
**Abstract:**

**Background**

It is well established that very few individuals with autism spectrum disorders (ASD) and an IQ below 70 are able to live independently as adults. However, even amongst children with an IQ in the normal range, outcome is very variable. Childhood factors that predict later stability, improvement or decline in cognitive functioning remain uncertain and, in particular, very little is known about trajectories in later adulthood.

**Method**

Changes in cognitive and language ability from childhood to adulthood were assessed in 60 individuals with autism, all of whom had an IQ in the average range as children. Mean age in childhood = 6 years (range 2–13 years); mean age in adulthood = 44 years (range 29–64 years). Trajectories of change and factors related to current cognitive abilities were explored.

**Results**

For the majority of participants (N = 45, 75%), who were testable both as children and adults, IQ remained very stable and language also improved over time. However, 15 individuals could not be assessed on standard tests as adults and their developmental level could be estimated only on the Vineland Adaptive Behavior Scales. Almost all these adults (apart from one who had suffered a major stroke) showed severe aggressive or self-injurious behaviours; none had ever developed language above a 3-year level, and seven had developed epilepsy.

**Conclusions**

For most individuals with autism who had an IQ in the average range (i.e. ≥70) as children, childhood IQ proved a reliable predictor of cognitive functioning well into mid- to- later adulthood. However, a significant minority was no longer testable on standard tests as adults. Their current very low levels of functional ability were generally associated with severe behavioural disturbance and persisting and severe language impairment; 50% of these individuals had also developed epilepsy, pointing to the role of organic brain dysfunction. Implications for early intervention are discussed.
Abstract

OBJECTIVE
The distinct trajectories of patients with autism spectrum disorders (ASDs) have not been extensively studied, particularly regarding clinical manifestations beyond the neurobehavioral criteria from the Diagnostic and Statistical Manual of Mental Disorders. The objective of this study was to investigate the patterns of co-occurrence of medical comorbidities in ASDs.

METHODS
International Classification of Diseases, Ninth Revision codes from patients aged at least 15 years and a diagnosis of ASD were obtained from electronic medical records. These codes were aggregated by using phenotype-wide association studies categories and processed into 1350-dimensional vectors describing the counts of the most common categories in 6-month blocks between the ages of 0 to 15. Hierarchical clustering was used to identify subgroups with distinct courses.

RESULTS
Four subgroups were identified. The first was characterized by seizures (n = 120, subgroup prevalence 77.5%). The second (n = 197) was characterized by multisystem disorders including gastrointestinal disorders (prevalence 24.3%) and auditory disorders and infections (prevalence 87.8%), and the third was characterized by psychiatric disorders (n = 212, prevalence 33.0%). The last group (n = 4316) could not be further resolved. The prevalence of psychiatric disorders was uncorrelated with seizure activity (P = .17), but a significant correlation existed between gastrointestinal disorders and seizures (P < .001). The correlation results were replicated by using a second sample of 496 individuals from a different geographic region.

CONCLUSIONS
Three distinct patterns of medical trajectories were identified by unsupervised clustering of electronic health record diagnoses. These may point to distinct etiologies with different genetic and environmental contributions. Additional clinical and molecular characterizations will be required to further delineate these subgroups.

Abstract
Autism Spectrum Disorders (ASDs) are neurodevelopmental disorders characterized by impairments in social interaction and communication, and the presence of restrictive and repetitive behaviors. Symptoms of ASD likely emerge from a complex interaction between pre-existing neurodevelopmental vulnerabilities and the child's environment, modified by compensatory skills and protective factors. Prospective studies of infants at high familial risk for ASD (who have an older sibling with a diagnosis) are beginning to characterize these developmental pathways to the emergence of clinical symptoms. Here, we review the range of behavioral and neurocognitive markers for later ASD that have been identified in high-risk infants in the first years of life. We discuss theoretical implications of emerging patterns, and identify key directions for future work, including potential resolutions to several methodological challenges for the field. Mapping how ASD unfolds from birth is critical to our understanding of the developmental mechanisms underlying this disorder. A more nuanced understanding of developmental pathways to ASD will help us not only to identify children who need early intervention, but also to improve the range of interventions available to them.
Abstract

The aim of this study was to examine the relationship between emotion dysregulation and the core features of Autism Spectrum Disorder (ASD), which include social/communication deficits, restricted/repetitive behaviors, and sensory abnormalities. An 18-item Emotion Dysregulation Index was developed on the basis of expert ratings of the Child Behavior Checklist. Compared to typically developing controls, children and adolescents with ASD showed more emotion dysregulation and had significantly greater symptom severity on all scales. Within ASD participants, emotion dysregulation was related to all core features of the disorder, but the strongest association was with repetitive behaviors. These findings may facilitate the development of more effective therapeutic strategies targeting emotion dysregulation in order to optimize long-term outcomes for individuals with ASD.

Abstract:

Background

The development of effective treatments for use by non-specialists is listed among the top research priorities for improving the lives of people with mental illness worldwide. The purpose of this review is to appraise which interventions for children with intellectual disabilities or lower-functioning autism spectrum disorders delivered by non-specialist care providers in community settings produce benefits when compared to either a no-treatment control group or treatment-as-usual comparator.

Methods and Findings

We systematically searched electronic databases through 24 June 2013 to locate prospective controlled studies of psychosocial interventions delivered by non-specialist providers to children with intellectual disabilities or lower-functioning autism spectrum disorders. We screened 234 full papers, of which 34 articles describing 29 studies involving 1,305 participants were included. A majority of the studies included children exclusively with a diagnosis of lower-functioning autism spectrum disorders (15 of 29, 52%). Fifteen of twenty-nine studies (52%) were randomized controlled trials and just under half of all effect sizes (29 of 59, 49%) were greater than 0.50, of which 18 (62%) were statistically significant. For behavior analytic interventions, the best outcomes were shown for development and daily skills; cognitive rehabilitation, training, and support interventions were found to be most effective for improving developmental outcomes, and parent training interventions to be most effective for improving developmental, behavioral, and family outcomes. We also conducted additional subgroup analyses using harvest plots. Limitations include the studies' potential for performance bias and that few were conducted in lower- and middle-income countries.

Conclusions

The findings of this review support the delivery of psychosocial interventions by non-specialist providers to children who have intellectual disabilities or lower-functioning autism spectrum disorders. Given the scarcity of specialists in many low-resource settings, including many lower- and middle-income countries, these findings may provide guidance for scale-up
efforts for improving outcomes for children with developmental disorders or lower-functioning autism spectrum disorders.


Abstract:
The genetic bases of neuropsychiatric disorders are beginning to yield to scientific inquiry. Genome-wide studies of copy number variation (CNV) have given rise to a new understanding of disease etiology, bringing rare variants to the forefront. A proportion of risk for schizophrenia, bipolar disorder, and autism can be explained by rare mutations. Such alleles arise by de novo mutation in the individual or in recent ancestry. Alleles can have specific effects on behavioral and neuroanatomical traits; however, expressivity is variable, particularly for neuropsychiatric phenotypes. Knowledge from CNV studies reflects the nature of rare alleles in general and will serve as a guide as we move forward into a new era of whole-genome sequencing.

**Abstract:**

In a small fraction of patients with schizophrenia or autism, alleles of copy-number variants (CNVs) in their genomes are probably the strongest factors contributing to the pathogenesis of the disease. These CNVs may provide an entry point for investigations into the mechanisms of brain function and dysfunction alike. They are not fully penetrant and offer an opportunity to study their effects separate from that of manifest disease. Here we show in an Icelandic sample that a few of the CNVs clearly alter fecundity (measured as the number of children by age 45). Furthermore, we use various tests of cognitive function to demonstrate that control subjects carrying the CNVs perform at a level that is between that of schizophrenia patients and population controls. The CNVs do not all affect the same cognitive domains, hence the cognitive deficits that drive or accompany the pathogenesis vary from one CNV to another. Controls carrying the chromosome 15q11.2 deletion between breakpoints 1 and 2 (15q11.2(BP1-BP2) deletion) have a history of dyslexia and dyscalculia, even after adjusting for IQ in the analysis, and the CNV only confers modest effects on other cognitive traits. The 15q11.2(BP1-BP2) deletion affects brain structure in a pattern consistent with both that observed during first-episode psychosis in schizophrenia and that of structural correlates in dyslexia.

Abstract
Since subthreshold autistic social impairments aggregate in family members, and since attentional dysfunctions appear to be one of the earliest cognitive markers of children with autism, we investigated in the general population the relationship between infants’ attentional functioning and the autistic traits measured in their parents. Orienting and alerting attention systems were measured in 8-month-old infants using a spatial cueing paradigm. Results showed that only paternal autistic traits were linked to their children’s: (1) attentional disengagement; (2) rapid attentional orienting and (3) alerting. Our findings suggest that an early dysfunction of orienting and alerting systems might alter the developmental trajectory of future ability in social cognition and communication.


Abstract
Face recognition difficulties are frequently documented in children with autism spectrum disorders (ASD). It has been hypothesized that these difficulties result from a reduced interest in faces early in life, leading to decreased cortical specialization and atypical development of the neural circuitry for face processing. However, a recent study by our lab demonstrated that infants at increased familial risk for ASD, irrespective of their diagnostic status at 3 years, exhibit a clear orienting response to faces. The present study was conducted as a follow-up on the same cohort to investigate how measures of early engagement with faces relate to face-processing abilities later in life. We also investigated whether face recognition difficulties are specifically related to an ASD diagnosis, or whether they are present at a higher rate in all those at familial risk. At 3 years we found a reduced ability to recognize unfamiliar faces in the high-risk group that was not specific to those children who received an ASD diagnosis, consistent with face recognition difficulties being an endophenotype of the disorder. Furthermore, we found that longer looking at faces at 7 months was associated with poorer performance on the face recognition task at 3 years in the high-risk group. These findings
suggest that longer looking at faces in infants at risk for ASD might reflect early face-processing difficulties and predicts difficulties with recognizing faces later in life.


Abstract

Objective
To test whether gut permeability is increased in autism spectrum disorders (ASD) by evaluating gut permeability in a population-derived cohort of children with ASD compared with age- and intelligence quotient-matched controls without ASD but with special educational needs (SEN).

Patients and Methods
One hundred thirty-three children aged 10–14 years, 103 with ASD and 30 with SEN, were given an oral test dose of mannitol and lactulose and urine collected for 6 hr. Gut permeability was assessed by measuring the urine lactulose/mannitol (L/M) recovery ratio by electrospray mass spectrometry-mass spectrometry. The ASD group was subcategorized for comparison into those without (n = 83) and with (n = 20) regression.

Results
There was no significant difference in L/M recovery ratio (mean (95% confidence interval)) between the groups with ASD: 0.015 (0.013–0.018), and SEN: 0.014 (0.009–0.019), nor in lactulose, mannitol, or creatinine recovery. No significant differences were observed in any parameter for the regressed versus non-regressed ASD groups. Results were consistent with previously published normal ranges. Eleven children (9/103 = 8.7% ASD and 2/30 = 6.7% SEN) had L/M recovery ratio > 0.03 (the accepted normal range cut-off), of whom two (one ASD and one SEN) had more definitely pathological L/M recovery ratios > 0.04.

Conclusion
There is no statistically significant group difference in small intestine permeability in a population cohort-derived group of children with ASD compared with a control group with SEN. Of the two children (one ASD and one SEN) with an L/M recovery ratio of > 0.04, one had undiagnosed asymptomatic celiac disease (ASD) and the other (SEN) past extensive surgery for gastroschisis.

**Abstract**

The current study aims to evaluate the psychometric properties of the Emotion Regulation and Social Skills Questionnaire (ERSSQ), a rating scale designed specifically to assess the social skills of young people with Autism Spectrum Disorder (ASD). The participants were 84 children and young adolescents with ASD, aged between 7.97 and 14.16 years with a mean IQ score of 90.21 ($SD = 18.82$). The results provide evidence for the concurrent and criterion validity of the ERSSQ Parent form, and the concurrent validity of the ERSSQ Teacher form. The clinical and theoretical implications are discussed, including the necessity of ratings across multiple contexts and the potential use of the ERSSQ in identifying individuals most in need of intervention and for planning and assessing the outcomes of social skills interventions.


**Abstract**

We comprehensively compared all available questionnaires for measuring quantitative autistic traits (QATs) in terms of reliability and construct validity in 3,147 non-clinical and 60 clinical subjects with normal intelligence. We examined four full-length forms, the Subthreshold Autism Trait Questionnaire (SATQ), the Broader Autism Phenotype Questionnaire, the Social Responsiveness Scale2-Adult Self report (SRS2-AS), and the Autism-Spectrum Quotient (AQ). The SRS2-AS and the AQ each had several short forms that we also examined, bringing the total to 11 forms. Though all QAT questionnaires showed acceptable levels of test–retest reliability, the AQ and SRS2-AS, including their short forms, exhibited poor internal consistency and discriminant validity, respectively. The SATQ excelled in terms of classical test theory and due to its short length.
Abstract
The study's aim was to evaluate the cost-effectiveness of CBT compared to treatment as usual (TAU). In total, 49 children aged 8–18 years with ASD and comorbid anxiety disorders, and their parents, participated; 24 were assigned to CBT and 25 were assigned to TAU. Outcome measures were the percentage of children free from their primary anxiety disorder and quality adjusted life years (QALYs). Costs were measured using a retrospective cost-questionnaire. Effects and costs were assessed at pre-, post-, and three months after treatment. Effects and costs were not statistically different between CBT and TAU, however the incremental cost-effectiveness ratio (ICER) demonstrated that CBT dominates TAU. Bootstrapped ICERs demonstrated that CBT has a high probability to be more effective than TAU, however, the probability that either CBT or TAU is more costly did not differ much. Secondary analyses demonstrated fairly robust results. CBT seems a cost-effective intervention compared to TAU, however, long-term follow-ups and comparisons between CBT and specific TAUs are necessary. Cost-effectiveness analyses may help inform policy makers to decide how to treat anxiety disorders in children with ASD.

Abstract

Research articles involving participants with an autism spectrum disorder and published from 2010 through 2012 in *Autism, Journal of Autism and Developmental Disorders, Journal of Child Psychology and Child Psychiatry,* and *Research in Autism Spectrum Disorders* were examined to determine the reported gender of participants. The overall male:female ratio was 4.62, which is similar to that reported in epidemiological studies, but the ratio was 6.07 in intervention studies. These findings suggesting that males were in a statistical sense over-represented in intervention studies, but not in other kinds of research. Most (82.21%) of these studies included both male and female participants, but direct comparisons of males and females with an autism spectrum disorder are scarce. Few of the articles we examined, 0.49% of the total, involved only female participants. Roughly half of the articles included comparison groups without an autism spectrum disorder. The percentage of male participants in these comparison groups was substantially and significantly lower than the percentage of males in groups with an autism spectrum disorder, which may in some cases constitute a methodological confound. We encourage researchers to carefully consider the gender of participants as both an extraneous variable and as an independent variable in future investigations.
Abstract

Objective

A reliable diagnosis of autism can be made as early as 24 months, yet many children are diagnosed much later. A delay in diagnosis translates into a missed opportunity to provide early intervention services and improve outcomes. The aim of the current study was to review the literature on early detection approaches in primary care and other community settings in the United States.

Methods

A search was conducted of the peer-reviewed and gray literature to identify studies published from January 1990 through January 2013 testing approaches to enhance the early detection of autism in community settings in the United States.

Results

The search identified 40 studies describing 35 approaches, which were grouped into the following categories: awareness (n=4), routine screening (n=21), and practice improvement to enhance screening (n=10). Awareness approaches were associated with positive changes in knowledge of autism-related topics. Routine screening yielded high or increased rates of screening and referrals; however, few studies assessed the effect of screening on age at diagnosis or services enrollment. Practice improvement approaches resulted in increased screening and referral rates and highlighted the importance of adopting a multipronged approach to enhance early detection.

Conclusions

While studies that tested screening approaches in community settings found positive results, the effectiveness of such efforts on reducing time to diagnosis and services enrollment remains largely untested. The fact that few studies reported outcomes beyond rates of referral indicates the need for enhanced methodological rigor particularly with respect to length of follow-up and quality of measures used.

**Abstract**

**Background**
The range of outcomes for young adults with Autism Spectrum Disorders (ASD) and the early childhood factors associated with this diversity have implications for clinicians and scientists.

**Methods**
This prospective study provided a unique opportunity to predict outcome 17 years later for a relatively large sample of children diagnosed with ASD at 2 years old. Diagnostic and psychometric instruments were administered between 2 and 19 with data from 2, 3, and 19 included in this study. Clinicians administered tests without knowledge of previous assessments whenever possible. Caregivers provided additional information through questionnaires.

**Results**
Significant intellectual disabilities at 19 were predicted by age 2 about 85% of the time from VIQ and NVIQ scores together, though prediction of young adult outcome for youths with average or higher intelligence was more complex. By 19, 9% of participants had largely overcome core difficulties associated with ASD and no longer retained a diagnosis. These youths with Very Positive Outcomes were more likely to have participated in treatment and had a greater reduction in repetitive behaviors between age 2 and 3 compared to other Cognitively Able youths (VIQ ≥70) with ASD. Very Positive Outcome youths did not differ phenotypically from Cognitively Able ASD individuals at 2 but both groups differed from Cognitively Less Able individuals (VIQ <70).

**Conclusion**
Those most at risk for intellectual disabilities and ASD can be reliably identified at an early age to receive comprehensive treatment. Findings also suggest that some cognitively able children with ASD who participate in early intervention have very positive outcomes, although replication with randomized, larger samples is needed. In order to improve understanding of very positive outcomes in ASD, future research will need to identify how variations in child characteristics and environmental factors contribute to the nature and timing of growth across individuals and areas of development.

**Abstract**

Daily living skills standard scores on the Vineland Adaptive Behavior Scales–2nd edition were examined in 417 adolescents from the Simons Simplex Collection. All participants had at least average intelligence and a diagnosis of autism spectrum disorder. Descriptive statistics and binary logistic regressions were used to examine the prevalence and predictors of a “daily living skills deficit,” defined as below average daily living skills in the context of average intelligence quotient. Approximately half of the adolescents were identified as having a daily living skills deficit. Autism symptomatology, intelligence quotient, maternal education, age, and sex accounted for only 10% of the variance in predicting a daily living skills deficit. Identifying factors associated with better or worse daily living skills may help shed light on the variability in adult outcome in individuals with autism spectrum disorder with average intelligence.


**Abstract**

Sensory processing abnormalities are common in autism spectrum disorders (ASD), and now form part of the Diagnostic and Statistical Manual 5th Edition (DSM-5) diagnostic criteria, but it is unclear whether they characterize the ‘broader phenotype’ of the disorder. We recruited adults (*n* = 772) with and without an ASD and administered the Autism Quotient (AQ) along with the Adult/Adolescent Sensory Profile (AASP), the Cardiff Anomalous Perceptions Scale (CAPS), and the Glasgow Sensory Questionnaire (GSQ), all questionnaire measures of abnormal sensory responsivity. Autism traits were significantly correlated with scores on all three sensory scales (*AQ/GSQ r = 0.478*; *AQ/AASP r = 0.344*; *AQ/CAPS r = 0.333*; all *p* < 0.001). This relationship was linear across the whole range of AQ scores and was true both in those with, and without, an ASD diagnosis. It survived correction for anxiety trait scores, and other potential confounds such as mental illness and migraine.
Abstract:
As a starting point for our review we use a developmental timeline, starting from birth and divided into major developmental epochs defined by key milestones of social cognition in typical development. For each epoch, we highlight those developmental disorders that diverge from the normal developmental pattern, what is known about these key milestones in the major disorders affecting social cognition, and any available research on the neural basis of these differences. We relate behavioural observations to four major networks of the social brain, that is, Amygdala, Mentalizing, Emotion and Mirror networks. We focus on those developmental disorders that are characterized primarily by social atypicality, such as autism spectrum disorder, social anxiety and a variety of genetically defined syndromes. The processes and aspects of social cognition we highlight are sketched in a putative network diagram, and include: agent identification, emotion processing and empathy, mental state attribution, self-processing and social hierarchy mapping involving social ‘policing’ and in-group/out-group categorization. Developmental disorders reveal some dissociable deficits in different components of this map of social cognition. This broad review across disorders, ages and aspects of social cognition leads us to some key questions: How can we best distinguish primary from secondary social disorders? Is social cognition especially vulnerable to developmental disorder, or surprisingly robust? Are cascading notions of social development, in which early functions are essential stepping stones or building bricks for later abilities, necessarily correct?

Abstract

Restricted interests and repetitive behaviors vary widely in type, frequency, and intensity among children and adolescents with autism spectrum disorder. They can be stigmatizing and interfere with more constructive activities. Accordingly, restricted interests and repetitive behaviors may be a target of intervention. Several standardized instruments have been developed to assess restricted interests and repetitive behaviors in the autism spectrum disorder population, but the rigor of psychometric assessment is variable. This article evaluated the readiness of available measures for use as outcome measures in clinical trials. The Autism Speaks Foundation assembled a panel of experts to examine available instruments used to measure restricted interests and repetitive behaviors in youth with autism spectrum disorder. The panel held monthly conference calls and two face-to-face meetings over 14 months to develop and apply evaluative criteria for available instruments. Twenty-four instruments were evaluated and five were considered “appropriate with conditions” for use as outcome measures in clinical trials. Ideally, primary outcome measures should be relevant to the clinical target, be reliable and valid, and cover the symptom domain without being burdensome to subjects. The goal of the report was to promote consensus across funding agencies, pharmaceutical companies, and clinical investigators about advantages and disadvantages of existing outcome measures.