Abstract

Objective

Disorders on the autism spectrum, as well as autistic traits in the general population, have been found to be both highly stable across age and highly heritable at individual ages. However, little is known about the overlap in genetic and environmental influences on autistic traits across age and the contribution of such influences to trait stability itself. The present study investigated these questions in a general population sample of twins.

Method

More than 6,000 twin pairs were rated on an established scale of autistic traits by their parents at 8, 9, and 12 years of age and by their teachers at 9 and 12 years of age. Data were analyzed using structural equation modeling.

Results

The results indicated that, consistently across raters, not only were autistic traits stable, and moderately to highly heritable at individual ages, there was also a high degree of overlap in genetic influences across age. Furthermore, autistic trait stability could largely be accounted for by genetic factors, with the environment unique to each twin playing a minor role. The environment shared by twins had virtually no effect on the longitudinal stability in autistic traits.

Conclusions

Autistic traits are highly stable across middle childhood and this stability is caused primarily by genetic factors.

Abstract

Autobiographical memory (AM) was assessed in 63 children (aged 8–17 years) with an autism spectrum disorder (ASD) and compared with 63 typically developing children matched for age, gender, IQ, and verbal ability. A range of methodologies was employed for eliciting past experience with particular focus on the ability to recall (a) specific events, (b) the recent and remote past, and (c) semantic versus episodic memories across different lifetime periods. Results indicated that the ASD group manifested difficulties in retrieving specific memories to word cues and had poorer access to the remote past. Deficits were found in the context of intact recent memory and preserved general memory abilities, with some impairment of visual memory. Problems in retrieving episodic and semantic AMs across the life span were also evident. Qualitative analysis of memory reports suggested that the ASD group was less likely to refer to emotion in their remote memories but more likely to describe emotions in their recent memories. Important predictors of AM performance in the ASD group were central executive abilities, in particular cognitive flexibility and verbal fluency.
Abstract

People with autism spectrum disorder (ASD) show abnormal processing of faces. A range of morphometric, histological, and neuroimaging studies suggest the hypothesis that this abnormality may be linked to the amygdala. We recorded data from single neurons within the amygdalae of two rare neurosurgical patients with ASD. While basic electrophysiological response parameters were normal, there were specific and striking abnormalities in how individual facial features drove neuronal response. Compared to control patients, a population of neurons in the two ASD patients responded significantly more to the mouth, but less to the eyes. Moreover, we found a second class of face-responsive neurons for which responses to faces appeared normal. The findings confirm the amygdala’s pivotal role in abnormal face processing by people with ASD at the cellular level and suggest that dysfunction may be traced to a specific subpopulation of neurons with altered selectivity for the features of faces.
Abstract

Background

Synaesthesia is a neurodevelopmental condition in which a sensation in one modality triggers a perception in a second modality. Autism (shorthand for Autism Spectrum Conditions) is a neurodevelopmental condition involving social-communication disability alongside resistance to change and unusually narrow interests or activities. Whilst on the surface they appear distinct, they have been suggested to share common atypical neural connectivity.

Methods

In the present study, we carried out the first prevalence study of synaesthesia in autism to formally test whether these conditions are independent. After exclusions, 164 adults with autism and 97 controls completed a synaesthesia questionnaire, autism spectrum quotient, and test of genuineness-revised (ToG-R) online.

Results

The rate of synaesthesia in adults with autism was 18.9% (31 out of 164), almost three times greater than in controls (7.22%, 7 out of 97, P <0.05). ToG-R proved unsuitable for synaesthetes with autism.

Conclusions

The significant increase in synaesthesia prevalence in autism suggests that the two conditions may share some common underlying mechanisms. Future research is needed to develop more feasible validation methods of synaesthesia in autism.

This study was published in the Molecular Autism, an open access journal and you can read full version of the paper by following this link:

http://www.molecularautism.com/content/pdf/2040-2392-4-40.pdf

Abstract

This study evaluated a manualized intervention for sensory difficulties for children with autism, ages 4-8 years, using a randomized trial design. Diagnosis of autism was confirmed using gold standard measures. Results show that the children in the treatment group (n = 17) who received 30 sessions of the occupational therapy intervention scored significantly higher (p = 0.003, d = 1.2) on Goal Attainment Scales (primary outcome), and also scored significantly better on measures of caregiver assistance in self-care (p = 0.008 d = 0.9) and socialization (p = 0.04, d = 0.7) than the Usual Care control group (n = 15). The study shows high rigor in its measurement of treatment fidelity and use of a manualized protocol, and provides support for the use of this intervention for children with autism. Findings are discussed in terms of their implications for practice and future research.

**Abstract**

**Background**

Although neurodevelopmental disorders are demarcated as discrete entities in the Diagnostic Statistical Manual of mental disorders, empirical evidence indicates that there is a high degree of overlap among them. The first aim of this investigation was to explore if a single general factor could account for the large degree of observed overlap among neurodevelopmental problems, and explore whether this potential factor was primarily genetic or environmental in origin. The second aim was to explore whether there was systematic covariation, either genetic or environmental, over and above that contributed by the potential general factor, unique to each syndrome.

**Method**

Parents of all Swedish 9- and 12-year-old twin pairs born between 1992 and 2002 were targeted for interview regarding problems typical of autism spectrum disorders, ADHD and other neurodevelopmental conditions (response rate: 80 percent). Structural equation modeling was conducted on 6,595 pairs to examine the genetic and environmental structure of 53 neurodevelopmental problems.

**Results**

One general genetic factor accounted for a large proportion of the phenotypic covariation among the 53 symptoms. Three specific genetic subfactors identified ‘impulsivity,’ ‘learning problems,’ and ‘tics and autism,’ respectively. Three unique environment factors identified ‘autism,’ ‘hyperactivity and impulsivity,’ and ‘inattention and learning problems,’ respectively.

**Conclusion**

One general genetic factor was responsible for the wide-spread phenotypic overlap among all neurodevelopmental symptoms, highlighting the importance of addressing broad patient needs rather than specific diagnoses. The unique genetic factors may help guide diagnostic nomenclature, whereas the unique environmental factors may highlight that neurodevelopmental symptoms are responsive to change at the individual level and may provide clues into different mechanisms and treatments. Future research would benefit from assessing the general factor separately from specific factors to better understand observed overlap among neurodevelopmental problems.

Abstract

Caring for a relative with autism spectrum disorder (ASD) entails being under chronic stress that could alter body homeostasis. Electrodermal activity (EDA) is an index of the sympathetic activity of the autonomic nervous system related to emotionality and homeostasis. This study compares EDA in response to acute stress in the laboratory between parents of people with (n = 30) and without (n = 34) ASD (caregivers and non-caregivers, respectively). Caregivers showed lower EDA in response to acute stress than non-caregivers. They also presented higher trait anxiety, anger, depression, and somatic symptoms than non-caregivers. Higher EDA was related to a worse mood and more severe somatic symptoms only in caregivers. These results could reflect an adaptive habituation to stress and establish that high EDA in response to acute stress depends on caregivers’ health.

Background
The objectives of this study were to explore associations between autistic traits and self-reported clinical symptoms in a population with anorexia nervosa (AN). Experimental and self-report evidence reveals similarities between AN and autism spectrum condition (ASC) populations in socio-emotional and cognitive domains; this includes difficulties with empathy, set-shifting and global processing. Focusing on these similarities may lead to better tailored interventions for both conditions.

Methods
A cross-sectional independent-groups design was employed. Participants with AN \( (n = 66) \) and typical controls \( (n = 66) \) completed self-report questionnaires including the Short (10-Item) Version Autism Spectrum Quotient (AQ-10) questionnaire (the first time this has been implemented in this population), the Eating Disorder Examination Questionnaire, the Hospital Anxiety and Depression Scale and the Work and Social Adjustment Scale. Group differences and the relationship between autistic traits and other questionnaire measures were investigated.

Results
The AN group had a significantly higher AQ-10 total score and a greater proportion scored above the clinical cut-off than the control group. Seven out of ten AQ-10 items significantly discriminated between groups. In the AN group, levels of autistic traits correlated with a greater self-reported anxiety and depression and a lower ability to maintain close relationships; however, eating disorder symptoms were not associated with autistic traits.

Conclusions
Women with anorexia possess a greater number of autistic traits than typical women. AQ-10 items that discriminated between groups related to ‘bigger picture’ (global) thinking, inflexibility of thinking and problems with social interactions, suggesting that autistic traits may exacerbate factors that maintain the eating disorder rather than cause the eating disorder directly. Using screening instruments may improve understanding of patients’ problems, leading to better tailoring of intervention. We conclude that further investigation of autistic traits in AN could inform new intervention approaches based on joint working between ASC and eating disorder services.

**Importance** The prevalence of psychological distress among mothers of children with autism spectrum disorder (ASD) suggests a need for interventions that address parental mental health during the critical period after the child’s autism diagnosis when parents are learning to navigate the complex system of autism services.

**Objective** To investigate whether a brief cognitive behavioral intervention, problem-solving education (PSE), decreases parenting stress and maternal depressive symptoms during the period immediately following a child’s diagnosis of ASD.

**Design, Setting, and Participants** A randomized clinical trial compared 6 sessions of PSE with usual care. Settings included an autism clinic and 6 community-based early intervention programs that primarily serve low-income families. Participants were mothers of 122 young children (mean age, 34 months) who recently received a diagnosis of ASD. Among mothers assessed for eligibility, 17.0% declined participation. We report outcomes after 3 months of follow-up (immediate postdiagnosis period).

**Interventions** Problem-solving education is a brief, cognitive intervention delivered in six 30-minute individualized sessions by existing staff (early intervention programs) or research staff without formal mental health training (autism clinic).

**Main Outcomes and Measures** Primary outcomes were parental stress and maternal depressive symptoms.

**Results** Fifty-nine mothers were randomized to receive PSE and 63 to receive usual care. The follow-up rate was 91.0%. Most intervention mothers (78.0%) received the full PSE course. At the 3-month follow-up assessment, PSE mothers were significantly less likely than those serving as controls to have clinically significant parental stress (3.8% vs 29.3%; adjusted relative risk [aRR], 0.17; 95% CI, 0.04 to 0.65). For depressive symptoms, the risk reduction in clinically significant symptoms did not reach statistical significance (5.7% vs 22.4%; aRR, 0.33; 95% CI, 0.10 to 1.08); however, the reduction in mean depressive symptoms was statistically significant (Quick Inventory of Depressive Symptomatology score, 4.6 with PSE vs 6.9 with usual care; adjusted mean difference, −1.67; 95% CI, −3.17 to −0.18).

**Conclusions and Relevance** The positive effects of PSE in reducing parenting stress and depressive symptoms during the critical postdiagnosis period, when parents are asked to
navigate a complex service delivery system, suggest that it may have a place in clinical practice. Further work will monitor these families for a total of 9 months to determine the trajectory of outcomes.


Abstract

Importance Disruptive behavior disorders, such as attention-deficient/hyperactivity disorder and oppositional defiant disorder, are common and stable throughout childhood. These disorders cause long-term morbidity but benefit from early intervention. While symptoms are often evident before preschool, few children receive appropriate treatment during this period. Group parent training, such as the Incredible Years program, has been shown to be effective in improving parenting strategies and reducing children’s disruptive behaviors. Because they already monitor young children’s behavior and development, primary care pediatricians are in a good position to intervene early when indicated.

Objective To investigate the feasibility and effectiveness of parent-training groups delivered to parents of toddlers in pediatric primary care settings.

Design, Setting, and Participants This randomized clinical trial was conducted at 11 diverse pediatric practices in the Greater Boston area. A total of 273 parents of children between 2 and 4 years old who acknowledged disruptive behaviors on a 20-item checklist were included.

Intervention A 10-week Incredible Years parent-training group co-led by a research clinician and a pediatric staff member.

Main Outcomes and Measures Self-reports and structured videotaped observations of parent and child behaviors conducted prior to, immediately after, and 12 months after the intervention.

Results A total of 150 parents were randomly assigned to the intervention or the waiting-list group. An additional 123 parents were assigned to receive intervention without a randomly selected comparison group. Compared with the waiting-list group, greater improvement was observed in both intervention groups ($P < .05$). No differences were observed between the randomized and the nonrandomized intervention groups.

Conclusions and Relevance Self-reports and structured observations provided evidence of improvements in parenting practices and child disruptive behaviors that were attributable to
participation in the Incredible Years groups. This study demonstrated the feasibility and effectiveness of parent-training groups conducted in pediatric office settings to reduce disruptive behavior in toddlers.


Abstract
Deficits in eye contact have been a hallmark of autism since the condition’s initial description. They are cited widely as a diagnostic feature and figure prominently in clinical instruments; however, the early onset of these deficits has not been known. Here we show in a prospective longitudinal study that infants later diagnosed with autism spectrum disorders (ASDs) exhibit mean decline in eye fixation from 2 to 6 months of age, a pattern not observed in infants who do not develop ASD. These observations mark the earliest known indicators of social disability in infancy, but also falsify a prior hypothesis: in the first months of life, this basic mechanism of social adaptive action—eye looking—is not immediately diminished in infants later diagnosed with ASD; instead, eye looking appears to begin at normative levels prior to decline. The timing of decline highlights a narrow developmental window and reveals the early derailment of processes that would otherwise have a key role in canalizing typical social development. Finally, the observation of this decline in eye fixation—rather than outright absence—offers a promising opportunity for early intervention that could build on the apparent preservation of mechanisms subserving reflexive initial orientation towards the eyes.


We have serious concerns regarding two recently highly publicized papers proposing early biomarker tests for autism or autism spectrum disorder (ASD) (Braunschweig et al. 2013, Walker et al. 2013). The paper of Braunschweig et al. concerns patterns of anti-brain antibodies detected in maternal plasma, while Walker et al. report on the occurrence of a microscopic morphological abnormality (the trophoblast inclusion) in placental tissue. Both groups suggest that their measure should be used clinically to test for autism/ASD risk and to influence early intervention, and websites promoting the tests have been established (pediatricbioscience.com; medicine.yale.edu/obgyn/kliman/autism/asd/index.aspx).
Braunschweig and colleagues state that the use of the maternal autoantibody-related (MAR) test would allow for early diagnosis and early intervention. In material on the Pediatric Biosciences website it is stated that the MAR test should be used by “…women prior to becoming pregnant as a family planning tool, or immediately after giving birth to allow early behavioral intervention for the newborn.” Walker and colleagues state that their placental trophoblast inclusion measure “…has the possibility of identifying newborns at risk for ASD who might benefit from targeted early interventions aimed at preventing or ameliorating behavioral symptoms and optimizing developmental outcomes.” In both cases, we believe the tests and the underlying research are fundamentally flawed and that clinical application of the tests would do much more harm than good.

Each of the studies has serious methodological problems. The statistical approach of the Braunschweig et al. study employed post hoc data analyses and was uncorrected for the number of possible antibody combinations. The Walker et al. study reported an intra-rater reliability (kappa) of only 0.56 and did not actually study placentas of children with diagnosed ASD. Instead, placentas of children at risk due to having an older sibling with ASD were examined and the children’s ASD outcomes were not reported. The reported sensitivities and specificities for both of the tests are thus of questionable validity. However, even if one accepts the reported sensitivities and specificities, both measures are extremely poor tests for ASD risk.

The maternal plasma antibody (MAR) test was reported to have a sensitivity of 23% and a specificity of 98.7%. If applied to the general population and using the CDC prevalence value of 1/88 (Wingate et al. 2012), the positive predictive value (PPV) of the MAR test would be 17%. This means that 83% of the time a positive MAR test would misidentify a typically developing offspring as being likely to develop ASD. Conversely, the reported sensitivity of 23% for the MAR test means that most (77%) mothers of offspring likely to develop ASD will receive a negative test. If the MAR test were applied to mothers over the age of thirty or with an older child with autism as suggested by Pediatrics Biosciences, the PPV might improve to about 29 and 75%, respectively.

The placenta test has a reported sensitivity of 41% and specificity of 92% when using the a priori criteria and has a calculated PPV of only 6%. Therefore, 94% of the time a positive placenta test would misidentify a typically developing child as being likely to develop ASD. The reported sensitivity of 41% for the placenta test means that 59% of families of a child likely to develop ASD will receive a negative test. Application of the placenta test to children...
with an older sibling with ASD would be pointless given that the test only deals with having risk equivalent to that of having an older sibling with ASD. Thus, both tests usually would provide false and misleading information regarding autism risk. The maternal antibody (Bauman et al. 2013; Braunschweig et al. 2013) and placental trophoblast inclusion (Anderson et al. 2007; Walker et al. 2013) observations are intriguing and further research in these areas is warranted. However, the marketing and clinical application of the MAR and placenta tests as they stand would have serious detrimental effects. Typically developing children misidentified as being at risk might be subjected to unnecessary, intrusive and expensive interventions. Such misidentified children would suffer from labeling effects and altered intra-family dynamics, and their families would experience needless anxiety and stress. Conversely, a large proportion of the families of children who go on to develop autism would be falsely reassured that their child was not at risk.

The search for early autism/ASD biomarkers is a worthy endeavor. However, at this time, by far the best way to assess risk and to determine need for intervention is for parents and healthcare providers to consider family history and observe carefully the behavior and development of the child.

**Abstract**

Autism spectrum disorders (ASDs) are neurodevelopmental in origin, affecting an estimated 1 in 88 children in the United States. We previously described ASD-specific maternal autoantibodies that recognize fetal brain antigens. Herein, we demonstrate that lactate dehydrogenase A and B (LDH), cypin, stress-induced phosphoprotein 1 (STIP1), collapsin response mediator proteins 1 and 2 (CRMP1, CRMP2) and Y-box-binding protein to comprise the seven primary antigens of maternal autoantibody-related (MAR) autism. Exclusive reactivity to specific antigen combinations was noted in 23% of mothers of ASD children and only 1% of controls. ASD children from mothers with specific reactivity to LDH, STIP1 and CRMP1 and/or cypin (7% vs 0% in controls; P<0.0002; odds ratios of 24.2 (95% confidence interval: 1.45-405)) had elevated stereotypical behaviors compared with ASD children from mothers lacking these antibodies. We describe the first panel of clinically significant biomarkers with over 99% specificity for autism risk thereby advancing our understanding of the etiologic mechanisms and therapeutic possibilities for MAR autism.

Abstract

BACKGROUND:
Gestation is a critical window for neurodevelopmental vulnerability. This study examined whether the presence of trophoblast inclusions (TIs) in the placenta could serve as a predictor for children at elevated risk for autism spectrum disorder (ASD).

METHODS:
Placentas were obtained from 117 births in the MARBLES (Markers of Autism Risk in Babies-Learning Early Signs) cohort of families who have one or more previous biological children with ASD, placing their newborn at elevated risk for neurodevelopmental compromise. Control samples were obtained from 100 uncomplicated term pregnancies of multiparous women with one or more typically developing biological children. Frequency of TIs was compared across the two groups.

RESULTS:
Placentas from at-risk pregnancies had an eightfold increased odds of having two or more TIs compared with control samples (odds ratio: 8.0, 95% confidence interval: 3.6-18.0). The presence of ≥2 TIs yielded a sensitivity of 41% and a specificity of 92% for predicting ASD risk status, whereas ≥4 TIs yielded a sensitivity of 19%, a specificity of 99.9%, and a positive likelihood ratio of 242 and conservatively predicted an infant with a 74% probability of being at risk for ASD.

CONCLUSIONS:
Our findings suggest that the placentas from women whose fetuses are at elevated risk for autism are markedly different from control placentas. These differences are manifested histologically as TIs. Their identification has the possibility of identifying newborns at risk for ASD who might benefit from targeted early interventions aimed at preventing or ameliorating behavioral symptoms and optimizing developmental outcomes.