "certainly true" rated 0–2 for negatively worded items, and inversely 2–0 for positively worded items. The problem domains are *hyperactivity problems* including items such as inattentiveness and distractibility, *conduct problems* including items such as disobedience and temper tantrums, *emotional problems* including items such as anxiety and worry, *peer problems* including items such as loneliness and preferring adult company. *Prosocial behaviour* consists of items such as being helpful and kind.

Combining the four problem subscales (0–10) computes the Total Difficulties Score (TDS) (0–40). The SDQ also includes an impact score (IS) which measures the impact of mental health problems. For each of the subscales, a score at or above the 90th percentile of the controls was defined as screen positive and a Total Difficulties Score at or above the 90th percentile as risk of having a psychiatric disorder.

*2.4. Psychiatric Disorders: Kiddie-SADS.* Parents of children with CP were interviewed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (6-18) 10.04.00 (Kiddie-SADS), a semistructured child psychiatric diagnostic interview designed to unveil psychiatric symptoms within the following groups of disorders: affective, anxiety, psychotic, eating, attention/hyperactivity, oppositional defiant, conduct, tics, substance abuse, and posttraumatic stress disorders, as well as encopresis and enuresis. Diagnostic conclusions were drawn according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Parents were interviewed, and we recorded present symptoms. All interviews were conducted by the first author, a child and adolescent psychiatrist. A *psychiatric disorder* was ascertained if criteria listed in the DSM-IV for each specific diagnosis were fulfilled, including severity and duration of specific symptoms.

*2.5. Mental Health Screening and Psychiatric Disorder.* Mental health problems recorded using the SDQ were compared to psychiatric disorders (DSM-IV criteria) for the following symptom-disorder pairs: SDQ-emotional problems compared to emotional disorders, SDQ-hyperactivity problems compared to ADHD/ADD, and SDQ-conduct problems were compared to ODD and conduct disorders. Finally, the SDQ-Total Difficulties, SDQ-peer problems, and SDQ-impact scores were compared to any psychiatric disorder.

*2.6. Statistical Analyses.* Independent $t$-tests were used to compare mean scores from children in the CP group to those from the general population. *Sensitivity* was defined as the proportion of actual positives which were identified as such. *Specificity* was defined as the proportion of actual negatives which were correctly identified as such. *Positive predictive value (PPV)* was defined as the proportion of positive tests that were true positives, and *negative predictive value* was defined as the proportion of negative tests that were true negatives. *Sensitivity, specificity, PPV, and NPV above 80% were regarded as high. Cross-tabulations and* 90th percentile cutoff were used to calculate these parameters.

Effect size was defined using Cohen's $d$ measuring the standardized mean difference between the study population and controls; a large effect size was defined as ≥0.8, a medium effect size as ≥0.5, and a small effect size as ≥0.3. Cross-tabulations were done to evaluate possibly significance between high scorers on SDQ-TDS and types and severity of CP.

A linear regression analysis was used to explore the influence of each of the five symptom items in the peer problem score, the latter being the dependent variable, and the five items were independent variables.

Table 1: Demographics and functional data for a population of children with cerebral palsy living in the Western Health Region of Norway at school starting age.

| | $N$ (%) |
|---|---|
| $N = 47$ | |
| Boys | 30 (64) |
| Cerebral palsy subtype | |
| Bilateral | 25 (53) |
| Unilateral | 18 (38) |
| Ataxia/dyskinesia | 4 (9) |
| GMFCS level[i] | |
| I-II | 38 (81) |
| III-IV | 9 (19) |
| Intellectual disability[ii] | 10 (21) |
| Epilepsy | 9 (19) |
| Visual impairment[iii] | 19 (40) |

[i] Gross Motor Function Classification System.
[ii] Defined as IQ < 70.
[iii] Defined as any visual impairment.

## 3. Results

*3.1. Population.* Of the 56 children in the present study, 47 completed the SDQ. The mean age was 7 years and 3 months (87.6 months, SD 6.5). Thirty (64%) were boys, more than half had CP diplegia, and four of five children had Gross Motor Function Classification System (GMFCS) levels I and II. One of five had an intellectual disability, and approximately the same number suffered from epilepsy (Table 1). Type and severity of CP conditions were not significantly associated with high scorers on SDQ-Total Difficulties Score.

*3.2. Mental Health Problems in Children with Cerebral Palsy Compared to a Population-Based Control.* Children with CP had significantly higher mean scores compared to controls, affecting all problem scales as well as impact score (Table 2). A large effect size was found for the Total Difficulties Score, hyperactivity problems, conduct problems, peer problems and impact score, and moderate effect size for emotional problems, and a small effect size for prosocial behaviour (Table 2).

*3.3. Coexisting Symptoms.* When comparing all SDQ screen positives across the problem scales, including TDS and impact score, with the following four groups of psychiatric disorders, emotional disorders, conduct disorders, ADHD/ADD, and any psychiatric disorders, we found a high prevalence of coexisting screen positives across groups of psychiatric disorders in children with CP (Table 3). There was a discrepancy between screen positives and children meeting criteria for a psychiatric disorder, most prevalent for SDQ-hyperactivity problems (3/24) and SDQ-conduct problems (2/4). For the 24 children meeting criteria for ADHD/ADD,

Table 2: Mental health for children with cerebral palsy (CP) using mean scores of the Strengths and Difficulties Questionnaire compared with controls.

| | CP group (47) | | Controls[a] (7007) | | | | 95% CI | | Cohen's *d* |
|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | *t* (df) | *P* | | | |
| Emotional problems | 2.6 | 2.2 | 1.3 | 1.7 | 4.0 (46) | <.001 | 0.6 | 1.9 | 0.66 |
| Conduct problems | 2.5 | 1.5 | 1.0 | 1.3 | 6.7 (45) | <.001 | 1.1 | 2.0 | 1.07 |
| Hyperactivity problems | 4.3 | 1.5 | 2.7 | 2.1 | 7.8 (47) | <.001 | 1.2 | 2.1 | 0.88 |
| Peer problems | 4.5 | 1.5 | 1.0 | 1.5 | 16.0 (46) | <.001 | 3.1 | 4.0 | 2.33 |
| Total difficulties scores | 13.9 | 5.3 | 5.6 | 5.0 | 10.7 (46) | <.001 | 6.8 | 9.9 | 1.61 |
| Prosocial behaviour[b] | 7.8 | 2.1 | 8.5 | 1.5 | −2.2 (45) | 0.03 | 1.3 | −0.1 | 0.39 |
| Impact score | 2.9 | 3.8 | 0.4 | 1.5 | 4.6 (46) | <.001 | 1.4 | 3.7 | 0.94 |

[a] Bergen Child Study, [b] higher scores indicate more prosocial behaviour.

Table 3: Coexisting mental health symptoms in children with cerebral palsy meeting criteria for a psychiatric disorder according to DSM-IV criteria assessed by Kiddie-SADS.

| | Children scoring above 90th percentile cutoff on the Strengths and Difficulties Questionnaire | | | | | |
|---|---|---|---|---|---|---|
| | Emotional problems | Conduct problems | Hyperactivity problems | Peer problems | TDS[a] | Impact score |
| Psychiatric disorder | | | | | | |
| Emotional (*N* = 5) | 5/5 | 3/5 | 1/5 | 5/5 | 5/5 | 3/5 |
| Conduct/ODD[b] (*N* = 4) | 2/4 | 2/4 | 2/4 | 4/4 | 4/4 | 4/4 |
| ADHD/ADD[c] (*N* = 24) | 9/24 | 10/24 | 3/24 | 23/24 | 19/24 | 19/24 |
| Any psych[d] (*N* = 27) | 12/27 | 12/26 | 4/27 | 26/26 | 22/26 | 20/27 |

[a] TDS: Total Difficulties Score; [b] ODD: oppositional/defiant disorder; [c] ADHD: attention-deficit/hyperactivity disorder; ADD: attention deficit disorder; [d] Any psych: any psychiatric disorder.

23 were screen positives for peer problems. To gain understanding of the large proportion experiencing peer problems in the present study, a regression analysis was done to identify the impact of each of the five items in the peer problem scale. We found preference for adult company, the most weighted item, followed by lack of close friendships, loneliness, being bullied, and not being liked in diminishing order.

*3.4. SDQ and Psychiatric Disorder.* Screening efficiency of the SDQ-TDS in children with cerebral palsy was assessed by comparing SDQ screen positives (i.e., scores above 90th percentile) with children meeting criteria for a psychiatric disorder according to Kiddie-SADS (Table 4). Sensitivity for all symptom groups varied between 0.13 and 1.0, and specificity varied from 0.55 to 0.87. For TDS, sensitivity was 0.85 and specificity 0.55 (Table 4).

## 4. Discussion

*4.1. Main Findings.* Children with CP in the present population based study had significantly higher means on all SDQ subscales compared to the general childhood population. There was considerable mental health symptom overlap across all categories, and peer problems were highly prevalent in all four groups of psychiatric disorders. Sensitivity for TDS was adequate for SDQ compared to any psychiatric disorders using a semistructured child psychiatric diagnostic interview (Kiddie-SADS).

*4.2. Mental Health Problems in Children with Cerebral Palsy.* Compared to controls, mean scores in children with cerebral palsy were significantly higher on all scales, which is consistent with previous findings. Previous studies have found high TDS mean scores 11.0–12.4, which are similar to those found in the present study [3, 6, 14, 15], even when children with GMFCS level V and intellectual disability (ID) were excluded and therefore as expected had less medical complications than a population consisting of all five GMFCS levels [1, 7].

Mean scores for emotional problems in the present study were similar to the study by Parkes et al. since 2008 [3] and Brossard-Racine et al. where all CP subgroups were included [15]. In the study by Parkes et al. including children with CP hemiplegia only however [14], a fourfold higher mean score for emotional problems was found. This may indicate that anxiety and depressive disorders are more prevalent in children having CP with a functional level closer to their healthy peers, as they perhaps more often are met with the same expectations in all areas as children without CP, leading to a sense of shortcoming.

For the conduct and hyperactivity subscales, mean scores in the present study were similar (2.5 and 4.3, resp.) to those found in comparable studies, 1.7–2.0 for conduct problems and 4.3–4.8 for hyperactivity problems [3, 14, 15]. This finding underlines a consistently high prevalence of behavioural problems in children with CP, which was also confirmed in a recent meta-analysis where one of four children with CP were found to have behaviour disorder [22]. Mean scores

Table 4: Mental health screening compared to having a psychiatric disorder (according to DSM-IV criteria assessed by Kiddie-SADS) for children with cerebral palsy at school starting age.

| SDQ-symptoms versus psychiatric disorders | Above 90th percentile on SDQ[a] *N* (%) | Psychiatric disorder present *N* (%) | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|
| Emotional symptoms versus emotional disorders[b] | 14 (29.8) | 5 (10.6) | 1.00 | 0.79 | 0.36 | 1.00 |
| Conduct problems versus conduct disorder/ODD[c] | 16 (34.8) | 4 (8.5) | 0.50 | 0.67 | 0.13 | 0.93 |
| Hyperactivity problems versus ADHD/ADD[b] | 6 (12.8) | 24 (51.1) | 0.13 | 0.87 | 0.50 | 0.49 |
| Total Difficulties Score versus any psychiatric disorder[c] | 31 (67.4) | 26 (56.5) | 0.85 | 0.55 | 0.71 | 0.73 |
| Peer problems versus any psychiatric disorder | 41 (89.1) | 26 (56.5) | 1.0 | 0.25 | 0.63 | 1.0 |
| Impact score versus any psychiatric disorder | 27 (57.4) | 27 (57.4) | 0.74 | 0.65 | 0.74 | 0.65 |

PPV: positive predictive value; NPV: negative predictive value; [a]SDQ: strengths and difficulties questionnaire [b]$N = 47$; [c]$N = 46$.

for peer problems however were higher in the present study compared to previous studies of children with cerebral palsy (2.7–3.0) [3, 14, 15]. Peer problems were found in nine of ten children with CP in the present study, whereas Parkes et al. found peer problems in one of three children in their studies and two of five children in the Canadian study by Brossard-Racine et al. Peer problems were highly prevalent across all diagnostic groups, that is, emotional disorders, conduct disorders/ODD, as well as hyperactivity disorders, and could be related symptomatically to autism spectrum disorders (ASD) which have been found to be prevalent in children with CP [23]. Similarly, ASD is often part of neurodevelopmental conditions in general with a considerable overlap of conditions as described in the ESSENCE model [8]. When analysing the peer problems construct in detail, preference for adult company and loneliness were highly prevalent in the present study. This finding is coherent with information given by parents during the Kiddie-SADS interview, where many parents pointed to their children taking part in organized school and leisure activities, although they often had few mutual own-aged friendships. This could indicate that some might be passively watching rather than being active participants in peer activities. Another possible hypothesis for peer problems is slow cognitive processing and speech, which for many children with CP with normal IQ may result in difficulties matching their peers in spontaneous play activities, perhaps resulting in a preference for adults to accompany during activities [24].

*4.3. Behaviour Problems.* For ADHD/ADD which was the most prevalent psychiatric disorder in the present study, the screening efficacy using SDQ in the present study was 13%, about half of that found in the studies by Parkes et al. and Brossard-Racine et al. [3, 14, 15], despite a high prevalence of ADHD/ADD (52%) when parents of the same children were interviewed with the Kiddie-SADS and diagnosed according to DSM-IV criteria. On the contrary, symptoms of conduct disorders in the present study were almost twice as high as those found in the studies by Parkes et al. and Brossard-Racine et al. [3, 14, 15], despite a much lower prevalence (8.5%) when diagnosing according to Kiddie-SADS. Other studies have pointed to cooccurrence of symptoms between ODD (oppositional defiant disorders) and ADHD/ADD, emotional problems and peer problems [25]. Although the studies by Parkes et al. and Brossard-Racine et al. include children with all CP subtypes, similar to the present one, mental health symptoms may be recognized as conduct or peer problems rather than hyperactivity problems in the study population. Attention problems may not be recognized as such, as these children in Norway to a large degree have individual support during most of their time at school, and parents are often primed to assist their children with all practical issues at home and may not recognize their children's challenges in memory or attention span. During the semistructured Kiddie-SADS interview, these issues were elaborated, and many children met criteria for attention problems when parents were asked to judge their child's attention span in a situation where they were left to do their school work or organize their belongings as would their peers or siblings. Perhaps the screening tools are more sensitive to symptoms such as peer and conduct problems in a population of children with CP than to hyperactivity problems and therefore may not fully capture the attention and/or hyperactivity problems these children suffer, as motor symptoms due to the CP condition may disguise restlessness and distractibility which may be interpreted differently.

*4.4. Coexisting Conditions.* In accordance with the ESSENCE model, we found an extensive overlap of mental health symptoms in children with CP meeting criteria for a psychiatric disorder. Gillberg et al. found a high prevalence of other psychiatric disorders such as emotional problems and ODD in children with ADHD [26], which has also been found in a previous study including children in the present study [7]. Similarly, ADHD was found in half of all children with mild mental retardation MMR in association with other developmental problems [27]. ADHD seems to be a common associated factor in many different developmental disorders or neurological conditions stemming from the brain and may be associated with the immature nervous system being

vulnerable to brain injury in the neonatal period. Perhaps this is one of the reasons for a high level of diversity and overlap of mental health symptoms in children with disorders such as CP which occurs in the neonatal period and why mental health symptoms in children with CP seem to present differently from the general childhood population. It may also explain why the SDQ seems to be a less accurate screening tool for ADHD/ADD in children with CP than one would expect from studies conducted in a general childhood population. The extensive overlap of symptoms constitutes a considerable challenge both in providing diagnostic tools and in gaining competence in recognizing psychiatric disorders in children with a complexity of interacting symptoms.

*4.5. Screening Efficiency of the SDQ.* The child psychiatric diagnostic interview Kiddie-SADS and the Strengths and Difficulties Questionnaire were both used to assess the same children which enabled us to evaluate the psychometric properties of the SDQ when using the Kiddie-SADS as the gold standard. When comparing specific mental health symptoms and psychiatric disorders, we found a large range in sensitivity and specificity between the least and the most sensitive symptom-disorder pairs in this study. Sensitivity for TDS compared to any psychiatric disorder according to Kiddie-SADS in the present study was 0.85 and specificity 0.55, which differ from those found in the general childhood population yielding sensitivity of 0.63 and specificity of 0.95 [12]. For a population of children referred to mental health services in Norway, sensitivity was 0.85 and specificity 0.52 for TDS [16], and for children with chronic illnesses in a Norwegian study, sensitivity was 0.81 and specificity 0.69 for TDS [17] which is comparable to the present study. For emotional, conduct, and hyperactivity disorders, however, we found that the positive predictive value was low, indicating that there may be a need for caution when using the SDQ to predict these disorders in children with CP in early childhood.

*4.6. Clinical Implications.* In the present study, 57% met criteria for a psychiatric disorder, and 67% were screen positive on Total Difficulties Score (TDS). Sensitivity of the SDQ for TDS may be considered adequate however predictive value for specific psychiatric disorders is found to be inadequate in the present study. Knowing that mental health problems seem to affect two in three children with CP, with a considerable overlap of mental health symptoms and psychiatric disorders, we are faced with challenges in disentangling and diagnosing a conglomerate of symptoms. Establishing mental health services as part of the regular follow-up program for children with CP seems relevant. In addition, using the SDQ as a screening instrument to identify children with CP without mental health problems, not in need for mental health services, may be legitimate, bearing in mind, however, the high rate of psychiatric diagnosis and the low diagnostic specificity especially for AD/HD which is one of the most frequent diagnosis.

*4.7. Limitations.* The version of Kiddie-SADS used in the present study did not contain a section on autism spectrum Disorders (ASD), which is a weakness, since all children diagnosed with a psychiatric disorder were screen positive for peer problems. Further, one of three had peer problems without having a psychiatric disorder, and these might represent children with an ASD. Likewise, we did not use the SDQ algorithm for predicting psychiatric disorders as we had a single informant.

A small study population was also a limitation to the study. Similarly, omitting children with GMFCS V and ID from the study may represent a weakness as information on mental health among severely affected children is lacking. Previous studies have attempted to include the most severely affected children; however, it has not been possible to draw diagnostic conclusions regarding psychiatric disorders due to the complexity of motor, cognitive, somatic, and epileptic disorders affecting these children [7, 28]. The current study was however representative of children with CP with GMFCS levels I–IV.

*4.8. Conclusions.* The present study supports the previous literature indicating a high prevalence of mental health problems in children with CP compared to controls. The SDQ disclosed problems relating to peers in more than three in four children, and further studies regarding ASD are recommended. We recommend establishing mental health services for children with CP as part of the regular follow-up program; however screening children with CP for mental health problems in the paediatric clinics using the SDQ seems relevant when established mental health service programs are not available.

## Ethical Approval

The study was approved by the Regional Committee for Medical Research Ethics in Western Norway.

## Conflict of Interests

The authors declare no conflict of interests.

## Authors' Contribution

H. M. Bjorgaas has contributed to the study design, collection of data, and writing the paper. I. Elgen has contributed to the study design, draft, and revision of the paper. T. Boe has contributed to the statistical analysis, draft, and revision of the paper. M. Hysing has contributed to data analysis, draft, and revision of the paper.

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*Research Article*

# Applying an ESSENCE Framework to Understanding Adult Autism Spectrum Disorder and ADHD: Retrospective Parent Reports of Childhood Problems

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Diagnoses of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are increasingly being made in adulthood. However, assessments can fail to address the diverse range of problems that patients have experienced. The current study applied an early symptomatic syndromes eliciting neurodevelopmental clinical examinations (ESSENCE) framework to explore retrospectively reported childhood developmental and behavioral problems. It examined if adult ASD and ADHD patients would show problems outside those reflected in the respective diagnostic criteria, and also if these patient groups would show more extensive childhood problems than other psychiatric patients. Parents of adults with ADHD ($n = 130$), ASD ($n = 57$), coexisting ADHD and ASD ($n = 38$), and other psychiatric disorders ($n = 56$) reported on a range of childhood problems. Descriptions of the ADHD, ASD, and ADHD+ASD groups reflected greater impairment than descriptions for patients with other psychiatric disorders in most problem areas. Although differences were observed between ADHD and ASD patients in the core diagnostic areas, these syndromes also shared a number of childhood difficulties. The ESSENCE approach can assist in understanding the symptom history of adult ADHD and ASD patients and can be helpful to distinguish their childhood experiences from other psychiatric patients' experiences.

## 1. Introduction

Adult diagnoses of autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) have increased in recent decades and are currently estimated to occur in one and four percent of the adult population, respectively [1, 2]. Although these two syndromes are relatively well-known childhood disorders, they have only recently come into the focus of adult psychiatry. Consequently, suitable approaches to understanding the complex needs of these adult patient groups are warranted.

Diagnosis of ASD is based on a qualitative impairment of social interaction and communication as well as restricted repetitive and stereotyped patterns of behavior, interest, and activities [3]. ADHD diagnosis is characterised by attention deficits and/or hyperactivity and impulsivity. Importantly, diagnosis of each of these syndromes requires that the symptoms begin in childhood [3]. Although ADHD and ASD present distinct problems, these two conditions can also appear to share characteristics [4–6], making them sometimes problematic to distinguish. For example, inattention and poor social skills are common to both disorders. However, ADHD and ASD may also share a high rate of comorbidity, with epidemiological studies, for example, estimating 30% prevalence of ADHD amongst ASD patients [7].

In addition to symptoms described in the diagnostic criteria, patients with ASD and/or ADHD tend to also experience a range of other behavioral and developmental problems. Both syndromes are associated with language [8, 9]

and motor skill deficits [10, 11] as well as mood disorders [12, 13] and sleep problems [14, 15]. They also tend to involve cognitive deficits including executive functions, time perception, and memory functions [16]. Furthermore, ASD and ADHD are thought to have more extensive developmental problems than other psychiatric conditions with typically later onset (such as mood disorders or anxiety disorders) [17, 18].

Both ASD and ADHD are associated with a range of difficulties, of which only some are located within the diagnostic criteria [19, 20]. However, clinical assessments often focus heavily on the core features of a suspected diagnosis and, as a result, can fail to examine the assortment of problems that an individual presents with. Gillberg has conceptualized the variety of problems characterising some young children in clinical settings as ESSENCE (early symptomatic syndromes eliciting neurodevelopmental clinical examinations) [21]. This approach describes the multifaceted developmental and behavioral symptoms often observed in children with neurodevelopmental syndromes, including ASD and ADHD. ESSENCE presents these problems as belonging to eight areas of functioning: (a) general development, (b) communication and language, (c) social interrelatedness, (d) motor skills, (e) attention, (f) activity, (g) behavior (conduct), and (h) mood and/or sleep. Gillberg observes that children presenting for clinical examination with one or more of these difficulties are usually treated by only one type of specialist, although specialists from a range of fields would often be more appropriate [21]. Syndromes such as ASD and ADHD, have significant comorbidities (such as depression) that can be overlooked or misinterpreted in "specialised" assessment and treatment. Consideration of broader problem areas, such as those suggested by ESSENCE, during the diagnostic process of ASD and ADHD would assist in capturing the full picture of an individual's impairments.

Although ADHD and ASD are usually diagnosed in childhood, adult diagnoses are rapidly increasing [22]. Furthermore, prevalence rates are likely to be higher than current estimates as many adult psychiatric patients go undiagnosed [23]. Consequently, there is a pressing need to extend knowledge in diagnosis and treatment of child ASD and ADHD to adult psychiatry. However, ASD and ADHD symptoms can reduce somewhat [24–26], or can take on new forms with age [27], further complicating assessments. As the diagnoses of ADHD and ASD require that symptoms persist throughout childhood [3], parent reports of childhood symptoms play an important role in the diagnostic process. Therefore, when evaluating adults, it is important that tools are available to assess an adult's broader childhood symptom history.

This study applies the ESSENCE framework to the adult assessment of ASD and ADHD. In Nordic psychiatry, the five to fifteen (FTF) questionnaire is a widely used instrument that addresses a variety of childhood neurodevelopmental problems [28]. In addition to the inclusion of problems diagnostic of each disorder, the FTF also addresses problem areas that ESSENCE presents as relevant to understanding the full picture of an individual's difficulties [21, 29, 30]. Using the FTF, the current study will explore to what extent retrospective parent reports of childhood symptoms reflect impairments in developmental areas other than those listed in the respective diagnostic criteria. As ESSENCE argues that childhood onset neurodevelopmental disorders such as ASD and ADHD are associated with extensive childhood problems, it is expected that adults with ASD and/or ADHD will have exhibited more childhood problems than patients with other (later onset) psychiatric disorders. The similarities and differences in childhood problems between these diagnostic groups will be examined.

## 2. Materials and Methods

*2.1. Participants and Procedure.* Participants ($n = 413$) were consecutive admissions referred to an outpatient tertiary psychiatric clinic in northern Stockholm (Sweden) by a clinician for diagnosis and treatment of ADHD or ASD. The catchment area of the clinic has a population of nearly 320,000 adult inhabitants from both high and low socioeconomic regions. Self-referrals or patients with an intellectual disability or obvious drug/alcohol problems were not included in the study.

Assessment for adult ADHD and ASD involved clinical interviews and assessments with patients and a parent by certified senior psychiatrists and licensed psychologists, with a diagnosis given after consensus between the two. The DSM-IV diagnostic criteria were applied; however, the criterion limiting concurrent diagnosis of ASD and ADHD was disregarded to allow an investigation of the coexisting ASD and ADHD. The assessment procedure for each patient took 12–18 hours to complete over a 2-week period. Ethics approval was provided by the Regional Ethics Committee in Stockholm.

At the first consultation, a parent was asked to complete a questionnaire addressing childhood problems (FTF). Parent reports of patients diagnosed by the clinic with ASD ($n = 57$), ADHD ($n = 130$), or coexisting ADHD+ASD ($n = 38$) were compared to a psychiatric disorders group ($n = 56$), mostly comprised of patients with major depression, OCD and other anxiety disorder diagnoses, who were identically assessed but did not receive an ASD and/or ADHD diagnosis. Of the initial sample, 281 participated (females $n = 142$, males $n = 139$; aged between 16 and 57 years of age; mean age = 30.57, SD = 9.86) (see Figure 1).

*2.2. Diagnosis of ADHD and ASD.* In addition to clinical interviews, the following instruments assisted in the diagnosis of ASD and ADHD. For ASD assessment, the Autism Spectrum Screening Questionnaire (ASSQ) [31] and the Asperger Syndrome Diagnostic Interview (ASDI) [32] were completed. The ASSQ is a screening test detecting the high-functioning autism in childhood and is completed by parents [31]. The ASDI is a structured diagnostic patient-interview addressing current symptoms including social impairment, narrow interests, repetitive routines, speech and language peculiarities, nonverbal communication problems, and motor clumsiness [32]. ASDI scores range from 20 to 60.

For ADHD symptoms, patients completed the Wender Utah Rating Scale (WURS), which addresses childhood symptoms of ADHD [33]. They were also assessed with the Wender-Reimherr Adult Attention Deficit Disorder

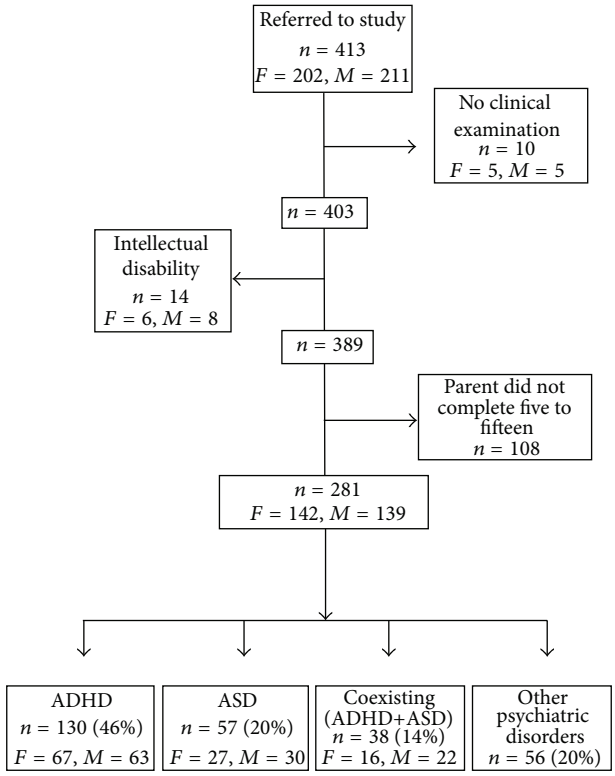


Figure 1: Flow scheme for participation.

Scale (WRAADDS) [34]. This structured patient interview addresses adult symptoms including attention difficulties, hyperactivity and/or restlessness, temper, affective lability, emotional overreactivity, disorganization, and impulsivity relating to present difficulties. A summed score (ranging from 0 to 140) is calculated to reflect severity of ADHD symptoms.

In addition, the assessment of general functioning was made using the global assessment of functioning (GAF) [35]. This provides an estimate of the level of social, psychological, and work-related functioning and degree of mental symptoms in the past year. Scores range between 0 and 100, with higher scores representing good functioning in a wider range of activities. The Wechsler adult intelligent scale, neuropsychological version (WAIS III and WAIS III-NI), was used to screen for intellectual disability.

*2.3. Childhood Problems: Five to Fifteen Questionnaire.* The five to fifteen (FTF) was used to describe a range of developmental and behavioral problems that patients displayed in childhood between ages five and fifteen years [28]. This instrument is a parent-report questionnaire consisting of 181 statements describing neuropsychiatric-neurodevelopmental problems in daily functioning. The FTF has been used extensively in both clinical and research settings, with gender and age norms available [28, 36–38]. Typically, parents complete this questionnaire when their child is being screened for a neurodevelopmental disorder. In the current study, a parent retrospectively completed the FTF about their adult child. Parents were told to focus on when their child was younger than 8 years. This corresponds approximately to the age when symptoms of ADHD or ASD must be present in order to fulfill the diagnostic criteria for these diagnoses and when parents typically recognize these childhood problems. Parents indicated how accurately each statement described their child's behavior in childhood in comparison to what would be considered as normal for this age range. Thus, a behavioral problem noted by the parent when the child was five years but gone at the age of 12 was checked as a problem in the FTF. Reponses are made on a 3-point scale ranging from 0 to 2 (*does not apply, applies sometimes or to some extent, and definitely applies*).

The items represent eight broader domains: (a) motor skills, (b) executive functions, (c) perception, (d) memory, (e) language, (f) learning, (g) social skills, (h), and emotional/behavioral problems. To examine childhood problems in more detail and illustrate the ESSENCE domains, the current study examined 19 FTF subdomains (see Table 2). The subdomain scores were calculated as the mean value of the included subdomain items as described in the FTF questionnaire instructions, with higher scores representing greater childhood difficulties. The current study then compared the median subdomain scores for each group with the FTF median norms available for children aged from 6 to 8 years. For a few subdomains norms for this age group were unavailable as they are related to school performances, and so norms for 9 to 12 years old were used instead (norms available on request at http://www.515.org/). Younger children receive higher ratings than older children [28]; thus, using young age group norms minimized the risk for over-stating the findings in the current study.

The FTF subdomains of "communication" and "social skills" refer to symptoms in ASD diagnostic criteria, while "attention" and the combined subdomains "hypoactivity and hyperactivity/impulsivity" and "attention" refer to symptoms in ADHD diagnostic criteria.

*2.4. Statistical Analyses.* Statistical analyses were performed in Statistica 7.1 [39]. All significance tests were two-tailed. A series of chi-square tests and Kruskal-Wallis ANOVAs were used to examine patient characteristics between the diagnostic groups. As the scores for each FTF subdomain were highly skewed, non-parametric tests were used. All between-group main effects for each subdomain were analysed using the Kruskal-Wallis ANOVA. Between-group comparisons were analysed pairwise using Mann-Whitney $U$ test. A significance $P$ value of $<.05$ was regarded as significant. As the analyses were largely exploratory, the application of a Bonferroni adjustment was not considered as fully applicable in this context.

## 3. Results

*3.1. Participant Characteristics.* The four patient groups shared a similar proportion of males and females as well as age distribution ($P = .10$) (see Table 1). Significantly, more

Table 1: Participant characteristics for each patient group.

| Patient characteristics | ADHD ($n$ = 130) | ASD ($n$ = 57) | ADHD+ASD ($n$ = 38) | Other psychiatric disorders ($n$ = 56) |
|---|---|---|---|---|
| Gender—male | 63 (48.5) | 30 (52.6) | 22 (57.9) | 24 (42.9) |
| Mean age (SD) | 30.2 (10.2) | 29.8 (9.8) | 29.7 (9.5) | 32.9 (9.1) |
| Single marital status | 99 (79.8) | 51 (94.4) | 27 (75.0) | 37 (75.5) |
| Work full-time | 21 (17.8) | 5 (9.8) | 3 (9.1) | 11 (23.9) |
| Meet friends less than monthly | 12 (10.9) | 27 (54.0) | 12 (37.5) | 10 (23.8) |
| Current symptoms and functioning | | | | |
| WRAADDS | 78.79 (23.74) | 46.88 (19.52) | 72.84 (24.81) | 48.53 (22.04) |
| ASDI | 25.32 (5.09) | 37.75 (6.73) | 33.05 (7.53) | 25.05 (4.24) |
| GAF | 55.53 (10.97) | 45.42 (10.87) | 47.44 (10.97) | 54.27 (12.62) |

Characteristic results = $n$ (%); current symptoms and functioning = mean (SD).

Table 2: Five to fifteen subdomain median scores.

| ESSENCE domain | FTF subdomain | ADHD | ASD | ADHD+ASD | Other psychiatric disorders | FTF norms |
|---|---|---|---|---|---|---|
| Motor coordination | Gross motor skills | 0.29 | 0.43 | 0.50 | 0.07 | .14 |
| Motor coordination | Fine motor skills | 0.20 | 0.10 | 0.35 | 0.00 | .10 |
| Attention | Attention | 1.2 | 0.60 | 1.22 | 0.22 | .25 |
| Activity | Hypoactive and hyperactive/impulsive | 0.69 | 0.46 | 0.50 | 0.15 | .00 and .22* |
| General development | Planning and organizing | 1.17 | 0.67 | 1.00 | 0.00 | .33 |
| Motor coordination | Relation in space | 0.20 | 0.20 | 0.60 | 0.00 | .00 |
| General development | Time concepts | 0.50 | 0.00 | 0.50 | 0.00 | .05 |
| Motor coordination | Body perception | 0.40 | 0.40 | 0.40 | 0.00 | .00 |
| General development | Visual perception | 0.00 | 0.00 | 0.00 | 0.00 | .00 |
| General development | Memory | 0.55 | 0.27 | 0.45 | 0.09 | .18 |
| Communication and language | Comprehension | 0.20 | 0.20 | 0.40 | 0.00 | .00 |
| Communication and language | Expressive language skills | 0.08 | 0.08 | 0.15 | 0.00 | .00 |
| Social interaction | Communication | 0.33 | 0.33 | 0.83 | 0.00 | .00 |
| General development | Reading/writing and math | 0.62 | 0.23 | 0.69 | 0.00 | −.12 and −.00* |
| General development | General learning | 0.50 | 0.50 | 0.75 | 0.00 | −.00 |
| General development | Coping in learning | 1.00 | 0.70 | 1.00 | 0.20 | −.20 |
| Social interaction | Social skills | 0.44 | 0.74 | 0.70 | 0.15 | .04 |
| Behavior/sleep/mood-mood | Internalising and externalising | 0.58 | 0.48 | 0.44 | 0.20 | .00 and .08* |
| Behavior/sleep/mood | Obsessive-compulsive | 0.13 | 0.25 | 0.13 | 0.00 | .00 |

*FTF norms for 9–12 years old because 6–8 years old norms are not available for these subdomains.

ASD patients were single ($x^2$ = 8.35; $df$ = 3; $P$ = .04) and had low social contact than the other groups ($x^2$ = 35.64; $df$ = 3; $P$ < .001). No significant differences in fulltime employment rates were observed between groups ($P$ = .15). Consistent with diagnoses, the ADHD and ADHD+ASD groups showed the highest WRAADDS scores, while the ASD and ADHD+ASD groups showed the highest ASDI scores. Poorer general functioning (lower GAF scores) was observed for the ASD and the ADHD+ASD groups compared to the ADHD group and other psychiatric disorders group (H(3, $n$ = 240) = 30.5, $P$ < .0001).

*3.2. Childhood Problems Reported for ASD and ADHD Patients.* To explore the extent to which ASD and ADHD patients were described as having childhood problems beyond those listed in the diagnostic criteria, median subdomain scores for each diagnostic group were compared to the FTF median norms. As shown in Table 2, scores for the ADHD, ASD and ADHD+ASD groups appeared higher than the nonclinical norms on nearly all subdomains. These included the ASD group showing higher "communication" and "social skills" impairment scores and the ADHD group having higher "hypoactivity and hyperactivity/impulsivity" impairment scores than the norms. Three exceptions were observed for "fine motor skills", "visual perception," and "time concepts".

*3.3. Childhood Problems in ADHD and ASD Compared with Other Psychiatric Patients.* The ADHD, ASD, and ADHD+ASD groups were then compared to patients with

Table 3: Comparisons in childhood problems between ADHD/ASD groups and other psychiatric disorders group.

| FTF subdomains | Main Effects | ADHD | ASD | ADHD+ASD |
|---|---|---|---|---|
| | *P* | *P* | *P* | *P* |
| Gross motor skills | <0.001 | <0.01 | <0.001 | <0.001 |
| Fine motor skills | <0.001 | <0.001 | <0.05 | <0.001 |
| Attention | <0.001 | <0.001 | <0.001 | <0.001 |
| Hypoactive and hyperactive/impulsive | <0.001 | <0.001 | <0.001 | <0.001 |
| Planning and organizing | <0.001 | <0.001 | <0.01 | <0.001 |
| Relation in space | <0.001 | <0.001 | <0.05 | <0.001 |
| Time concepts | <0.001 | <0.001 | n.s. | <0.001 |
| Body perception | <0.001 | <0.001 | <0.001 | <0.001 |
| Visual perception | <0.01 | <0.01 | n.s. | <0.01 |
| Memory | <0.001 | <0.001 | <0.001 | <0.001 |
| Comprehension | <0.001 | <0.001 | <0.01 | <0.001 |
| Expressive language skills | <0.05 | n.s. | <0.05 | <0.01 |
| Communication | <0.001 | 0.01 | <0.001 | <0.001 |
| Reading/writing and math | <0.001 | <0.001 | <0.05 | <0.001 |
| General learning | <0.001 | <0.001 | <0.001 | <0.001 |
| Coping in learning | <0.001 | <0.001 | <0.001 | <0.001 |
| Social skills | <0.001 | <0.001 | <0.001 | <0.001 |
| Internalising and externalising | <0.001 | <0.001 | <0.001 | <0.001 |
| Obsessive-compulsive | <0.05 | n.s. | <0.01 | n.s. |

Comparisons between the other psychiatric disorders and the ADHD, ASD, and ADHD+ASD groups; n.s.: nonsignificant; overall group differences were calculated using the Kruskal-Wallis ANOVA; pairwise group comparisons were made using the Mann-Whitney test.

other psychiatric disorders to examine if the latter group showed fewer childhood problems. As shown in Table 3, significant main effects were observed on all subdomains. The pairwise comparisons showed that on nearly all subdomains, the ADHD, ASD, and ADHD+ASD groups had higher scores than the other psychiatric disorders group. These included ASD having higher "communication" and "social skills" impairment scores and ADHD having higher "hypoactivity and hyperactivity/impulsivity" and "attention" difficulty scores than the other psychiatric disorders group.

However, there were no significant differences between the ASD group and patients with other psychiatric disorders in "time concepts" and "visual perception". There were also no differences observed between the ADHD group and the other psychiatric disorders group in "obsessions-compulsions" or "expressive language skills". Finally, no differences were observed between ADHD+ASD and the other psychiatric disorders group in "obsessions-compulsions".

*3.4. Similarities and Differences between ADHD, ASD, and ADHD+ASD in Childhood Problems.* Although the majority of main effects for differences amongst the ASD and ADHD groups were nonsignificant, several differences were observed (see Table 4). Pairwise comparisons showed that the ADHD group showed higher scores than the ASD group in the following five subdomains: "attention" ($P < .001$), "hypoactivity and hyperactivity/impulsivity" ($P < .01$), "planning and organization" ($P < .001$), "time concepts" ($P < .01$), and "memory" ($P < .05$).

In comparison, the ASD group showed greater difficulties than the ADHD group in "social skills" ($P < .001$). Furthermore, the ADHD+ASD group had higher scores than the ASD group in "attention" ($P < .01$) and "time concepts" ($P < .05$). They also had higher scores than the ADHD group for "communication" ($P < .05$) and "social skills" ($P < .01$).

## 4. Discussion

The current study applied the ESSENCE framework to evaluating the symptom history of adult psychiatric patients assessed for ADHD and ASD. It examined retrospective parent reports of patients' childhood developmental and behavioral problems and found that these descriptions reflected impairments in a range of areas, including and extending beyond those listed in the diagnostic criteria. Furthermore, ASD and ADHD patients showed greater difficulties than patients with other psychiatric disorders in nearly all of the FTF subdomains. In support of ESSENCE, the findings indicate that a range of impairments can be expected in childhood neurodevelopmental disorders such as ADHD and ASD.

The childhood problems described by parents generally reflected impairments characterising the diagnostic criteria for ADHD and ASD. However, the two groups did not differ on "communication" scores. This may be due to the conceptualization of the FTF "communication" items. Only one of the three "communication" items, namely, *"difficulty carrying on a conversation"* describes problems explicitly relevant to ASD, although this can even be problematic for children with

Table 4: Main effects for comparisons amongst ADHD and ASD groups.

| FTF subdomain | Main effects $P$ |
|---|---|
| Gross motor skills | n.s |
| Fine motor skills | n.s |
| Attention | <0.001 |
| Hypoactive and hyperactive/impulsive | 0.006 |
| Planning and organizing | 0.002 |
| Relation in space | n.s |
| Time concept | 0.007 |
| Body perception | n.s |
| Visual perception | n.s |
| Memory | 0.048 |
| Comprehension | n.s |
| Expressive language skills | n.s |
| Communication | 0.033 |
| Reading/writing and math | n.s |
| General learning | n.s |
| Coping in learning | n.s |
| Social skills | <0.001 |
| Internalising and externalising problems$^r$ | n.s |
| Obsessive-compulsive | n.s |

Comparisons amongst ADHD, ASD, and ADHD+ASD groups; overall group differences were calculated using the Kruskal-Wallis ANOVA; pairwise group comparisons were made using the Mann-Whitney test and presented in text.

ADHD. The other two items refer to abilities to explain events and keep focused when speaking, which are relevant to both ASD and ADHD. ASD however, is characterised by particular difficulties in nonverbal communication (such as eye contact and body language) as well as voice expression, and the FTF addresses these abilities within "social skills". Although they are theoretically distinct constructs, social skills and communication can be difficult to distinguish in practice and measurement. Consistent with this, the diagnostic criteria for ASD in DSM-5 will merge difficulties in social skills and communication into a single criterion [40].

Our results are consistent with the ESSENCE framework and previous studies showing significant problems for ADHD and ASD patients beyond the diagnostic criteria [6, 41, 42]. Adult patients with ADHD and/or ASD were reported to have had childhood difficulties in motor coordination [10, 11], sleep and externalising/internalising behaviors [12, 13], communication and language (comprehension and expressive problems) as well as in aspects of general development (reading/writing, general learning, and coping in learning) [43, 44].

Although the ADHD and ASD groups shared difficulties in several areas of functioning outside the diagnostic criteria, parent reports also revealed trends specific to each condition relating to executive functions. Greater memory function problems were reported for ADHD patients than for ASD patients. This is consistent with impairments reported in other studies for ADHD patients in working memory and long-term memory [42, 45–47] and is likely due to attention and inhibition deficits [46]. Descriptions of ADHD patients also reflected greater difficulty in planning and organizing than those for ASD patients. Although both disorders are associated with problems in these areas [48, 49], the FTF items refer to "perceiving consequences" and "completing tasks". This focus incorporates impulsivity and possibly explains why ADHD patients' scores reflected greater impairment. A third area of difference was in "time concept", which involves skills in concentration, inhibition, and memory [50, 51], and is important for orientating to future goals and working towards them [52]. Although difficulties in relating to time are described for both ASD and ADHD [50, 51], in the current study, they were more relevant to adult ADHD and ADHD+ASD patients.

The current findings illustrate that ASD and ADHD share many problems during childhood that may often be overlooked in specialised treatment and research focusing on exclusively one of these two specific disorders. However, there are some limitations that should be considered when evaluating the findings. Firstly, participants in this study were diagnosed in adulthood. As individuals diagnosed earlier in development (childhood or adolescence) tend to have a more severe condition than those diagnosed at a later stage [53], our participants may have relatively limited impairments compared to the broader ADHD and ASD population. However, they can be considered representative of the Swedish adult population seeking assessment for ADHD and ASD.

Secondly, there is a possibility that parent reports may be influenced by their adult child's symptoms rather than purely reflecting childhood difficulties. Given that all differences amongst the diagnostic groups were in the expected direction (although symptoms for both ADHD and ASD can decrease with age), this influence appears unlikely. Future research could further validate the retrospective use of the FTF by using a prospective design comparing parent reports made in childhood and adulthood.

Thirdly, as multiple comparisons were made, there was an increased risk of making a type-I error, falsely rejecting the null hypothesis. However, given that the analyses were largely exploratory, the application of a Bonferroni adjustment was not considered as fully applicable. Nevertheless, if such an adjustment had been applied, nearly all of the current findings would still apply.

## 5. Conclusion

The current study adds to the evidence that neurodevelopmental syndromes such as ADHD and ASD are associated with a considerable range of developmental and behavioral problems. It also extends prior research by demonstrating that adult ADHD and ASD patients are likely to have displayed more difficulties in childhood when compared to other psychiatric patients and that retrospective parent reports can assist in building a symptom history. The ESSENCE framework and instruments such as the FTF appear to be useful for identifying areas of difficulty that are not diagnostic of ADHD and/or ASD but are nevertheless

important for understanding the complexity of patients' needs.

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*Research Article*

# Language Delay Is Not Predictable from Available Risk Factors

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*Aims*. To investigate factors associated with language delay in a cohort of 30-month-old children and determine if identification of language delay requires active contact with families. *Methods*. Data were collected at a pilot universal 30-month health contact. Health visitors used a simple two-item language screen. Data were obtained for 315 children; language delay was found in 33. The predictive capacity of 13 variables which could realistically be known before the 30-month contact was analysed. *Results*. Seven variables were significantly associated with language delay in univariate analysis, but in logistic regression only five of these variables remained significant. *Conclusion*. The presence of one or more risk factors had a sensitivity of 89% and specificity of 45%, but a positive predictive value of only 15%. The presence of one or more of these risk factors thus can not reliably be used to identify language delayed children, nor is it possible to define an "at risk" population because male gender was the only significant demographic factor and it had an unacceptably low specificity (52.5%). It is not possible to predict which children will have language delay at 30 months. Identification of this important ESSENCE disorder requires direct clinical contact with all families.

## 1. Introduction

Although there is substantial variation in the rate of language acquisition between developmentally normal individuals, most children acquire good verbal communication by the age of three years [1]. Not only is language delay among the most common developmental disorders (prevalence 1–19% depending on definition [2]) but is also an ESSENCE disorder [3] commonly associated with negative long-term outcomes [4–6]. These include social and behavioural problems, lack of school readiness [7], school exclusion [8], future academic problems [9], neuropsychiatric disorders [10], and poor employment [11].

A number of studies (e.g., [4, 12]) have supported the argument that early interventions can affect long-term outcomes, but there are many methodological weaknesses in trial design [13], and findings of trials based on community screening are inconsistent [13, 14]. There has thus been no international consensus to date on the wisdom of screening for language delay. There is no screening programme currently in the UK, largely because of the lack of historical evidence of effectiveness [15, 16]. The evidence base has, however, developed substantially in the past decade. Miniscalco et al. [17] evaluated a simple Swedish language screening instrument and found that it accurately identified language delay in 2.5-year-old children. Further, a cluster randomised trial of language screening for toddlers in The Netherlands concluded that screening can reduce the number of children who require special education and leads to improved language performance at age eight [18]: the authors recommended nationwide implementation of the screening instrument. Contrasting conclusions have emerged from recent work in Australia [14]. There remain significant methodological challenges to the development and adoption of a universally accepted screening instrument [19].

Child health screening activity for the whole population has been substantially curtailed in the UK [16] and in Scotland at the time of writing there is currently no universal health surveillance contact for children beyond 16 weeks of age [20]. Before 16 weeks, families are usually visited at home on a number of occasions by their community child health nurse (health visitor) who offers support and assesses developmental or social vulnerabilities. After the neonatal medical

examination, there is only one scheduled developmental assessment, at six weeks of age. Parents are nevertheless free to contact their general medical practitioner or their health visitor if they have concerns about a child's development. The arguments for the dismantling of a universal child health surveillance system were based upon both lack of evidence of effectiveness [16] and social inequity. This latter issue is often described as the "Inverse Care Law" [21]: the selective uptake of preventative health services by those who least need them. The withdrawal of universal developmental screening in Scotland was predicated upon assumptions that appropriately informed parents would attend services with concerns about their children's development, in tandem with the view that high risk children could be identified by methods other than universal routine health checks: for example, because of social deprivation, involvement of hospital services, or through the early postnatal assessments carried out by health visitors [20].

The Scottish model for supporting early child development is thus founded on two principles: parental awareness and targeted surveillance based on known risk factors. We have recently reported on pilot work carried out by health visitors with 30-month-old children in West Glasgow [22] and demonstrated that a substantial proportion of developmental problems had not hitherto been suspected, raising concerns about reliance on parental awareness as a trigger to service contact.

In the present paper, we test the second assumption that known risk factors can be used by child health nurses to predict the key ESSENCE disorder, language delay.

## 2. Methods

Health visitors in West Glasgow Community Health and Care Partnership were asked to visit all families in their caseload when their child reached the age of 30 months. Details of the population base and the organisation of this visit are given in Thompson et al. [22]. At the contact, health visitors completed three questionnaires with the principal carer of the child (usually the mother):

(i) the Richman Behaviour Checklist [23], a list of 21 problematic childhood behaviours scored as 0, 1, or 2;

(ii) the Parenting Daily Hassles Scale (PDHS) [24], which lists 20 perceived parental stresses, each scored both in terms of frequency and severity;

(iii) a language screen consisting of two questions [17]:

(a) can your child put two or more words together?

(b) can your child say at least 50 words?

The language screen is a modification of Miniscalco's screening instrument: a vocabulary of fewer than 50 words at 30 months was found to be a reasonable indication of language delay, with a sensitivity of 0.69 and specificity of 0.93 [17].

The health visitors were asked to record other information, including but not limited to the following.

(i) Any existing medical problems with the child or other family members. For the sake of brevity, this question did not go into further detail so items were recorded entirely at the discretion of the health visitor.

(ii) Details of service provision to date.

(iii) HPI (health plan indicator) status [25]; each child is assigned by the health visitor to Core, Additional, or Intensive status which indicates the level of continued contact needed. For most Scottish children, the HPI status would have been allocated in the first year of life and not reconsidered thereafter [26]. Children assigned to the Core category would not normally be seen by the health visitor on a planned routine basis.

(iv) Details of who lives with the child.

No more detailed examination of the child was performed on a routine basis.

The data collection sheet is provided in Appendix A. Information collected from these contacts along with Scottish Index of Multiple Deprivation (SIMD) rankings for the datazones of residence of the family [27] were collated for analysis. SIMD is an area-based measure of deprivation referenced to the whole Scottish population: Glasgow has a relatively high level of deprivation and about half of our sample is in the most deprived Scottish SIMD quintile. This study used SIMD data from 2009, the year of data collection. Health visitors were able to insert free text on the data collection sheet including, in some cases and at their discretion, whether the family used more than one language at home. The potential predictor variables that we used in our analyses thus correspond to those that a health visitor might reasonably be expected to be able to access for a child who had not been seen since infancy.

*2.1. Statistical Analysis.* Disagreement with the "can your child say at least fifty words" statement was used to represent presence of language delay. All the children reported to be unable to make two-word utterances were also reported as being unable to say 50 words.

Thirteen potential predictor variables for language delay which were potentially available to the health visitor could feasibly have been known before the 30-month contact. They include demographic, service use and personal and family medical history and are listed in Appendix B. Univariate associations were tested using Fisher's exact tests. Those variables that showed some evidence ($P < 0.1$) of association with language delay were entered into a multiple logistic regression model, and a backward stepwise procedure was used to derive a model including only those factors showing an independent association with language delay at a 5% significance level. The diagnostic performance of the number of predictive factors was assessed in terms of sensitivity, specificity, and positive predictive value.

Ethics committee review was not required for this piece of work as it formed part of an NHS service evaluation.

## 3. Results

Three hundred and thirty families (40% of 819 eligible) received a visit and data for the language screen were available for 315 children (95% of the 330 visited). Language delay,

Table 1: Univariate analysis. Prevalence of language delay at 30 months in relation to potential risk factors, with Fisher's exact test $P$ values.

| | $N$ | $N$ (%) with language delay | $P$ value |
|---|---|---|---|
| SIMD quintile (26 missing) | | | |
| Q 1 | 121 | 17 (14.0%) | |
| Q 2 | 42 | 4 (9.5%) | |
| Q 3 | 47 | 4 (8.5%) | $P = 0.342$ |
| Q 4 | 26 | 3 (11.5%) | |
| Q 5 | 53 | 2 (3.8%) | |
| Attends nursery (2 missing) | | | |
| No | 178 | 25 (14.0%) | $P = 0.025$ |
| Yes | 135 | 8 (5.9%) | |
| Is there any known problem with drug or alcohol use in the family? (4 missing) | | | |
| No | 294 | 28 (9.5%) | $P = 0.233$ |
| Yes | 17 | 3 (17.6%) | |
| HPI status at start of visit | | | |
| Core | 200 | 14 (7.0%) | |
| Additional | 84 | 12 (14.3%) | $P = 0.012$ |
| Intensive | 31 | 7 (22.6%) | |
| Involvement with community paediatrics team | | | |
| No | 313 | 31 (9.9%) | $P = 0.011$ |
| Yes | 2 | 2 (100.0%) | |
| Social work involvement | | | |
| No | 296 | 30 (10.1%) | $P = 0.434$ |
| Yes | 19 | 3 (15.8%) | |
| Involvement with other services | | | |
| No | 293 | 27 (9.2%) | $P = 0.018$ |
| Yes | 22 | 6 (27.3%) | |
| Gender (26 missing) | | | |
| Female | 146 | 10 (6.8%) | $P = 0.054$ |
| Male | 143 | 20 (14.0%) | |
| Father not at home (2 missing) | | | |
| No | 258 | 28 (10.9%) | $P = 0.813$ |
| Yes | 55 | 5 (9.1%) | |
| Child's behavioural and developmental problems (7 missing) | | | |
| No | 296 | 25 (8.4%) | $P < 0.001$ |
| Yes | 12 | 7 (58.3%) | |
| Parental mental illness (10 missing) | | | |
| No | 288 | 28 (9.7%) | $P = 0.396$ |
| Yes | 17 | 3 (17.6%) | |
| Familial behavioural and developmental problems (9 missing) | | | |
| No | 297 | 28 (9.4%) | $P = 0.052$ |
| Yes | 9 | 3 (33.3%) | |
| Bilingualism (bilingual family) | | | |
| No | 288 | 26 (9.0%) | $P = 0.014$ |
| Yes | 27 | 7 (25.9%) | |

defined as reported inability to say 50 words, was evident in 33 children (10.5% of 315). Table 1 shows the prevalence of language delay in relation to the potential predictor variables. There was no evidence ($P > 0.1$) that language delay using our definition was associated with deprivation (SIMD quintile), known problems with alcohol or drug abuse in the family, involvement with social work services, the father not being at home, or parental mental illness.

Only two children had an involvement with the Community Paediatrics Team, and both showed signs of language delay ($P = 0.011$). This variable would not, however, have any value in a logistic regression model due to the small number

Table 2: Multivariate analysis. Effects of candidate predictor variables, reported as odds ratio for language delay with 95% confidence interval and $P$ value.

| Predictor | Model 1<br>Estimate (95% CI), $P$ value | Model 2<br>Estimate (95% CI), $P$ value |
|---|---|---|
| Attends Nursery | | |
| Yes versus no | 0.53 (0.20, 1.44), $P = 0.212$ | |
| HPI status at start of visit | | |
| Additional versus core | 0.82 (0.25, 2.70), $P = 0.740$ | |
| Intensive versus core | 1.02 (0.21, 4.93), $P = 0.979$ | |
| Involvement with non-SW services | | |
| Yes versus no | 4.58 (1.16, 18.10), $P = 0.030$ | 4.31 (1.25, 14.86), $P = 0.021$ |
| Gender | | |
| Female versus male | 2.90 (1.06, 7.89), $P = 0.038$ | 2.66 (1.00, 7.11), $P = 0.050$ |
| Child's behavioural and developmental problems | | |
| Yes versus no | 8.26 (1.73, 39.43), $P = 0.008$ | 8.02 (1.89, 33.97), $P = 0.005$ |
| Family behavioural and developmental problems | | |
| Yes versus no | 6.06 (0.87, 42.40), $P = 0.069$ | 6.85 (1.07, 43.82), $P = 0.042$ |
| Bilingual Family | | |
| Yes versus no | 5.62 (1.76, 18.01), $P = 0.004$ | 5.89 (1.87, 18.57), $P = 0.003$ |

Model 1: all predictors with $P < 0.1$ at univariate analysis. Model 2: best fitting model found by backwards selection, starting with model 1, with stepwise exclusion of terms with $P > 0.05$.

of children with the factor. Consequently, we combined this indicator with "Involvement with Other Services," which was also positively associated with language delay ($P = 0.018$), to create a variable "Involvement with non-Social Work Services" to be used in the logistic regression analysis. This factor identified 24 children, of whom 8 (33%) were positive on the language delay screen, compared to 25/291 (8.6%) without this factor ($P = 0.001$).

Table 2 reports the results of logistic regression modelling. Attendance at nursery and HPI status at the start of the visit did not show evidence of independent associations with language delay. Language delay was independently associated with male gender, involvement with services other than social work, behavioural and developmental problems of the child or the family, and with bilingual families.

Table 3 and Figure 1 show the prevalence of language delay in relation to the number of risk factors identified by logistic regression, overall and separately for boys and girls. There was a strong association between the number of risk factors and language delay at 30 months. Whilst the presence of one or more risk factors had a sensitivity of 89%, this threshold included all male children, and the specificity was low, at 45%: more importantly, the positive predictive value was only 15%. The presence of two or more risk factors had a specificity of 93%, but a sensitivity and positive predictive value of only 48% and 43%.

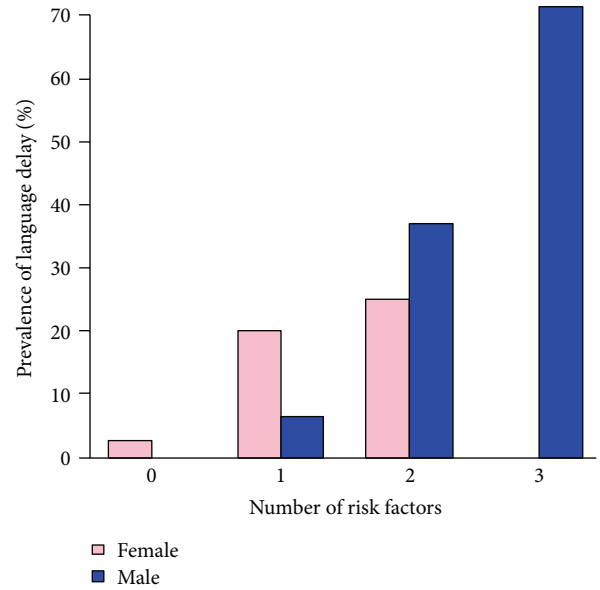


Figure 1: Prevalence of language delay at 30 months in relation to number of risk factors, by gender.

## 4. Discussion

We first aimed to establish which preexisting factors are significantly associated with language delay at 30 months. Five predictor variables were identified; male gender, involvement with services other than social work, behavioural and developmental problems of the child or the family, and living in a bilingual household. Given the lack of universal child health screening contacts in Scotland, we also sought to establish whether preexisting data could be used to identify children at risk of language delay with an acceptable degree of accuracy.

The association of language delay with "involvement with services other than social work" variable is unsurprising. The number of such children was relatively small (24; 8%) and the variable covers a wide range of services which were not individually specified. It is likely that at least some

Table 3: Prevalence of language delay at 30 months in relation to number of risk factors, overall and by gender, with Fisher's exact test $P$ values. $N = 273$ (27 with language delay) after excluding 32 children with missing data for one or more risk factors.

| | Number of risk factors | | | | $P$ value |
|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | |
| Overall | | | | | |
| No language delay | 111 | 118 | 15 | 2 | $P < 0.001$ |
| Language delay | 3 | 11 | 8 | 5 | |
| Prevalence | 2.6% | 8.5% | 34.8% | 71.4% | |
| Males | | | | | |
| No language delay | 0 | 102 | 12 | 2 | $P < 0.001$ |
| language delay | 0 | 7 | 7 | 5 | |
| Prevalence | — | 6.4% | 36.8% | 71.4% | |
| Females | | | | | |
| No language delay | 111 | 16 | 3 | 0 | $P = 0.005$ |
| Language delay | 3 | 4 | 1 | 0 | |
| Prevalence | 2.6% | 20.0% | 25.0% | — | |

types of service use (e.g., community paediatric services) are already used by nurses in their approaches to identification of developmental vulnerability.

Our finding of an association between being in a bilingual household and language delay must be considered tentative. Previous studies have noted that bilingual children can be at a greater risk of either being misdiagnosed with language difficulties, or of being overlooked because language problems in this group are difficult to be diagnosed accurately [28]. Problems of reporting bias may also have influenced the data on bilingualism: health visitors were not specifically asked to report on bilingualism and may have done so more readily if the child had language delay. These findings need confirmation in a more robust design.

The remaining predictive factors are male gender and preexisting behavioural and developmental problems in either the child or the family. The utility of both of these categories in the identification of children at risk for developmental delay is doubtful. Behavioural and developmental problems do not at present meet UK national screening criteria and consequently screening is not offered [29], although there may be an increasingly strong case for screening for persistent conduct disorder [30]. As there is no reliable method of identifying developmental and behavioural problems without some sort of assessment of the child or family, it is not feasible to use knowledge of preexisting behavioural and developmental problems in a targeting strategy to identify the children at high risk of language delay.

While using gender as a predictive tool would be easy, and there is a significant association between male gender and language delay, the utility of this predictor is clearly limited: many girls have language delay and selective screening of boys would clearly be discriminatory.

Each of the predictive factors identified in this study thus has flaws which make them unsuitable for use as screening tools. Furthermore, 11.1% of the children with language delay had no risk factors (including male gender) and a significant proportion of children with language delay would be missed, even with "selective" targeting of most of the population.

*4.1. Strengths and Limitations of the Study.* Although our sample consisted of under half (40%) of the eligible population, our analyses of the missing data suggest that most was due to differential engagement of the staff in the pilot area [22, 31] rather than nonparticipation by families. As well as good representativeness in terms of socioeconomic status, our sample's preexisting risk assessment (HPI) categories did not differ significantly from the population, with most families in the core category [22]. While our sample was representative of the population of the area in terms of socioeconomic status and HPI, it may have differed from the whole population on unmeasured variables. The fact that this study was carried out in the context of a service evaluation, rather than a research project, may have improved the generalizability of our findings.

Relatively few potentially predictive variables were available for analysis: for example, details of family history and household language were not recorded systematically in most cases. Because this was a service evaluation, not a research project, it is likely that families were not asked the questions about language delay in a consistent way. The language screen itself was very basic and it is possible that questions about receptive language ability may have been more sensitive in identifying all children with verbal communication problems. Nevertheless, we consider it likely that the majority of the children (10.5% of the whole sample) would have significant verbal communication problems. Our sample was nevertheless relatively small which may have impacted on the outcome of multivariate analyses.

*4.2. Comparison with the Existing Literature.* When comparing this study's results with those in previous literature, the association between behavioural and developmental problems and language delay is not unexpected: it has been consistently demonstrated over the years. A cross-sectional study [32] in a London borough in the 1970s found that 58% of the language delayed children had behaviour problems compared to only 14% of the nonlanguage delayed children. A decade later, Baker and Cantwell [33] also reported that children with language difficulties had a high rate of emotional and behavioural problems. More recently Van Daal et al. [34] found that 40% of children with language impairment displayed serious significant behaviour problems. More detail of the overlap between reported behavioural problems and language delay in the sample reported here is given in the study of Thompson et al. [22]. Our finding that language delay was independently associated with male gender is also supported by many previous studies (e.g., [35, 36]).

Several authors have reported a significant association between socioeconomic deprivation and delayed language development. This association has been attributed to several interlinked factors: for example, maternal educational levels (and consequently vocabulary) are generally greater in higher socioeconomic groups, and rates of maternal depression,

drug, and alcohol misuse are greater in more deprived socioeconomic groups [37, 38].

The present study is not unique, however, in finding no apparent association between language delay and socioeconomic status or factors associated with lower socioeconomic status, that is, family mental health problems and family drug or alcohol misuse. Other studies have had similar results: Berglund et al. [35] and Choudhury and Benasich [36] both found that socioeconomic status was not significantly related to language ability. This indicates that it is entirely possible that socioeconomic status is unrelated to abnormal language development in West Glasgow, although it is likely that the range of normal language development would vary with maternal educational attainment [39]. In line with O'Callaghan et al. [37], we found that marital status of the child's parents was unrelated to language delay.

Berglund et al. [35] reported that children who attended day-care centres had higher language abilities than those who did not. In our univariate analysis, attending nursery was significantly associated with a lower rate of language delay, but this association became nonsignificant after adjustment for confounders such as socioeconomic status.

## 5. Conclusions and Recommendations

It is not feasible to use the presence of preexisting available risk factors to identify language delay at 30 months with any reasonable degree of accuracy. It is also not possible to define an "at risk" population group because, apart from the poorly predictive association with male gender, there were no demographic factors significantly associated with language delay. Previous studies have come to similar conclusions; Baker and Cantwell [33], Zubrick et al. [40], Reilly et al. [39], and Schjølberg et al. [41] found no demographic variables which could realistically be used to identify high risk children. Our findings, which add variables related to services use and risk category allocated in infancy to demographic predictors, provide strong support for the view that universal language screening programs are the only effective way of identifying children with language delay.

It appears that the use of specific questions about language delay, rather than simply asking parents if they are concerned about their child's language development, is necessary. Miniscalco et al. [17] and others reported that parental concern is not a reliable guide to language skills in toddlers and Westerlund and Sundelin [42] found that only 64% of the 3-year-old children in their study with language delay would have been identified by parental concern alone.

We think that there is a compelling case for community child health services to approach all families with children who aged two years. A finding of language delay should trigger further assessment of motor function, social communication, attention, hyperactivity, and overall cognitive performance—the ESSENCE disorders [3]. Since the work reported in this paper was conducted, the Scottish Government has reintroduced a universal child health screening contact, focussed on language, behaviour, and social development, at 27 months [43].

## Appendices

## A. The Visit Cover Sheet

See supplementary material available online at http://dx.doi.org/10.1155/2013/947018.

## B. Variables Tested for Association with Language Delay

*Continuous Variable*

*SIMD Rank*. Scottish index of multiple deprivation ranking for each child's household.

*Categorical Variables*. The following categorical variables were all derived from yes/no answers to the following questions.

(i) Is the child attending nursery?

(ii) Is there any known problem with drug or alcohol use in the family?

(iii) Are there any 1st degree relatives not living within the household?

(iv) Are there any significant diagnoses (in the child) with long-term implications for the child's development?

(v) Is there any relevant family medical history likely to have an impact on the child's development?

(vi) HPI status at start of visit.

(vii) Involvement with community paediatric team.

(viii) Social work involvement.

(ix) Involvement with other services.

(x) Gender.

*New Categorical Variables.* Three of the categorical variables had additional details provided in the dataset that were used to create new more specific variables.

(i) Father not at home.

From the "first degree relatives not living within the household" variable a "father not at home" variable was created.

(i) Child's behavioural and developmental problems.

(ii) Child medical conditions with child's behavioural developmental problems not included.

From the "significant diagnoses for the child" variable a "child's behavioural and developmental problems" variable was created.

(i) Parental mental illness.

(ii) Familial behavioural and developmental problems.

(iii) Family medical history with familial behavioural and developmental problems not included.

From the "relevant family history" variable "parental mental illness" and "familial behavioural and developmental problems" variables were created.

(i) Bilingual family.

The free text in the dataset comprised information that the health visitors felt was noteworthy. From this information it was clear that several children came from bilingual families, so this information was used to create a new bilingual variable.

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*Clinical Study*

# Autism in the Faroe Islands: Diagnostic Stability from Childhood to Early Adult Life

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Childhood autism or autism spectrum disorder (ASD) has been regarded as one of the most stable diagnostic categories applied to young children with psychiatric/developmental disorders. The stability over time of a diagnosis of ASD is theoretically interesting and important for various diagnostic and clinical reasons. We studied the diagnostic stability of ASD from childhood to early adulthood in the Faroe Islands: a total school age population sample (8–17-year-olds) was screened and diagnostically assessed for AD in 2002 and 2009. This paper compares both independent clinical diagnosis and Diagnostic Interview for Social and Communication Disorders (DISCO) algorithm diagnosis at two time points, separated by seven years. The stability of clinical ASD diagnosis was perfect for AD, good for "atypical autism"/PDD-NOS, and less than perfect for Asperger syndrome (AS). Stability of the DISCO algorithm subcategory diagnoses was more variable but still good for AD. Both systems showed excellent stability over the seven-year period for "any ASD" diagnosis, although a number of clear cases had been missed at the original screening in 2002. The findings support the notion that subcategories of ASD should be collapsed into one overarching diagnostic entity with subgrouping achieved on other "non-autism" variables, such as IQ and language levels and overall adaptive functioning.

## 1. Introduction

Almost since the beginning of its history in clinical medicine, childhood autism/autistic disorder (AD) has been regarded as one of the most, if not the most, stable diagnostic categories applied to young children with psychiatric/developmental disorders [1, 2]. In the last several years, a number of studies have documented that autism is not a distinct "either/or" phenomenon, but often can be seen as a dimensionally distributed trait in the general population [3–5]. Recent hypotheses include those that see autism (or autism spectrum disorder (ASD), or pervasive developmental disorder (PDD)) as the lowermost portion on a spectrum of "autistic traits" shading into normally distributed similar traits in the population and that its basis is genetic, regardless of whether one is dealing with "caseness" or "the broader/normal phenotype" [6, 7]. However, the question remains as to whether, just as in intellectual developmental disorder (IDD), ASD as a clinical diagnosis, in some cases, represents pathological (and qualitatively different) variants that cannot be explained as

a normally distributed trait (perhaps associated with brain damage or other non-genetic factors). Diagnostic stability would, hypothetically, be high for ASD under such a model.

Papers reporting on diagnostic stability of ASD from 2005 onwards have concentrated on very young and preschool age children. Only one study reported a follow-up interval of 7 years (from age 2 through 9 years). Most studies compared the stability of clinical diagnosis over a 2-year period. The overarching category of ASD (encompassing all the diagnostic subcategories, including autistic disorder (AD), Asperger syndrome (AS), and PDD/not otherwise specified (NOS) [8, 9]) has repeatedly been reported as very stable (>90%), and the "core autism" (AD) and AS categories have been found to be more stable than the PDD-NOS category [10, 11]. Clinical diagnosis has consistently been shown to be more stable than any instrument diagnosis [12], such as diagnoses made using the Autism Diagnostic Interview-Revised (ADI-R) [13]; the Early Screening of Autistic Traits (ESAT) [14], Wing's [15] Autistic Disorder Interview (WADIC), and Autism Diagnostic Observation Schedule-Generic (ADOS-G) [16–18]; or the Childhood Autism Rating Scale (CARS) [19] and ADOS [17, 20].

A clinical diagnosis is usually considered the "gold standard." However, for research purposes there has been a demand for some time for a "quantified" diagnostic measure and this has led to the development of some of the frequently used instruments: semi- or highly structured interviews (the ADI-R, or the Diagnostic Interview for Social and Communication Disorders (DISCO)), questionnaires (e.g., the Autism Spectrum Screening Questionnaire (ASSQ) [21–24], or the Social Communication Questionnaire (SCQ) [25]), and observation schedules (e.g., the ADOS [26]). There has also been a need to develop these scales for the purpose of training less experienced, junior clinicians or researchers to assist in the diagnostic process. This has led to the need for continuous research into diagnostic stability of ASD diagnoses made on the basis of different approaches (clinical "best estimate" or instrument diagnosis) and of compatibility across types of diagnosis made. It is essential that these instruments are compared with the clinical "gold standard."

The stability over time of a diagnosis of ASD is not only theoretically interesting but important for a number of clinical reasons. Resources for psychoeducation and early intervention in ASD are currently allocated at a relatively high level in many western countries. The same holds for diagnostic services. Often, intervention provision is heavily dependent on availability of diagnostic services and knowledge about diagnostic stability, therefore, of particular importance.

We have had the opportunity to study the diagnostic stability of ASD from childhood to early adult life in a total population sample in the Faroe Islands. This paper details the results of that study, both as regards independent clinical comprehensive diagnosis and in respect of DISCO algorithm diagnosis of ASD at two time points, separated by seven years.

The Faroe Islands—considered a genetic isolate—are situated in the heart of the Gulf Stream in the North Atlantic Ocean, northwest of Scotland and half way between Norway and Iceland at 62°00′ N. It is a group of 18 islands, several of them now connected by under-sea tunnels. The total population of the Faroe Islands is about 49,000. There are only two towns—a capital Torshaven (around 19,000 inhabitants) and Klaksvik (around 5000). The rest of the population live in rural (including remote) areas and small villages.

Given the genetic isolate character, the Faroe Islands constitute an interesting environment in which to conduct epidemiological studies. Many variables are unusually stable, for example, socioeconomic status, education, health care, familial/genetic history, and diet among others. Several epidemiological studies so far have been interested in the apparently high prevalence of certain diseases in this community—among them Parkinson disease [27, 28] and autism [29].

## 2. Methods

In a general population setting in the Faroe Islands (in the North Atlantic Sea), we have been performing prevalence, clinical, and genetic studies of ASD for more than a decade. The school age child population as a whole (8–17-year-olds) on the islands was screened and diagnostically assessed for ASD in 2002 [29], and the same age cohort was screened and assessed again in 2009 [30].

*2.1. Procedure.* The same procedures for screening (ASSQ, school and hospital screening) and diagnostic assessments (clinical interview/assessment and Wechsler testing of the individual, DISCO interview with a parent) were employed at both time points. The ADOS was included only at Time 2. The clinician examining the individuals and interviewing the parents at Time 2 was usually not the same as had been involved at Time 1. Parents and teachers completed the ASSQ. Registers of schools and the Torshavn hospital (the only hospital in the Faroe Islands) were searched. Parents of screen positive individuals were interviewed using the DISCO-10. Screen positive individuals were themselves assessed using a semistructured interview, regarding their interests, skills patterns, family, and peer relationships. Their IQ levels were tested with the Wechsler Intelligence Scales for Children (WISC-R or WISC-III) [31, 32] or the Wechsler Adult Intelligence Scale-III [33] (in individuals over the age of 16 years).

*2.2. Participants.* The whole Faroese population of 8–17-year-old children (born in 1985 through 1994) was screened and diagnostically assessed for ASD throughout all schools and registers in 2002 (Time 1). The same age cohort was screened and assessed again in 2009 (Time 2). The details of the screening and diagnostic procedures included at Time 1 and Time 2 have already been published [29, 30]. Clinical interviews/assessments of the screen positive individuals were performed by one of two clinical psychologists (AE and HK) at Time 1 and by another psychologist (RB) (with no prior knowledge of the individuals and their diagnosis—this researcher was "blind") at Time 2.

*2.3. Instruments. DISCO interviews* were done at both time points. They were performed by one of two clinical

psychologists (AE and HK) at Time 1. DISCO-11 interviews were performed by a third clinical psychologist (RB) in the majority of cases ("old" and "new") at Time 2. In 9 of the cases, for practical purposes, one of the two Faroese psychologists active at Time 1 performed the DISCO-11 interviews. In these cases, at Time 2, they each met a parent that they had interviewed personally at Time 1. The DISCO is an investigator-based structured and semistructured instrument developed with a view to serving as a research and clinical interview with a collateral informant (usually one of the parents, as in the present context) for differential diagnosis within the spectrum of autism and other social communication disorders [34, 35]. It has been used in a large number of studies (see Leekam [36] for a recent overview) and has been shown to have good to excellent psychometric properties including excellent interrater reliability and good validity for diagnoses within the autism spectrum [37]. It takes 2–4 hours to complete. It is currently available in its eleventh version (DISCO-11). The difference between the tenth (DISCO-10) and the eleventh version is minor. The DISCO-10 was used at Time 1 and the DISCO-11 at Time 2.

The DISCO provides a computerized diagnostic algorithm, allowing the following (mutually not exclusive) diagnoses to be made: "childhood autism/autistic disorder," "atypical autism/PDD-NOS," "Asperger syndrome according to ICD-10/DSM-IV, Asperger syndrome according to Gillberg" [38], "social impairment," and "ASD" according to Wing [39]. Thus, the diagnosis is made by the computer on the basis of the clinical information given by the collateral informant and coded by the interviewer (AE and HB at Time 1 and in a few instances at Time 2, RB at Time 2) and is *not* at this "algorithm diagnostic stage" influenced by clinical comprehensive assessment, nor was the clinical diagnosis influenced by the DISCO algorithm diagnosis.

*Wechsler Intelligence Scales* were used age-appropriately for the cognitive assessment: WISC-III in the majority of cases at Time 1 and WAIS-R at Time 2. Those who were not tested at Time 1 were tested at Time 2. The Wechsler Intelligence Scale for Children is an individually administered intelligence test for children between the ages of 6–16 years. The WISC-R (Revised version) [31] and the WISC-III [32] has 15 subtests which are organized into verbal and performance scales and provide scores for Verbal IQ (VIQ), Performance IQ (PIQ), Processing Speed Index (PSI), and Full Scale IQ (FSIQ). Individuals over the age of 16 were tested with the Wechsler Adult Intelligence Scale (WAIS) [33].

*ADOS assessment* was performed only at Time 2. The ADOS is an instrument used for diagnosing and assessing autism. The protocol consists of a series of structured and semistructured tasks that involve social interaction between the examiner and the subject. The examiner observes and identifies segments of the subject's behaviour and assigns these to predetermined observational categories. Categorized observations are subsequently combined to produce quantitative scores for analysis. Research-determined cutoffs identify the potential diagnosis of autism or related ASD, allowing a standardized assessment of autistic symptoms.

*2.4. Screening and Diagnosis Time 1.* There were 56 children aged 8–17 years identified at screening with a suspicion of ASD from the population of 7,689 at Time 1 and 43 of these met DSM-IV PDD/ASD diagnostic criteria or, in the case of "Asperger syndrome," they met criteria for this condition operationalised by Gillberg [38]. The parents of two of the 43 children did not wish for their child to participate in the in-depth assessment study but both these children had been worked up comprehensively and diagnosed with ASD by Faroese or Danish clinicians prior to the research study.

*2.5. Screening and Diagnosis Time 2.* All 41 participating individuals with ASD at Time 1, now aged 15–24 years, were contacted at Time 2 (2009) and 31 of these (76%) agreed to participate in the follow-up study. In addition, there were 30 individuals newly referred because of the suspicion of ASD during the 2009 screening, and 22 of these met diagnostic criteria for ASD. Two additional cases had received their clinical diagnosis elsewhere, but were confirmed by the Time 2 clinician (RB). This means that there were 55 cases available at Time 2 (31 + 22 + 2).

The reasons for refusal to participate in the study at Time 2 among the original group diagnosed at Time 1 included (as recorded by the DISCO interviewer) (a) parent's denial of any problems related to autism ($n = 2$); (b) autism individual's own denial of any problems ($n = 2$); (c) parent blaming the health system for not offering enough help ($n = 2$); (d) parents' refusal due to very low general functioning of the person with autism ($n = 1$); (e) involvement of genetic analysis in the study ($n = 1$); and (f) other "unspecified reasons" or "no information available" ($n = 3$).

*2.6. Time 1 Final Sample.* A total of 43 individuals received the diagnosis of ASD (autism, atypical autism, or Asperger syndrome) in 2002, corresponding to total population prevalence for ASD in 8–17-year-old children in the Faroe Islands of 0.56%.

*2.7. Time 2 Final Sample.* A total of 67 individuals received the diagnosis of ASD (autism, atypical autism/PDDNOS, or Asperger syndrome) in 2009, corresponding to total population prevalence for ASD in 15–24-year-old young adults in the Faroe Islands of 0.94% [30]. Of these, 24 were "new cases," not found in the study at Time 1. For these, of course, there were no Time 1 assessments, clinical or DISCO algorithm ASD diagnoses available. Only in those individuals who had been assessed both at Time 1 and Time 2 was it possible to study diagnostic stability over time ($n = 31$ for clinical diagnosis, $n = 30$ for DISCO algorithm diagnosis).

The source of referral to the study for ASD diagnostic assessment after screening of the 24 new cases at Time 2, who were missed at Time 1, included (a) the Torshavn Hospital Adolescent Psychiatry Outpatient Unit where they had been treated for other mental health problems: anxiety ($n = 2$), depression ($n = 2$), ADHD ($n = 2$), and other ($n = 5$); (b) adult psychiatrists who had treated them as outpatients for other mental health problems: depression ($n = 1$), psychosis ($n = 1$), and other ($n = 6$); or (c) the Torshavn Hospital Adult

Table 1: Stability of clinical diagnosis from 2002 to 2009 ($n = 30$).

| Clinical diagnosis 2002 | Clinical diagnosis 2009 | | | |
|---|---|---|---|---|
| | Atypical autism | Asperger syndrome | AD | Total |
| Atypical autism | 5 | 1 | 0 | 6 |
| Asperger syndrome | 4 | 10 | 0 | 14 |
| AD | 0 | 0 | 10 | 10 |
| Total | 9 | 11 | 10 | 30 |

Kappa score: 0.747 ~ good (95% ci: 0.548–0.945).

Psychiatry Inpatient Unit where they were treated for other psychiatric disorders: depression ($n = 4$) and OCD ($n = 1$).

The mean age of the DISCO algorithm diagnostic stability study group at followup was 19.5 (SD 3.1) years. There were 5 females (17%) and 25 males (83%). IQ subcategories were defined as follows: IQ 20–50, $n = 9$ (30%); 51–70, $n = 3$ (10%); 71–85, $n = 7$ (23%); >85, $n = 11$ (37%).

Eleven of the Time 1 sample and 6 of the Time 2 sample of individuals failed to take part in the DISCO-11 assessment, leaving 50 probands at Time 2 for whom there was both a DISCO-11 algorithm diagnosis and an independent clinical diagnosis (including 20 for whom there was no Time 1 diagnosis).

*2.8. Statistical Analysis.* All statistics were calculated via SPSS 17.0 software on anonymous data, using two-tailed $P$ values. $P$ values < 0.05 were considered statistically significant. An agreement between diagnostic raters at two time points in 2002 and 2009 was quantified by using Kappa statistics. Kappa score was assigned according to Landis and Koch scale [40] using 95% confidence intervals.

*2.9. Ethics.* The study was approved by the Faroe Islands Board for Ethics in Medicine. All families provided informed consent (parents or, in the case of individuals 18 years or over, by the individuals with a diagnosis of ASD (from Time 1) or with suspected autism spectrum problems (from Time 2) themselves).

## 3. Results

*3.1. Stability of Clinical Diagnosis.* When combining the AD, AS, and atypical autism/PDDNOS into a collapsed ASD group, 30 of 31 (97%) remained in this overarching clinical diagnostic category. When separating them into specific ASD diagnostic subcategories (Table 1), those with an AD diagnosis in 2002 ($n = 10$) all maintained their diagnosis, whereas in the group with an original diagnosis of AS in 2002 ($n = 15$), 5 were no longer diagnosed in this category (4 with atypical autism/PDDNOS and 1 with no ASD diagnosis at all at Time 2). All but one of those with an atypical autism diagnosis in 2002 ($n = 6$) were still diagnosed in this category at followup (one male in this subgroup was diagnosed with AS at Time 2).

An agreement between clinical diagnoses in 2002 and 2009 was quantified by using Kappa statistics. Kappa score was 0.747 (95% confidence interval: from 0.548 to 0.945). The strength of agreement is considered to be "good" (substantial).

*3.2. Clinical Subgroup Characteristics according to Change/No Change of Diagnostic Category.* The 6 individuals (5 males) whose original clinical diagnosis of AS or atypical autism/PDDNOS had changed at Time 2 had a mean age at followup of 21.0 (SD 3.6) years; their IQ ranged from 50 to 102; 5 individuals had low scores (0-1) on the ADOS "Stereotypical/Repetitive Behaviour" scale. This was markedly different from the group of 10 (8 males) individuals with an original clinical diagnosis of AD (all of whom were again diagnosed clinically as AD at Time 2). Their mean age was 19.3 (SD 3.6) years (n.s.), all but 1 had IQ < 50 ($P < .001$), and all had ADOS Stereotypical/Repetitive Behaviour scores of 2 or more ($P < .01$). However, the AS/atypical autism/PDDNOS group that remained stable ($n = 15$, 12 males) did not differ from those that changed, in terms of ADOS Stereotypical/Repetitive Behaviour scores, but they were younger at followup (18.7, SD 2.8 years, $P < .05$) and IQ tended to be a bit higher (range 73–114).

*3.3. Stability of DISCO Algorithm Diagnosis.* Of all five DISCO algorithm diagnoses, the category of AD was the most stable between 2002 and 2009 (8 of the 10 individuals remained in the same category) (Table 2). The DISCO algorithm diagnoses of AS and atypical autism showed considerable variability; however, no individual moved out of the overarching ASD category altogether.

An agreement between DISCO algorithm diagnoses in 2002 and 2009 was quantified by using Kappa statistics. Kappa score was 0.299 (95% confidence interval: from 0.099 to 0.500). The strength of agreement is considered to be "fair."

*3.4. Correspondence between Clinical Diagnosis and DISCO Diagnosis at Followup (n = 50).* The highest agreement/stability between the Clinical ICD-10/DSM-IV diagnosis and DISCO algorithm diagnosis in 2009 was noted for AD (67% complete agreement) and AS (52% complete agreement) (Table 3).

An agreement between clinical ICD-10 diagnosis and DISCO diagnosis in 2009 was quantified by using Kappa statistics. Kappa score was 0.502 (95% confidence interval: from 0.278 to 0.726). The strength of agreement is considered to be "moderate."

Table 2: Stability of DISCO algorithm diagnosis from 2002 to 2009 ($n$ = 30).

| DISCO algorithm diagnosis 2002 | DISCO algorithm diagnosis 2009 | | | | | |
|---|---|---|---|---|---|---|
| | SID* | ASD** | Atypical autism | Asperger syndrome*** | AD | Total |
| SID* | 1 | 0 | 1 | 0 | 0 | 2 |
| ASD** | 0 | 0 | 0 | 0 | 0 | 0 |
| Atypical autism | 2 | 0 | 1 | 2 | 0 | 5 |
| Asperger syndrome*** | 2 | 3 | 2 | 4 | 2 | 13 |
| AD | 1 | 0 | 1 | 0 | 8 | 10 |
| Total | 6 | 3 | 5 | 6 | 10 | 30 |

*Social interaction disorder according to Wing and Gould criteria.
**Autism spectrum disorder according to Wing and Gould criteria.
***Asperger syndrome according to Gillberg and Gillberg criteria.
Kappa score: 0.299 ~ fair (95% ci: 0.099–0.500).

Table 3: Correspondence between clinical diagnosis and DISCO diagnosis at followup ($n$ = 50).

| Clinical ICD-10 diagnosis 2009 | DISCO diagnosis 2009 | | | |
|---|---|---|---|---|
| | Atypical autism | Asperger syndrome | AD | Total |
| Atypical autism | 5 | 1 | 0 | 6 |
| Asperger syndrome | 5 | 12 | 2 | 19 |
| AD | 2 | 2 | 8 | 12 |
| Total | 12 | 15 | 10 | 37 |

Kappa score: 0.502 ~ moderate (95% ci: 0.278–0.726).

*3.5. Gender Effects.* Among the females ($n$ = 6) who participated in the follow-up study, 5 remained in the original diagnostic category whereas 1 woman, earlier diagnosed with Asperger syndrome, now received the diagnosis of atypical autism.

There were more females identified at Time 2 ($n$ = 11 ~ 45.8%): 1 with childhood autism, 8 with Asperger syndrome, and 2 with atypical autism diagnosis, in comparison to the original study at Time 1 ($n$ = 7 ~ 16.3%): 4 with childhood autism and 3 with Asperger syndrome diagnosis, indicating that more females were missed at younger ages.

## 4. Discussion

Interestingly, the stability of clinical ASD diagnoses was perfect for AD, good for atypical autism/PDD-NOS, and less than perfect for AS. Stability of the DISCO algorithm subcategory diagnoses was more variable but still good for AD. In terms of "any ASD" diagnosis, both systems showed excellent stability over the seven-year period with only one case of "clinical ASD" at Time 1 receiving "no clinical diagnosis" at Time 2 and one case of "No DISCO ASD-diagnosis" at Time 1 receiving a "DISCO-ASD diagnosis" (AS) at Time 2.

Before going on to discuss the implications of the findings, several things need to be addressed. First, what is the representativeness of the sample? Even though relatively small, the groups studied are representative of the total population of young people with ASD in the Faroe Islands, as has been argued in more detail in a previous publication by our group [30]. The fact that they were recruited in a genetic isolate could, by some, be taken to indicate that they might be atypical, and findings therefore not generalisable to other populations. Even though this cannot be absolutely excluded, several members of the research group have experience of working with thousands of individuals with ASD, and their conclusion is that the Faroe Islands ASD groups are typical of similar age groups with ASD in other countries.

Second, was the clinical diagnostic process sufficiently expert and in-depth to allow generation of valid comprehensive clinical ASD diagnoses? We would argue that indeed it was. The individuals in the study were examined for many hours, and on several different occasions, by experienced psychologists and psychiatrists. These experts were working in the context of an internationally well-known and clinically highly experienced research group, who has demonstrated excellent reliability for autism diagnoses [41].

Third, is the DISCO an instrument with established psychometric properties? The DISCO has excellent inter- and (short-term) intrarater reliability and is valid for ASD diagnoses, both as derived from clinical assessment and after interview using an alternative investigator-based collateral informant interview, the ADI-R [37]. The DISCO generates much more information about early development and ASD-associated (not just "ASD-diagnostic") symptoms and problems, and so it is our contention that it is at least as useful in ASD diagnostics as is the ADI-R.

Finally, were the diagnosticians independent of each other and in relation to the DISCO algorithm diagnoses when they made their clinical diagnosis within the spectrum of autism? All clinical diagnoses were made on the basis of all available information obtained by each Faroese clinician (sometimes with the help of the Swedish clinical researchers) without any knowledge of the DISCO algorithm

ASD diagnoses delivered by the computer. It could not be ruled out that information obtained at DISCO interview might have influenced the Faroese clinician when assigning a clinical diagnosis, but the algorithm diagnosis (a complex combination of a very large number of items from all the many areas covered by the DISCO) and its constituent parts were not known to the clinician when the diagnosis was made. On balance, therefore, we conclude that the findings obtained are highly relevant as a basis for discussion of the stability and interrelationship of clinical and DISCO diagnoses of ASD in a long-term perspective.

There were no significant gender effects as regards stability/change of diagnosis, either in respect of clinical or DISCO algorithm diagnoses. However, the number of female cases included in the study was low (even though several previously undiscovered cases were identified at the second study), meaning that conclusions can only be tentative in this respect. In effect, one might argue that the relatively high number of "new" female cases emerging at Time 2 could be seen as an indication of the poor "diagnostic stability" of ASD in females (noncaseness turning into caseness at a considerable rate over a seven-year period, in spite of the "true" onset of the ASD having been in early childhood in all the "new" female cases).

It appears, then, that the take home message from this study is that both clinical and DISCO algorithm diagnoses are stable over the period from school age through late adolescence and early adult life so long as one is referring to ASD and not to individual categories within the ASD umbrella concept. For autistic disorder/childhood autism the clinical diagnosis is very stable, and the DISCO algorithm diagnosis fairly stable over a 7-year period from school age to early adult life. Asperger syndrome "caseness," on the other hand had relatively poor predictive ability for the same diagnosis at Time 2, with a "hit rate" of 67% for clinical and only 27% for DISCO algorithm identical diagnosis at followup.

In summary, the results of this study could be taken to lend support for the notion that a single diagnostic category, "autism," or "ASD" would be better suited to clinical realities than the current subdivision into autistic disorder, Asperger syndrome, childhood, and PDDNOS/atypical autism. At the time of writing, a single autism diagnostic entity is what is being proposed by the DSM-5 committee for neurodevelopmental disorders (and most likely the corresponding ICD-11 committee also).

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*Research Article*

# Autism in Toddlers: Can Observation in Preschool Yield the Same Information as Autism Assessment in a Specialised Clinic?

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We wanted to know whether preschool observation of children suspected of suffering from autism can provide the same information about core autism symptoms as the Autism Diagnostic Observation Schedule (ADOS) performed in a clinic. Forty 2–4-year-old children (9 girls, 31 boys), referred for assessment of suspected autism spectrum disorder participated in the study. The symptom areas covered by the ADOS algorithm were scored by an education specialist after free-field observation of each child in the preschool without using the prescribed ADOS materials. The ADOS was then completed in a clinic setting by examiners blind to the preschool results. Excellent agreement across results obtained at the two different types/settings of observations was found. The only significant difference found was with regard to spontaneous initiation of joint attention. The present study does not address the issue of whether or not one of the methods used is superior to the other when it comes to determining the "true" level of "autism problems" in these children. However, it is of interest that free-field preschool observation of children with suspected autism using a structured checklist yields very similar information as that obtained at ADOS assessment performed in a clinic setting.

## 1. Introduction

Autism spectrum disorder (ASD) has symptom onset early in life and a prevalence of about one percent of the general population [1]. ASD involves severe and pervasive restrictions regarding reciprocal social interaction, social communication, and imagination/behaviour and occurs at all levels of cognitive functioning. Most children with ASD have problems with generalisation, which affects their behaviour in different contexts. Young children with ASD have more nonfunctional and repetitive play than typically developing children [2], and impairment in play, imitation, and joint attention are important predictors of autism [3, 4]. Systematic research has highlighted the importance of early intervention for children with ASD [5–7]. It follows that early detection is crucial and that valid assessment tools designed for young children (and taking possible gender differences into account) are needed [8, 9].

One of the most widely advertised and used autism assessment tools is the Autism Diagnostic Observation Schedule (ADOS) [10]. The ADOS is a standardised, semi-structured instrument, shown to be valid for a clinical diagnosis of autism [11]. It is intended for use in a structured clinical setting. There are four different modules, depending on the level of expressive language (ranging from preverbal to fluent speech). For young children, module 1 is used for non-verbal children and module 2 for children with phrase speech. Module 3 is used for older children with fluent speech, and module 4 is intended for verbally fluent adolescents and adults. The ADOS is intended for use by specially trained professionals in the clinic. Observations of communication, social interaction, play and imagination, and stereotyped behaviours/interests are made in a play/interaction situation using structured activities and materials/toys. One test manager interacts with the child, and usually one professional observes the child during the test, which takes about

Table 1: Participants by module, age, gender, and clinical diagnosis. Module 1 = preverbal, module 2 = phrase speech.

| Module | Mean age (months) | Girls | Boys | AS | ASD | NS | Total number of individuals |
|---|---|---|---|---|---|---|---|
| 1 | 38 | 5 | 19 | 20 | 3 | 1 | 24 |
| 2 | 42 | 4 | 12 | 2 | 9 | 5 | 16 |
| Total | 40 | 9 | 31 | 22 | 12 | 6 | 40 |

30–50 minutes. Immediately after the ADOS procedure both professionals, that is, the test manager and the observer, score the child's performance together according to the manual. An algorithm covering 17 different autism-related areas for module 1 and 16 areas for module 2 is used, and the scoring result provides a cutoff for diagnosis at various levels of ASD, based on the total score for communication and reciprocal social interaction problems.

A few other observational instruments have recently been reported to have potential for the diagnostic assessment of autism in young children. One of these, the Classroom Observation Schedule to Measure Intentional Communication (COSMIC) [12], focuses on communication in natural settings. Relevant items from the COSMIC showed significant associations with the five selected corresponding items on the ADOS, and Interrater reliability was high. The items from the ADOS were (1) overall level of nonechoed language, (2) echolalia, (3) pointing, (4) gestures, and (5) spontaneous initiation of joint attention. Another recently reported instrument, the Playground Observation Checklist (POC) [13], discriminated in respect of social behaviour between children with autism, mental retardation, and typical development. However, no comparison with the ADOS was made. Both the COSMIC and the POC were used with children aged 4–11 years who had been clinically diagnosed with autism before the studies were performed.

According to a newly published report from the Swedish Council of Health Technology Assessment (SBU) there is a great need for further knowledge and development of diagnostic instruments regarding ASD and other neuropsychiatric disorders [14]. There is a particular need to further develop and evaluate methods for ASD observation in the child's everyday environment such as in day nurseries, preschools, and classrooms. We need instruments that can be used in order to identify symptoms of autism even if the child, for whatever reason, cannot participate in a formal test situation at the clinic and to establish whether or not it would be possible to "pick up" or make a preliminary diagnosis of autism even in the absence of full assessment in a clinical setting. This would also be important for epidemiological studies, where "quick and dirty," but ecologically valid, instruments are much needed. Clinical experience suggests that naturalistic observation of the child with suspected ASD in the "natural" environment of his/her preschool and observation in the clinic using the ADOS, often provides additional information about the child. This is also emphasised in the diagnostic manuals, including the DSM-IV [15].

The aim of this study is to determine whether structured observation (of free-field behaviour) in a preschool setting of 2–4-year-old children suspected of suffering from ASD, yields the same overlapping or different information as the ADOS used in a specialised autism clinic?

## 2. Method

The study was conducted within the AUDIE project (AUtism Detection and Intervention in Early life) [16]. The aim of the AUDIE is to detect toddlers in the general population with suspected ASD/other developmental disorders, make comprehensive clinical assessments, and provide early intervention. In brief, all 30-month-old Gothenburg children are screened for language, communication, and ASD problems in well-baby clinics. All children screening positive are referred for ASD in-depth assessment to the Child Neuropsychiatry Clinic (CNC), which is a local, regional, and nationwide clinic for assessment of ASD and other Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations (ESSENCE) [1].

*2.1. Participants.* Forty children (9 girls, 31 boys), aged 29–51 months (mean age 40 months) (Table 1), participated in the study. They had all been referred to the CNC for suspected ASD. These 40 children were consecutively referred through the AUDIE project with a clinical referral diagnosis of suspected ASD and who regularly attended a preschool ($n$ = 39) or another day-care facility group that included several other children ($n$ = 1).

*2.2. Diagnostic Assessment at the CNC.* As part of the AUDIE project, all children underwent the following assessments: (a) medical-neurological-psychiatric examination of the child; (b) child and family medical/psychiatric history taken from parent; (c) Griffiths' Developmental Scales [17] and whenever appropriate according to developmental age of the child the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) [18]; (d) Vineland Adaptive Behavior Scales (VABS) [19]; (e) MacArthur Communicative Development Inventory [20, 21] and the Reynell Developmental Language Scales III [22]; (f) Diagnostic Interview for Social and Communication Disorders (DISCO-11) [23]; (g) ADOS; and (h) preschool observation in accordance with a newly constructed protocol developed for the present study (see below). The professionals included in the CNC team were (a) a physician; (b) a neuropsychologist; (c) a speech and language pathologist; and (d) a special education teacher.

All the various assessments (a) through (h) were performed independently of each other, and the research clinicians remained blind to other assessors' results until the

conjoint diagnostic case conference, which was held after the completion of all assessment as listed under from (a) to (h). At this conference, the assessment team made consensus clinical diagnoses according to the DSM-IV criteria for disorders first evident in childhood or adolescence, on the basis of all available information. As regards ASD/PDD, the participating children in the present study were clinically diagnosed as autistic disorder (AS) ($n = 22$), other ASD ($n = 12$), and non spectrum (NS) ($n = 6$) (Table 1). Note that these diagnoses were only made *after* the preschool observation and ADOS assessments had been completed.

*2.3. ADOS Assessment at the CNC.* Two special education teachers (examiner 1 (GWA) and examiner 2 (UJ)) performed the ADOS-G assessments at the clinic. To avoid bias, examiner 1 performed the preschool observation of child 1 who was then (blindly) assessed by examiner 2 using the ADOS in the clinic together with another observer. Examiner 2 then performed the preschool observation of child 2 who was (blindly) ADOS assessed by examiner 1 in the clinic together with another observer. All ADOS clinical assessments were videotaped in order to perform reliability measures and were scored by the examiner and the observer together.

*2.4. Preschool Observation according to a New Structured Protocol.* In order to allow reasonable comparisons to be made, the "symptom areas" covered by the ADOS algorithm items were used as a "template" for the construction of the preschool observation checklist that would be used by a special education teacher with long-term experience of autism, and trained in the use of ADOS (see Appendix at the Supplementary Material available online at http://dx.doi.org/10.1155/2013/384745). These areas included in the ADOS algorithm were used both in the clinic and in the preschool. The examiner was aware that the observed child was under assessment for suspected ASD, but other than age and gender, the examiner was "blind" and had no further information about the child at the time of observation.

The preschool teachers were instructed to be around the children as they normally would in everyday indoor situations. The "ADOS-similar" observations were made mainly in group activities and free play. If the child did not spontaneously perform activities, allowing observation of a particular area, the examiner herself interacted with the child, presented the task to her/him, or asked the teacher to do so. The classrooms were designed for typically developing children, and the number of children in the groups ranged from 15 to 30 children. No ADOS-specific materials were used; instead all material used in this observation belonged to the preschool. In other words, only the symptom areas checked during the preschool observation were the same as those scored using the ADOS. The observation took about an hour to perform and was scored in accordance with the ADOS algorithm. All completed preschool observation research protocols were sealed and stored away, so that other research clinicians could not take part of the results until the final conjoint diagnostic assessment was made.

Table 2: Results of Interrater reliability measurements of ADOS ($n = 10$) and preschool observation ($n = 10$). Calculated in percent agreement—point-by-point method and weighted kappa.

| | Interrater measurement | |
|---|---|---|
| | Percent agreement | Weighted kappa |
| ADOS | | |
| Communication | 88 | 0.85 |
| Reciprocal social interaction | 93 | 0.91 |
| Play and imagination | 100 | 1.0 |
| Stereotyped behaviours and restricted interests | 90 | 0.89 |
| Preschool observation | | |
| Communication | 90 | 0.89 |
| Reciprocal social interaction | 94 | 0.93 |
| Play and imagination | 88 | 0.82 |
| Stereotyped behaviors and restricted interests | 83 | 0.82 |

*2.5. Interrater Reliability.* Interrater reliability was calculated as percent agreement using the point-by-point method and as weighted kappa [24], calculated in MedCalc version 10.2 [25].

Interrater reliability between the two examiners in the preschool observations was calculated on all the variables in the ADOS algorithm for communication, reciprocal social interaction, play and behaviour/interests, of the preschool observation results for 10 children. These children were included in the larger AUDIE project, but not in the present study. Examiner 1 and 2 observed the same child at the same time at preschool and scored according to the protocol (see Appendix at the Supplementary Material available online at http://dx.doi.org/10.1155/2013/384745), not talking to each other about what they observed. To measure the Interrater reliability of the clinical ADOS examination, another 10 children were blindly examined using videotapes of the ADOS assessment. Examiner 1 (blindly) examined 5 videotaped observations, performed "live" by examiner 2, and examiner 2 (blindly) examined 5 videotaped observations performed by examiner 1 (Table 2).

*2.6. Statistics.* The Wilcoxon signed rank test was used to compare child behaviours in preschool and clinic. There were some methodological challenges stemming from the fact that 24 children were coded using module 1 (preverbal), and 16 were coded using module 2 (phrase speech). We analysed the data in different ways to ensure that the conclusions do not depend on how we handled differences across instruments. Specifically, ADOS modules 1 and 2 contain 11 common variables. In addition, in module 1 there are another 6 variables unrelated to the common ones, and in module 2, there are 5 such unrelated variables. This is shown in Table 3. The material was analysed in three different stages.

Table 3: Agreement between ADOS and preschool observation findings (module 1, $n = 24$; module 2, $n = 16$). Number of higher score in each type of observation is described.

| Domains | $N$ | Agreement | ADOS higher | Preschool higher | $P$ value | Weighted Kappa |
|---|---|---|---|---|---|---|
| Communication | | | | | | |
| Frequency of vocalization directed to others | 24 | 17 (71%) | 4 (17%) | 3 (13%) | 1.0000 | 0.33 |
| Amount of social overtures | 16 | 10 (63%) | 5 (31%) | 1 (6.3%) | 0.2188 | 0.35 |
| Stereotyped/idiosyncratic use of words or phrases | 40 | 28 (70%) | 4 (10%) | 8 (20%) | 0.3877 | 0.43 |
| Use of others body to communicate | 24 | 13 (54%) | 7 (29%) | 4 (17%) | 0.5488 | 0.26 |
| Conversation | 16 | 9 (56%) | 2 (13%) | 5 (31%) | 0.4531 | 0.38 |
| Pointing | 40 | 24 (60%) | 10 (25%) | 6 (15%) | 0.4545 | 0.52 |
| Gestures | 40 | 23 (58%) | 9 (23%) | 8 (20%) | 1.0000 | 0.44 |
| Reciprocal social interaction | | | | | | |
| Unusual eye contact | 40 | 32 (80%) | 4 (10%) | 4 (10%) | 1.0000 | 0.56 |
| Facial expressions directed to others | 40 | 25 (63%) | 6 (15%) | 9 (23%) | 0.6072 | 0.53 |
| Shared enjoyment in interaction | 24 | 12 (50%) | 3 (13%) | 9 (38%) | 0.1460 | 0.21 |
| Showing | 24 | 15 (63%) | 6 (25%) | 3 (13%) | 0.5078 | 0.41 |
| Spontaneous initiation of joint attention | 40 | 26 (65%) | 12 (30%) | 2 (5.0%) | 0.0129 | 0.57 |
| Response to joint attention | 24 | 13 (54%) | 4 (17%) | 7 (29%) | 0.5488 | 0.42 |
| Quality of social overtures | 40 | 25 (63%) | 4 (10%) | 11 (28%) | 0.1185 | 0.47 |
| Quality of social response | 16 | 7 (44%) | 2 (13%) | 7 (44%) | 0.1797 | −0.07 |
| Amount of reciprocal social communication | 16 | 10 (63%) | 3 (19%) | 3 (19%) | 1.0000 | 0.33 |
| Overall quality of rapport | 16 | 8 (50%) | 3 (19%) | 5 (31%) | 0.7266 | 0.35 |
| Play and imagination | | | | | | |
| Functional play with objects | 24 | 15 (63%) | 4 (17%) | 5 (21%) | 1.0000 | 0.43 |
| Imagination/creativity | 40 | 26 (65%) | 8 (20%) | 6 (15%) | 0.7905 | 0.57 |
| Stereotyped behaviours and restricted interests | | | | | | |
| Unusual sensory interest in play material/person | 40 | 30 (75%) | 6 (15%) | 4 (10%) | 0.7539 | 0.14 |
| Hand and finger and other complex mannerism | 40 | 26 (65%) | 6 (15%) | 8 (20%) | 0.7905 | 0.51 |
| Unusual repetitive interests or stereotyped behaviours | 40 | 22 (55%) | 8 (20%) | 10 (25%) | 0.8145 | 0.42 |

The comparison data is presented as $n$ (%).
The $P$ values are calculated using a Sign test.

(1) Comparison of the overall results of each domains of modules 1 and 2 and the combined result of communication and reciprocal social interaction, which, in ADOS, gives cutoff for diagnosis. Thus, no attempt was made to correct for differences in the modules.

(2) To get a larger number of comparable variables, the overall summarised results of only the common variables for both module 1 and 2 were calculated. This score will be referred to as the "collapsed global" score. Children were compared also on this score from the preschool observation and from the ADOS assessment.

(3) Each variable within each domain was analysed.

Note that numbers of variables in Table 3 vary depending on whether the item belonged to module 1 ($n = 24$), module 2 ($n = 16$) or was shared by module 1 and module 2 ($n = 40$).

*2.7. Ethics.* The study was approved by the Human Ethics Committee at the Medical Faculty at the University of Gothenburg, Sweden. Informed consent was obtained from at least one of the parents/responsible carers in each case.

## 3. Results

*3.1. Reliability Results.* The results are shown in Table 2. For Interrater reliability for preschool observation, the percent agreement ranged from 83% to 94%, and weighted kappa

statistics ranged from 0.82 to 0.93. For Interrater reliability on the ADOS, percent agreement ranged from 88% to 100%, and weighted kappa ranged from 0.85 to 1.0. Interrater reliability measures were considered good to very good.

*3.2. Study Results.* In Table 3 data from both module 1 and module 2 in ADOS are presented for all children divided into four domains: (1) communication, (2) reciprocal social interaction, (3) play and imagination, and (4) stereotyped behaviours and restricted interests. The ADOS clinical and the preschool observation both showed a mean result of more than 12 points in combined total score for communication and reciprocal social interaction (Table 4), indicating a diagnosis of autism according to ADOS algorithm, at least at group level. Sign test comparisons of the variables rated in preschool and corresponding items in the clinic showed a significant difference only with regard to spontaneous initiation of joint attention ($P = 0.0129$). For all other observed variables there was good agreement according to sign test, percentage agreement, and weighted kappa across the two methods and the two settings. In some cases the score was somewhat higher in ADOS clinical, and in some cases it was higher in the preschool observation. This is shown in the "ADOS higher" and "preschool higher" columns in Table 3.

## 4. Discussion

The main finding of this study was that preschool observation by an autism-experienced rater of children with suspected ASD, yielded almost the same amount and type of information, as highly structured ADOS assessment performed by two specially trained clinicians in a specialised clinic setting. Initiation of joint attention, suggested to be one of the key difficulties in young children with ASD [3, 4], was the only domain where the ADOS at the clinic indicated more problems than preschool observation of the child in interaction with typically developing children. However, based on the results of the present study we cannot determine which of the two observation settings is more informative about the child's "true" level of joint attention.

Unlike in the study of COSMIC [12] and the POC [13], the researchers remained blind to the children's diagnosis when the observations were made, and our participants were of considerably younger age. Another contrast to the COSMIC study is that we used the same symptom areas, but in different contexts.

The findings, if confirmed by other researchers, suggest that preschool observation using the protocol included here (which is not equivalent to that of the ADOS, albeit covering the same areas) and performed by ASD experienced examiners could be used for rating observable autism symptoms. This could have important implications for field trials and epidemiological studies of autism, but also for autism diagnostic services, for example, in rural and sparsely populated areas. While preschool observation entails cost for travel for the examiner (including time costs), ADOS observation at the clinic often consists of two specially trained experts resulting in financial costs for both clinic and family, as well as inconvenience for the parents involved. However, in other instances the clinic ADOS assessment could be a more efficient and effective assessment tool than preschool observation. Conclusions and recommendations in this respect would have to be made on an individual basis.

Further, at the preschool visit one gets information about the child, that is not included in the clinic ADOS, for example, how the child can handle different situations in daily life. Some of this information may actually be even more important than the diagnosis of autism per se [15]. However, it is important to note that scoring above an algorithm cutoff is not the same as actually "getting" a diagnosis. It is crucial to interpret results from ADOS and preschool observations in relation to other information obtained at comprehensive neuropsychiatric assessment, including child and family medical/psychiatric history taken from parent, developmental quotient, and language measures.

Although we found very strong agreement across the two assessment methods, and even though we realise that this could be taken as support for an either/or approach in the delivery of diagnostic long-term clinical services, our experience suggests that in clinical practice, flexibility is important. Given that every child with ASD is a unique individual, one needs to remain open for individualisation, even in clinics where there is an agreed core protocol for ASD assessment. Preschool teachers, often have a high level of knowledge about the child, and this is important to take advantage of in the ASD diagnostic process. Preschool teachers should be encouraged to make observations and documentations of the child in everyday situations, so as to better enable identification of the child's strengths and difficulties. It is crucial that teachers in preschool receive information and formal training about children with ASD. When preschool teachers have good ASD "know-how," their commitment will be much greater in terms of early intervention in the preschool setting [6, 7, 26].

*4.1. Limitations.* There was no comparison group, so we do not know how typically developing children would be scored at this type of ASD assessment. However, the aim of this work was to *compare two settings* for an observation aiming to detect ASD symptoms and signs, and it was *not* intended to be *a comparison of participants' problems*. A larger study group would have been preferred, but the constraints of the AUDIE project did not allow inclusion of more cases.

*4.2. Further Research.* This study is focused on preschool children only. This means that we know nothing about what the result would be for older children. It would be valuable to perform similar studies in children with suspected ASD at older ages. It would also be important to perform a confirmatory study including a larger number of participants, not least so as to enable comparison of girls and boys. The ADOS severity metric [27] is a tool that could be useful for these comparisons. Finally, it would be of interest to determine the relative predictive validity of preschool observation as against ADOS performed in the clinic in respect of the "final" ASD consensus diagnosis.

Table 4: Comparison between the total score in the different domains of preschool observation and ADOS.

| Domains | Preschool M (SD) Min–max | ADOS M (SD) Min–max | Differences M (SD) Min–max | *P* value |
|---|---|---|---|---|
| Total: communication ($N = 40$) | 4.13 (2.46) | 4.50 (2.42) | −0.38 (1.86) | 0.1034 |
| | 0.00–10.00 | 0.00–9.00 | −4.00–6.00 | |
| Module 1 ($n = 24$) | 5.33 (2.22) | 5.71 (2.10) | −0.38 (1.95) | 0.1564 |
| | 1.00–10.00 | 2.00–9.00 | −3.00–6.00 | |
| Module 2 ($n = 16$) | 2.31 (1.54) | 2.69 (1.62) | −0.38 (1.78) | 0.4785 |
| | 0.00–6.00 | 0.00–7.00 | −4.00–3.00 | |
| Total: reciprocal social interaction ($N = 40$) | 8.13 (4.33) | 7.70 (4.26) | 0.43 (2.70) | 0.4196 |
| | 0.00–14.00 | 0.00–14.00 | −5.00–6.00 | |
| Module 1 ($n = 24$) | 10.21 (3.67) | 9.71 (3.86) | 0.50 (2.72) | 0.5178 |
| | 1.00–14.00 | 2.00–14.00 | −5.00–6.00 | |
| Module 2 ($n = 16$) | 5.00 (3.29) | 4.69 (2.85) | 0.31 (2.75) | 0.6573 |
| | 0.00–10.00 | 0.00–10.00 | −4.00–5.00 | |
| *Combined total; communication and reciprocal social interaction* ($N = 40$) | 12.25 (6.56) | 12.20 (6.37) | 0.05 (3.85) | 0.7180 |
| | 0.00–23.00 | 1.00–23.00 | −7.00–12.00 | |
| Module 1 ($n = 24$) | 15.54 (5.52) | 15.42 (5.50) | 0.13 (3.76) | 0.5574 |
| | 2.00–23.00 | 6.00–23.00 | −7.00–12.00 | |
| Module 2 ($n = 16$) | 7.31 (4.67) | 7.38 (4.19) | −0.06 (4.11) | 1.0000 |
| | 0.00–16.00 | 1.00–17.00 | −7.00–7.00 | |
| Total: play and imagination ($N = 40$) | 2.08 (1.65) | 2.08 (1.62) | 0.00 (1.04) | 1.0000 |
| | 0.00–4.00 | 0.00–4.00 | −3.00–4.00 | |
| Module 1 ($n = 24$) | 3.13 (1.23) | 3.04 (1.30) | 0.08 (1.21) | 0.8418 |
| | 0.00–4.00 | 0.00–4.00 | −3.00–4.00 | |
| Module 2 ($n = 16$) | 0.50 (0.63) | 0.63 (0.72) | −0.13 (0.72) | 0.7266 |
| | 0.00–2.00 | 0.00–2.00 | −1.00–1.00 | |
| Total: stereotyped behaviours and restricted interests ($N = 40$) | 1.83 (1.39) | 1.83 (1.41) | 0.00 (1.26) | 0.9660 |
| | 0.00–5.00 | 0.00–5.00 | −3.00–2.00 | |
| Module 1 ($n = 24$) | 2.21 (1.50) | 2.25 (1.51) | −0.04 (1.37) | 0.9089 |
| | 0.00–5.00 | 0.00–5.00 | −3.00–2.00 | |
| Module 2 ($n = 16$) | 1.25 (1.00) | 1.19 (0.98) | 0.06 (1.12) | 1.0000 |
| | 0.00–3.00 | 0.00–3.00 | −2.00–2.00 | |
| *Collapsed global score (module 1 and module 2)* | | | | |
| Communication | 2.23 (1.67) | 2.28 (1.45) | −0.05 (1.18) | 0.8179 |
| | 0.00–6.00 | 0.00–5.00 | −3.00–3.00 | |
| Reciprocal social interaction | 4.58 (2.89) | 4.60 (2.62) | −0.03 (1.54) | 0.8876 |
| | 0.00–8.00 | 0.00–8.00 | −5.00–4.00 | |
| Total; communication and reciprocal social interaction | 6.80 (4.33) | 6.88 (3.91) | −0.08 (2.34) | 0.3980 |
| | 0.00–13.00 | 1.00–13.00 | −5.00–7.00 | |
| Play and imagination | 1.25 (0.84) | 1.28 (0.85) | −0.03 (0.66) | 1.0000 |
| | 0.00–2.00 | 0.00–2.00 | −1.00–2.00 | |
| Stereotyped behaviours and restricted interests | 1.83 (1.39) | 1.83 (1.41) | 0.00 (1.26) | 0.9660 |
| | 0.00–5.00 | 0.00–5.00 | −3.00–2.00 | |

The data is presented as mean (SD)/Min–Max.
Differences are preschool values minus ADOS values.
The *P* values are calculated using a Wilcoxon signed rank test.
Collapsed global scores only include tests involving both modules.

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