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Optimal outcome in individuals with a history of autism

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Background: Although autism spectrum disorders (ASDs) are generally considered lifelong disabilities, literature suggests that a minority of individuals with an ASD will lose the diagnosis. However, the existence of this phenomenon, as well as its frequency and interpretation, is still controversial: were they misdiagnosed initially, is this a rare event, did they lose the full diagnosis, but still suffer significant social and communication impairments or did they lose all symptoms of ASD and function socially within the normal range? **Methods:** The present study documents a group of these optimal outcome individuals (OO group, $n = 34$) by comparing their functioning on standardized measures to age, sex, and nonverbal IQ matched individuals with high-functioning autism (HFA group, $n = 44$) or typical development (TD group, $n = 34$). For this study, 'optimal outcome' requires losing all symptoms of ASD in addition to the diagnosis, and functioning within the nonautistic range of social interaction and communication. Domains explored include language, face recognition, socialization, communication, and autism symptoms. **Results:** Optimal outcome and TD groups' mean scores did not differ on socialization, communication, face recognition, or most language subscales, although three OO individuals showed below-average scores on face recognition. Early in their development, the OO group displayed milder symptoms than the HFA group in the social domain, but had equally severe difficulties with communication and repetitive behaviors. **Conclusions:** Although possible deficits in more subtle aspects of social interaction or cognition are not ruled out, the results substantiate the possibility of OO from autism spectrum disorders and demonstrate an overall level of functioning within normal limits for this group. **Keywords:** Autism, outcome, optimal.

Introduction

Autism spectrum disorders (ASDs) are generally regarded as lifelong conditions, affecting communication, relationships, adaptive skills, academic and vocational attainment (Piven, Harper, Palmer, & Arndt, 1996). While children with ASD exhibit outcomes that vary widely (Eaves & Ho, 2008), moving off the autism spectrum into social and communicative function that is within normal limits is not generally considered a realistic goal, and, indeed, is not a common outcome (Billstedt, Gillberg, & Gillberg, 2005; Venter, Lord, & Schopler, 1992).

The purpose of the current study was to document cognitive, language, and social functioning in a group of children diagnosed with an ASD at a young age, who no longer carried this diagnosis. This report is part of a larger study designed to better understand the phenomenon of 'optimal outcome' (OO) in ASD, to explore possible persistent cognitive and emotional difficulties in this population, to document the range of treatments they received, and to explore biological characteristics in these individuals through structural and functional imaging.

Beginning with Rutter's (1970) pioneering study, most longitudinal studies have identified a minority of their sample who no longer met criteria for an ASD at follow-up, although the general assumption (explicit or implicit) has been that this outcome is anomalous or reflects initial misdiagnosis. Rutter reported that 1.5% of adults were functioning normally, although Sigman et al., almost 30 years later (1999), reported that 17% had lost their ASD diagnosis. Such an outcome is more likely in individuals with high IQs (Howlin, Goode, Hutton, & Rutter, 2004; Szatmari, Bartolucci, & Bremner, 1989) or an initial diagnosis of Asperger's disorder (Cederlund, Hagberg, Billstedt, Gillberg, & Gillberg, 2008). Reviewing long-term outcomes, Helt et al. (2008) concluded that between 3% and 25% of individuals with ASD eventually lost their diagnosis, although very few of the studies reporting these outcomes explicitly addressed the question of whether their social and communication abilities were fully typical. Helt et al. also concluded that early predictors of better outcomes included higher IQ, receptive language, imitation, and motor skills, earlier diagnosis and treatment, and a diagnosis of PDD-NOS rather than Autistic Disorder.

Lovaas (1987) introduced the idea of 'best outcome' or 'recovery' from autism. He reported that

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47% of his cohort receiving intensive behavioral intervention were mainstreamed in first grade and had IQs in the normal range. Although some subsequent studies confirmed Lovaas' results (Howard, Sparkman, Cohen, Green, & Stanislaw, 2005; Sallows & Graupner, 2005), others reported fewer individuals with 'optimal' or 'best' outcomes (e.g., Cohen, Amerine-Dickens, & Smith, 2006; Eikeseth, Smith, Jahr, & Eldevik, 2007). In response to Lovaas' claims, Mundy (1993) pointed out that normal IQ and functioning in regular education is possible in high-functioning autism and does not by itself constitute 'recovery'. He also noted that even if an individual no longer meets criteria for ASD, he or she might manifest traits reflecting persistent core features of ASD, comorbidities, or nonautism problems requiring intervention. We agree with Mundy that normal IQ and mainstream classroom placement are insufficient for a claim of 'optimal outcome', and that absence of autism symptoms must also be documented. In our definition of 'optimal outcome', we require that the individual be without any significant autism symptoms and function within the normal intellectual range; however, other difficulties, such as weaknesses in executive functioning or vulnerability to anxiety and depression may still exist.

In addition to the difficulties Mundy described (1993), including depression, odd thinking and poor executive functions, attention problems are also likely to persist. Fein, Dixon, Paul, and Levin (2005) and Zappella (1999) reported on children with clear ASD who had lost their ASD symptoms, but showed diagnosable ADHD. Kelley, Fein, and Naigles (2006) reasoned that persistent difficulties might also appear in language, as it is a core deficit in ASD. They examined 5- to- 9-year-old children with a history of ASD, who no longer showed significant autism symptoms, compared to a group of typical children, matched on age, sex, and vocabulary. No significant differences were found on any standardized language tests, but the OO group was poorer on verbal theory of mind tasks, on understanding mental state verbs, and on constructing narratives. These findings supported the overall excellent language functioning of the OO group, but suggested subtle residual pragmatic and semantic language deficits. In a follow-up study, Kelley, Naigles, and Fein (2010) examined a sample largely comprised of these same OO children, ages 8–13 years, who were found to be comparable to the TD group on *all* language measures and showed psychiatric vulnerability only in attention.

While these studies documented lack of current ASD symptoms, they could not address the issue of possible misdiagnosis in early childhood. Sutera et al. (2007) followed a group of 73 children from initial diagnosis around age 2 to a follow-up around age 4; 18% no longer showed signs of autism on follow-up. The group who lost the diagnosis had initially higher cognitive and especially motor functioning, and higher frequency of PDD-NOS as the initial diagnosis. Turner and Stone (2007) followed 48 children diagnosed at age 2 to follow-up at age 4. The 37% of children who lost the diagnosis had milder social symptoms, higher cognitive functioning, and were younger at initial diagnosis, but tended to have persisting language problems. Another study addressing the question of initial (mis)diagnosis was Mraz, Dixon, Dumont-Mathieu, and Fein (2009), who examined head circumference growth in children with persistent ASD versus those with OO. They reasoned that if the OO group was misdiagnosed and did not truly have autism, or constituted a distinct biological subtype, they would not show the accelerated head circumference growth previously reported for ASD (Courchesne et al., 2001). In fact, the results showed accelerated head growth in both ASD and OO groups compared to both national norms and local controls, confirming that the OO group showed an early biomarker characteristic of autism.

Several tentative conclusions thus seem warranted based on prior research: (a) losing the ASD diagnosis is a possibility for a minority of children and, at least for some children, is not due to misdiagnosis; (b) 'optimal outcome' is associated with higher cognitive functioning and somewhat milder initial symptoms; (c) residual difficulties with language, attention, executive or emotional functioning may persist and need to be characterized. Definitively documenting the existence and characteristics of individuals who lose the diagnosis of autism has important implications for understanding the neurobiology of autism, the impact of intervention on functioning, and the mechanisms underlying improvement. Structural and functional imaging of this group may shed light on whether brain anatomy and function have normalized, or whether normal behavior has been achieved through compensatory mechanisms. The current project aims to document a group of such OO individuals, explore possible persistent weaknesses in areas central to ASD, characterize the range of treatments they received, and look for biological characteristics through structural and functional MRI.

The purpose of this paper is to describe the methods of the study and the basic characteristics of the OO children, and to determine whether residual weaknesses exist in major domains of functioning in the OO group.

Method

Participants

Thirty-four individuals with a history of ASD and OO, 44 high-functioning individuals with a current ASD diagnosis (HFA), and 34 typically developing peers (TD) were tested. Participants ranged from 8 years, 1 month to 21 years, 8 months. The groups were matched on age, gender, and nonverbal IQ (NVIQ), but were significantly different on verbal IQ (VIQ), with the OO and TD groups having a VIQ about seven points higher than the

HFA group (See Table 1). Six HFA participants and three OO participants were evaluated at Queens University in Kingston, Ontario, Canada. Their performance did not significantly differ from the other participants on any measure. The participants tested at UConn were primarily from the northeast US. Participants were predominantly Caucasian, with three OO individuals, two HFA individuals, and three TD individuals reporting other races or ethnicities. The study was approved by the Institutional Review Boards of the University of Connecticut, the Institute of Living Hartford Hospital, Children's Hospital of Philadelphia, and Queens University.

Phone screenings based on study criteria were conducted with parents of each potential participant. The screening included information about demographics, exclusions for MRI (e.g., metal in body, braces, claustrophobia), previous head injury, other health problems, previous psychiatric and neurological diagnoses, medications, current and past seizures, hearing impairment, current social difficulties, and current friendships with typical peers. See Figure 1 for a flow chart of inclusion and exclusion. Recruitment was done through media outlets (newspaper stories, radio interviews), private practices, and clinic referrals. In some cases, therapists contacted parents of children known to have OOs, and in some cases, parents saw media reports and contacted the investigators.

Inclusion criteria All participants had verbal, nonverbal, and full-scale IQ standard scores greater than 77 (within 1.5 *SD* of the average of 100). Additional OO criteria were:

1. Participants had a documented ASD diagnosis made by a physician or psychologist specializing in autism before the age of 5, verified in a written diagnostic report provided by parents. Early language delay (no words by 18 months or no phrases by 24 months) documented in the report was required. As a second step in confirming diagnosis, the report was edited to remove information about diagnosis, summary, and recommendations, but leaving descriptions of behavior. One of the co-investigators (MB), an expert in diagnosis of ASD and Director of the University of Connecticut Psychological Services Clinic, reviewed these reports, blind to early diagnosis and current group membership. In addition to potential OO participants, she reviewed 24 'foil' reports for children with non-ASD diagnoses, such as global delay or language disorder. Four potential OO participants were rejected for insufficient early documentation, and were dropped from the study. All 24 foils were correctly rejected.
2. On the phone screening, parent had to report that the participant had typically developing friends. During evaluation, participants could not currently meet criteria for any ASD according to the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) administered by a research-reliable interviewer. In addition, the ADOS videotapes of all potential OO cases were reviewed by a clinician with more than 15 years of autism diagnostic experience (IME, MB, or DF) who confirmed that ADOS scores were below ASD thresholds and that in their expert clinical judgment, an ASD was not present.

Table 1 Participant characteristics of the three comparison study groups ($N = 112$): higher-functioning individuals with a current ASD diagnosis (HFA); those with a history of ASD and optical outcome (OO); and typically developing peers (TD). Table reports means, followed by SDs and ranges

	HFA	OO	TD	F/χ^2	p	Tukey/ Games-Howell	Cohen's d
n	44	34	34				
Sex	40 M; 4 F	27 M; 7 F	31 M; 3 F	2.92	.23		
Age	13.9 (2.7) 8:7–20:0	12.8 (3.5) 8:1–21:2	13.9 (2.6) 9:11–21:8	1.66	.20		
VIQ	105.4 (14.4) 81–142	112.7 (13.7) 80–137	112.0 (11.2) 93–138	3.62	.03	HFA < OO	HFA/OO: .52
NVIQ	110.2 (12.8) 78–147	110.3 (15.1) 81–142	112.8 (11.3) 89–139	0.45	.64		
ADOS–Communication	3.50 (1.42) 2–7	0.47 (0.62) 0–2	0.41 (0.56) 0–2	124.20	<.001	HFA > OO, TD	HFA/OO: 2.68 HFA/TD: 2.77
ADOS–Socialization	6.77 (2.21) 4–13	1.09 (1.31) 0–4	0.50 (0.75) 0–2	183.75	<.001	HFA > OO, TD	HFA/OO: 3.07 HFA/TD: 3.66
ADOS–Total*	10.27 (3.13) 7–19	1.56 (1.71) 0–5	0.91 (1.14) 0–4	213.10	<.001	HFA > OO, TD	HFA/OO: 3.38 HFA/TD: 3.84

ADOS, Autism Diagnostic Observation Schedule; HFA, high-functioning autism; OO, optimal outcome; TD, typical development; VIQ, verbal IQ; NVIQ, nonverbal IQ.

*By ADOS classification, 21 individuals in the HFA group fall into the autism spectrum category (cutoff total score of 7); 23 fall into the Autism category (cutoff total score of 10).

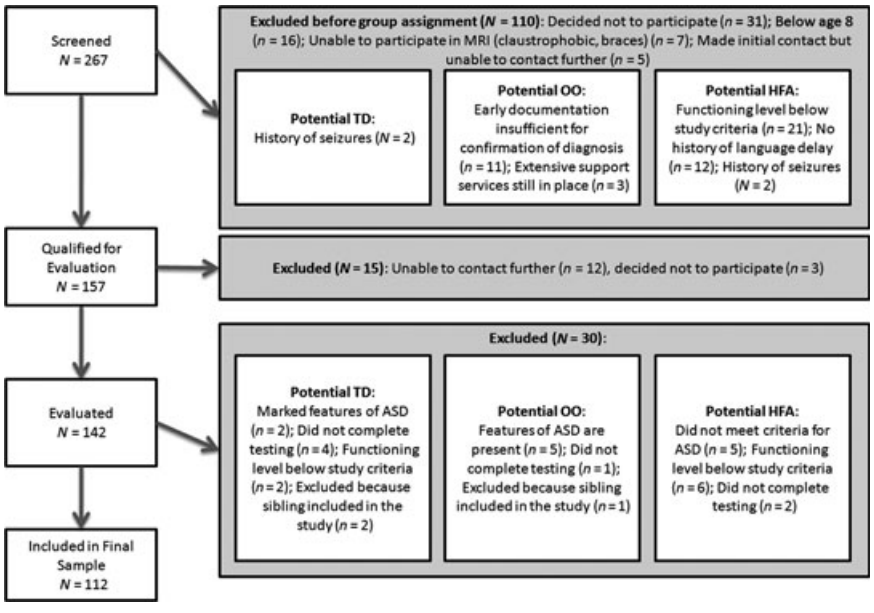

Figure 1 Flow chart of participant inclusion in the study and details for those excluded

To confirm that ASD was not present by clinical judgment, the ADOS scores were reviewed, and any possible DSM-IV symptom suggested by an elevated ADOS item was considered. Most of these concerns were in the area of nonverbal communication (indexed by ADOS items on eye contact, gesture, and facial expressiveness). Seven of the 34 OO participants were clinically judged to have some impairment (although not marked) in nonverbal social interaction, either in facial expressiveness, gesture, or eye contact; these difficulties were judged to be secondary to inhibition, anxiety, depression, inattention and impulsivity, embarrassment, or hostility, and not to have an autistic quality. Five potential OO participants were judged to have social impairments with an autistic quality and were excluded from the OO group (see Figure 1 and ADOS results, below).

3. Participants' scores on the Communication and Socialization domains of the Vineland (see below) had to be greater than 77 (within 1.5 standard deviations of the mean of 100) (see Table 4).
4. Participants had to be fully included in regular education classrooms with no one-on-one assistance and no special education services to address autism deficits (e.g., no social skills training). However, participants could be receiving limited special education services or psychological support to address impairments not specific to ASDs, such as attention or academic difficulties.

For the HFA group:

1. Following Collaborative Programs of Excellence in Autism diagnostic guidelines (Luyster et al., 2005), participants had to meet criteria for ASD on the ADOS (both Social and Communication domains and total score) and according to best estimate clinical judgment.

For the TD group:

1. Participants could not meet criteria for any ASD at any point in their development, by parent report.
2. Participants could not have a first-degree relative with an ASD diagnosis.
3. Participants could not meet current diagnostic criteria for an ASD on the ADOS, or by clinical judgment (see Table 1). There was no attempt to exclude TD children for other learning or psychiatric disorders (but see general exclusion criteria).
4. Scores on the Communication and Socialization domains of the Vineland had to be greater than 77 (see Table 4).

Exclusion criteria Potential participants for any group were excluded from the study if (a) at the time of the telephone screening they exhibited symptoms of major psychopathology (e.g., active psychotic disorder) that would impede full participation, (b) they had severe visual or hearing impairments, or (c) they had a seizure disorder, Fragile X syndrome, or significant head trauma with loss of consciousness. Two in the TD group and two in the HFA group were excluded because of possible seizure disorder; none were excluded for other reasons (see Figure 1).

Procedure

Potential participants who passed the telephone screening were scheduled for an assessment. For participants under 18, parent consent and child assent was obtained prior to testing. For participants 18 and over, their informed consent was obtained. The evaluation was administered in a quiet room over the course of two or three testing sessions at the University of Connecticut, the Institute of Living of Hartford Hospital, Queens University, or in the home. Testing lasted approximately 6 hr. In most cases, parent interviews were conducted concurrently by a second examiner and lasted approximately 3 hr for the OO and HFA groups and 1.5 hr for the TD group. Participants received a monetary incentive for participation, even if the testing could not be completed.

Measures

Results from tests of executive function, academics, psychiatric functioning, verbal memory, inferential language, history, as well as structural and functional imaging will be reported separately; the purpose of this paper is to document the overall functioning of the group of OO individuals, and to investigate specific residual difficulties that might be expected in major domains, including social cognition (measured by face recognition), language (measured by a composite language battery), and social interaction (measured by socialization and communication on the ADOS and the Vineland).

Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000). Module 3 or 4 (depending on age) was used to determine current diagnostic status for the OO and HFA groups, to rule out autistic features in the TD group, and to compare social interaction in the OO and TD groups. Administrations were videotaped and five administrations per group were coded by a rater blind to group status. Interrater reliability was coded based on the method of the test authors and was high for both the algorithm and total items, at 86.7% and 85.7%.

Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994). The ADI-R is a structured parent interview based on the DSM-IV criteria for Autistic Disorder, was administered to parents in OO and HFA groups. The 'ever' or 'most abnormal age 4–5' part of the ADI-R was used as a general measure of the severity of early autism. The ADI-R was not used to verify early ASD retrospectively because, although some items ask for whether a symptom was 'ever' observed, many items ask specifically about the 4–5 year age period, by which time the autism symptoms of some of the OO children had already improved. In addition, it has cutoffs for Autistic Disorder, but not for ASD. Current diagnoses for the HFA and OO groups were based on the ADOS, as outlined above.

Social Communication Questionnaire (SCQ; Berument, Rutter, Lord, Pickles, & Bailey, 1999). The SCQ is a 40-item parent questionnaire based on the ADI-R. The 'lifetime' score was used to screen out TD children with a history of possible autism, and to compare the overall severity of lifetime autism in the HFA and OO groups. The lifetime score is based on three items concerning present functioning, 16 items based on 'ever' displaying specific symptoms, and 21 symptoms based on the 4- to-5-year-old age period.

Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). Verbal and nonverbal IQ were measured using the WASI, which has two verbal (Vocabulary and Similarities) and two nonverbal (Block Design and Matrices) subtests.

Vineland Adaptive Behavior Scales (VABS; Sparrow, Balla, & Cicchetti, 1985). The VABS is a parent report measure that evaluates Communication, Daily Living, and Socialization.

Benton Facial Recognition Test (Benton, Sivan, Hamsher, Varney, & Spreen, 1994). Participants match test faces to a target face with different lighting and orientation.

Clinical Evaluation of Language Fundamentals-IV (CELF-IV; Semel, Wiig, & Secord, 2003). Subtests included: Concepts and Following Directions (for participants up to age 12), Word Definitions (for age 13 and up), Formulating Sentences, Recalling Sentences, and Word Classes.

Edinburgh Handedness Inventory (Oldfield, 1971). Left-handedness (Fein, Waterhouse, Lucci, Pennington, & Humes, 1985) or delayed maturation of handedness (Escalante-Mead, Minshew, & Sweeney, 2003) is overrepresented in autism. Participants reported their preferred response or pantomimed how they would perform a series of 10 familiar actions. Laterality Quotient = $(R - L)/(R + L) \times 100$. Participants with a score of ±70 or greater were categorized as right- or left-handed; a quotient of less than ±70 was considered 'mixed.'

For categorical variables (sex, handedness), groups were compared with chi-square. For continuous variables, one-way ANOVAs were used. For significant ANOVAs, when Levene's test for homogeneity of variances was found to be violated, the Games-Howell post hoc test was used; in other cases, the Tukey HSD post hoc test was used.

Results

Sex, age, and NVIQ did not differ among groups (see Table 1). VIQ was significantly lower in the HFA group than in the OO and TD group (see Table 1) and was therefore covaried in further analyses of language measures.

ADOS

As required by inclusion criteria, ADOS scores for the HFA group were above threshold for the Communication, Socialization, and total scores. As expected, the HFA scores were significantly higher than the other groups' scores, with a large effect size; no domain or total score differed between the TD and OO groups (see Table 1).

No child in the OO or TD group met criteria for ASD and if any child's social interaction was clinically judged to have an autistic quality, they were excluded (see Figure 1 and Methods, above). Minor elevations in Communication or Socialization for individual OO and TD children were generally due to anxiety or shyness, resulting in less eye contact or less outgoing conversation. Specifically, seven OO individuals were judged to show mild, nonautistic social impairment secondary to anxiety, depression, inhibition, embarrassment, hostility, or inattention/impulsivity. Twenty-one TD, 20 OO, and no HFA individuals had all zero's (most typical functioning) on the ADOS Communication algorithm items; 22

TD, 16 OO, and no HFA individuals had all zeros on ADOS Social algorithm items (chi-squares for TD-OO nonsignificant).

ADI-R lifetime scores

Socialization scores were significantly less impaired for OO than for HFA group, with a large effect size (as shown in Table 2). Communication and Repetitive Behaviors did not differ between HFA and OO.

SCQ As shown in Table 3, parent report confirmed that the lifetime severity of autism symptoms for the OO group was somewhat milder than that of the HFA group; the ranges are largely overlapping, but the mean is significantly lower for the OO group, with a large effect size. Both clinical groups, as expected, had significantly higher scores than the TD group.

VABS Adaptive behavior (see Table 4) did not differ in any of the three domains between the TD and OO groups. Socialization scores were virtually identical in OO and TD groups and Communication was slightly (nonsignificantly) higher in the OO group. Adaptive functioning was mildly delayed for the HFA group, and significantly below the other groups; this is not surprising, as the HFA scores, but not those of OO and TD groups, were allowed to range below normal, and because adaptive skills are often lower in individuals with ASD than would be suggested by their cognitive abilities (Eaves & Ho, 2008; Saulnier & Klin, 2007). For the HFA group, where cognitive scores were within the average range, 11/40 (28%) were low on Communication and 22/40 (55%) were low on Socialization. For Daily Living scores, which were allowed to freely vary for all groups, 14/40 (35%) of the HFA group had low scores, whereas 5/33 (15%) of the OO group and 4/34 (12%) of the TD group had low scores.

Benton facial recognition test As shown in Table 5, each individual's score on the Benton was transformed to a *z*-score for age. The HFA group mean was about half a standard deviation below average, whereas mean scores of the OO and TD groups were around 0 and did not differ. The bottom of the range was low for both OO and HFA groups; three of the OO group (9%), 11 of the HFA group (26%), and none of the TD group scored at or below −1.5.

Table 2 ADI-R-lifetime scores of HFA and OO comparative study groups. Table reports means, followed by SDs and ranges

	HFA	OO	*F*	*p*	Cohen's *d*
N	44	33			
ADI-R–Socialization	20.30 (5.33) 6–29	15.24 (6.43) 2–25	14.05	<.001	0.88
ADI-R–Communication	15.51 (5.07) 5–25	14.30 (4.73) 0–23	1.12	.29	
ADI-R–Restricted and stereotyped behaviors	6.19 (2.30) 1–12	5.85 (2.33) 1–9	0.40	.53	

ADI-R, Autism Diagnostic Interview-Revised; HFA, high-functioning autism; OO, optimal outcome.

Table 3 Social Communication Questionnaire – lifetime scores for three study comparison groups. Table reports means, followed by SDs and ranges

	HFA	OO	TD	*F*	*p*	Games-Howell	Cohen's *d*
n	34	30	32				
SCQ-Lifetime	22.65 (6.15) 10–33	17.10 (6.68) 5–30	1.50 (1.24) 0–4	140.43	<.001	HFA > OO > TD	HFA/OO: 0.88 HFA/TD: 4.77 OO/TD: 3.35

HFA, high-functioning autism; OO, optimal outcome; TD, typical development.

Table 4 Vineland Adaptive Behavior Scales (VABS) scores for three study groups. Table reports means, followed by SDs and ranges

	HFA	OO	TD	*F*	*p*	Games-Howell	Cohen's *d*
n	40	33	34				
VABS–Communication	82.70 (13.86) 42–108	98.30 (12.66) 79–122	93.44 (9.12) 78–119	15.96	<.001	HFA < OO, TD	HFA/OO: 1.19 HFA/TD: 0.91
VABS–Socialization	75.51 (16.02) 46–109	102.03 (8.44) 80–118	101.74 (8.56) 6–120	62.04	<.001	HFA < OO, TD	HFA/OO: 2.04 HFA/TD: 2.02
VABS– daily living	75.40 (14.26) 46–110	92.30 (15.88) 65–120	88.76 (9.26) 74–115	16.81	<.001	HFA<OO, TD	HFA/OO: 1.14 HFA/TD: 1.11

HFA, high-functioning autism; OO, optimal outcome; TD, typical development.

Table 5 Benton facial recognition test scores for three comparison study groups. Table reports means, followed by SDs and ranges

	HFA	OO	TD	*F*	*p*	Games-Howell	Cohen's *d*
n	43	33	33				
Benton	*z* = −0.49	*z* = −0.02	*z* = 0.27	4.55	.013	HFA < TD	0.72
	(1.25)	(1.19)	(0.79)				
	−3.63 to +1.67	−3.00 to +2.70	−1.45 to +2.03				

HFA, high-functioning autism; OO, optimal outcome; TD, typical development.

Table 6 Comprehensive evaluation of language fundamentals, 4th edition (CELF-IV). Table reports means, followed by SDs and ranges. All subtest scores are scaled scores with a mean of 10 and SD of 3. The CELF-IV Core Language Composite is a standard score with a mean of 100 and SD of 15. Numbers of participants, *n*, are as noted at the top of the table, unless otherwise specified

	HFA	OO	TD	*F*	*p*	Games-Howell	Cohen's *d*
n	43	33	34				
Concepts & following directions	10.50 (2.75) 4–13 *n* = 13	10.73 (1.67) 8–13 *n* = 16	12.00 (1.73) 9–14 *n* = 11	3.07	0.06	TD > HFA	TD/HFA: 0.67
Formulated sentences	9.67 (3.21) 1–15 *n* = 42	11.67 (2.19) 7–15	13.12 (1.27) 10–16	19.22	<0.01	TD > OO > HFA*	HFA/OO: 0.72 HFA/TD: 1.38 TD/OO: 0.83
Recalling sentences	9.44 (2.99) 4–15	10.27 (2.81) 4–14	11.97 (1.77) 8–15	9.01	<0.01	TD > HFA*	1.01
Word classes total	9.88 (3.26) 1–16	11.74 (2.73) 3–18	13.06 (1.97) 9–17	12.89	<0.01	TD > HFA*	1.16
Word definitions	11.43 (2.70) 6–16 *n* = 30	13.24 (2.14) 7–16 *n* = 17	13.78 (0.99) 12–16 *n* = 23	8.72	<0.01	TD > HFA*	1.12
Core language composite standard score	100.00 (13.79) 70–126 *n* = 30	108.35 (11.59) 79–126 *n* = 31	117.15 (7.06) 106–132 *n* = 33	20.78	<0.01	TD > OO > HFA*	HFA/OO: 0.67 HFA/TD: 1.61 TD/OO: 0.94

HFA, high-functioning autism; OO, optimal outcome; TD, typical development.

CELF language Scores (Table 6) were within the average range for all participants in all groups. Overall ANOVA was significant for all scores (except a trend for Concepts and Following Directions); the only significant post hoc pairwise difference was between the HFA and TD groups for most of the subtests. On Formulated Sentences and the Composite Score, the OO-TD group difference reached significance, but the OO scores were above average for all subtests and for the composite; thus the group

Table 7 Edinburgh Handedness Inventory scores for the three comparison study groups. Table reports means, followed by SDs and ranges. The Edinburgh Handedness Questionnaire's laterality quotient ranges from −100 to +100, with −100 indicating that the individual always uses his or her left hand, while +100 indicates the individual always uses his or her right hand.

	HFA	OO	TD	F/χ^2	*p*
N	44	33	34		
Handedness	39 Right; 5 Left	31 Right; 2 Left	29 Right; 5 Left	3.63	.46
Laterality quotient	70.10 (56.20) −100 – +100	84.60 (44.74) −100 – +100	68.95 (61.50) −88.24 – +100	0.87	.42

HFA, high-functioning autism; OO, optimal outcome; TD, typical development.

difference was due to the very high scores of the TD group. The findings remained significant when VIQ was covaried.

Handedness As shown in Table 7, the proportion of left-handers and the laterality index did not differ among groups.

Discussion

Thirty-four OO participants had a clear documented history of ASD, yet no longer met criteria for an ASD as per the ADOS and clinical judgment. Sex, age, nonverbal IQ, and handedness did not differ among the three groups. VIQ was 7 points lower in the HFA group than in the TD and OO groups, which were virtually identical and in the high average range. OO Communication and Socialization ADOS scores did not differ from the TD scores, although seven OO participants were judged to have social functioning mildly affected by nonautism conditions, such as anxiety, depression, or impulsivity. The number of OO and TD subjects who showed total social and communication ADOS algorithm scores above zero were not significantly different. A full exploration of psychiatric functioning in all three groups will be reported separately. By early history, the OO group had somewhat milder social symptoms than the HFA group, but did not differ in communication or repetitive behavior symptoms.

Adaptive behaviors were in the average range on all scales and virtually identical for the OO and TD groups. Scores above 77 on Communication and Socialization, but not Daily Living scales were required for OO and TD groups and this restricted the range of allowable scores; nevertheless, Daily Living could vary freely, and the allowable range above 77 on Communication and Socialization would still permit an OO-TD difference to emerge if it had existed.

Facial Recognition score was average for the OO group and not significantly different from the TD group, whereas the HFA group's average score was below average. Language subtests showed average performance on all subtests for all groups, and the OO scores were above average, although lower than the TD group on one subtest and the composite.

The results clearly demonstrate the existence of a group of individuals with an early history of ASD, who no longer meet criteria for any ASD, and whose communication and socialization skills, as measured by Vineland parent report and ADOS scores, are on par with that of TD individuals matched for IQ, sex, and age. A small group of OO individuals (3 of 34) had some weakness on a difficult face recognition test. Because 7% of the normal population would be expected to fall at or below 1.5 standard deviations, the 9% low scores obtained in the current OO group is not beyond what would be expected by chance. However, the 26% low scores obtained in the HFA group indicates a significant impairment.

The fact that impairments on facial recognition, socialization, communication, and formal language tests were not found does not necessarily mean that subtle residual deficits do not exist in the OO group. An extensive battery of tests of cognitive ability, language, academics, and executive function are being examined for possible weaknesses in the OO group. Although ADOS and Vineland scores revealed no differences between the OO and TD groups on social functioning, more fine-grained coding of social behavior might detect residual awkwardness not captured by ADOS coding; we are exploring this possibility. To conclusively demonstrate normal social functioning, peer interaction and quality of friendships would also have to be shown to be typical, using ecologically valid observation measures.

The ADI-R and SCQ-Lifetime results suggest that the OO group had somewhat milder autism in early childhood. This is consistent with the findings of Sutera et al. (2007) and Turner and Stone (2007). However, to the extent that parent recollections of up to 15 years can be relied on, the milder presentation applied to social, but not to communication and repetitive behaviors. Contrary to some findings suggesting that repetitive behaviors early in life may presage a poorer outcome (e.g., Watt, Wetherby, Barber, & Morgan, 2008) and that repetitive behaviors are less likely to improve than socialization and communication (Fountain, Winter, & Beaerman, 2012; Piven et al., 1996; Seltzer, Shattuck, Abbeduto, & Greenberg, 2004), the current data suggest that repetitive behaviors in early childhood do not seem to preclude an OO. It is possible that parent recollection may have been colored by the participant's outcome.

Another unexpected finding was that the OO group had mean IQs in the high average range, since they were only selected for having IQs above 77. It is possible that above average cognition allowed individuals with ASD to compensate for some of their deficits, using explicit and controlled processing to substitute for weak implicit social processing. It is also possible that families with higher IQ children volunteered for the study at higher rates.

A general point that should be noted is that by defining the OO group as having scores within the normal range on specific cognitive and adaptive measures, we reduced the likelihood of finding OO-TD differences. Allowing scores to range more freely would allow more exploration of residual differences from normal functioning, but would result in a less 'optimal' group of OO individuals. In addition, other scores in multiple domains were allowed to range freely, permitting exploration of at least some possible residual difficulties.

This study cannot address several important questions about OO in ASD. How many children with ASD have the capacity to achieve these outcomes? Sutera et al.'s (2007) prospective study concluded that about 18% of the children diagnosed at age 2

and receiving (mostly behavioral) intervention had lost the diagnosis by age 4. A definitive answer would require a prospective study with follow-up over a number of years. Although the ideal study has not been done, a review of outcome studies (Helt et al., 2008) concluded that between 3 and 25% of most cohorts appear to lose the diagnosis; the percent who would have reached this outcome without intervention remains unknown.

Another crucial question is what intervention can produce the highest rate of OO, and whether intervention is even always necessary. The children in the current study were predominantly from the northeast US, and therefore tended to get behavioral interventions, although children from other parts of the US and from Canada were also included. Intervention data have been collected and are being examined.

A pressing theoretical question is to what extent brain structure and function have normalized in the OO children. It is possible that effective early intervention plus maturation have resulted in the normalization of pathways and functions or even anatomical structure. Dawson et al. (2012) were able to show EEG evidence of normalization of cortical activation in response to faces versus objects in children receiving Early Start Denver Model intervention for 2 years in early childhood, supporting this possibility. Alternatively, successful intervention may have resulted in compensatory functions, such that overt behavior is normal, but atypical pathways or levels of activation are needed to achieve these behavioral results, as has been shown, for example, in dyslexia by Eden et al. (2004). Structural and functional MRI data were obtained from a subset of each group in the present study and are being analyzed.

Limitations in the current study included lack of diversity among the participating families. Recruitment strategies, as well as conducting the study in Connecticut, which is more heavily Caucasian than the US in general, may have resulted in these demographics. It is also possible that OO is rarer in children from minority or lower SES families because of less optimal interventions or resources or the presence of other family stresses (Fountain et al., 2012). It was the clinical impression of our team that the OO parents were generally highly involved in the children's treatment programs and in their social lives. Parents who advocate vigorously for the best interventions and who carry over treatments into other hours of the day do not guarantee the kind of OO we describe here, but may maximize the chance of one. Whether OO is more likely for children whose families have fewer social stresses and more resources can only be answered by an epidemiological-scale, prospective study.

Even if the child's inherent characteristics limit the cognitive and social progress that can be made, fulfilling his or her own potential can be considered a good outcome, and is made more likely by involved parents and quality treatment. It should also be pointed out that our definition of 'optimal outcome' included losing the ASD diagnosis AND functioning within the normal cognitive range. There is an additional group of children who lose the diagnosis, but still have significant intellectual or language disability (see for example Turner & Stone, 2007, and Sutera et al., 2007) and this is certainly another kind of good outcome for these children.

The purpose of the current study was primarily to demonstrate the existence of a cohort who had clear autism at a young age and no longer demonstrated any significant autistic impairments. The data clearly support the existence of this group. The possible presence of subtle limitations or differences in social behavior, social cognition, communication, or executive functions remain to be elucidated in further analyses, as do many other crucial questions, such as the biology of remediable autism, the course of improvement, and the necessary and sufficient conditions, including treatment, for such improvement.

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Key points

- Autism outcomes vary widely. Moving off the autism spectrum into normal functioning has been suggested as a possibility.
- The current study documents a group of individuals with clear early histories of autism who currently show normal language, face recognition, communication and social interaction, and no autism symptoms.
- Results have implications for prognosis by widening the range of possible outcomes for autism.

References

Benton, A.L., Sivan, A.B., Hamsher, K.D., Varney, N.R., & Spreen, O. (1994). *Contributions to Neuropsychological Assessment* (2nd edn). New York: Oxford University Press.

Berument, S., Rutter, M., Lord, C., Pickles, A., & Bailey, A. (1999). Autism screening questionnaire: Diagnostic validity. *The British Journal of Psychiatry*, *175*, 444–451.

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

Cederlund, M., Hagberg, B., Billstedt, E., Gillberg, I., & Gillberg, C. (2008). Asperger syndrome and autism: A comparative longitudinal follow-up study more than 5 years after original diagnosis. *Journal of Autism and Developmental Disorders*, *38*, 72–85.

Cohen, H., Amerine-Dickens, M., & Smith, T. (2006). Early intensive behavioral treatment: Replication of the UCLA model in a community setting. *Journal of Developmental and Behavioral Pediatrics*, *27* (Suppl. 2), S145–S155.

Courchesne, E., Karns, C., Davis, H., Ziccardi, R., Carper, R., Rigue, Z., … & Courchesne, R. (2001). Unusual brain growth patterns in early life in patients with autistic disorder. *Neurology*, *57*, 245–254.

Dawson, G., Jones, E., Merkle, K., Venema, K., Lowy, R., Faja, S., … & Webb, S. (2012). Early behavioral intervention is associated with normalized brain activity in young children with autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, *51*, 1150–1159.

Eaves, L.C., & Ho, H.H. (2008). Young adult outcome of autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *38*, 739–747.

Eden, G., Jones, K., Cappell, K., Gareau, L., Wood, F., Zeffiro, T., & Flowers, D. (2004). Neural changes following remediation in adult developmental dyslexia. *Neuron*, *44*, 411–422.

Eikeseth, S., Smith, T., Jahr, E., & Eldevik, S. (2007). Outcome for children with autism who began intensive behavioral treatment between ages 4 and 7: A comparison controlled study. *Behavior Modification*, *31*, 264–278.

Escalante-Mead, P.R., Minshew, N.J., & Sweeney, J.A. (2003). Abnormal brain lateralization in high-functioning autism. *Journal of Autism and Developmental Disorders*, *33*, 539–543.

Fein, D., Dixon, P., Paul, J., & Levin, H. (2005). Brief report: Pervasive developmental disorder can evolve into ADHD: Case illustrations. *Journal of Autism and Developmental Disorders*, *35*, 525–534.

Fein, D., Waterhouse, L., Lucci, D., Pennington, B., & Humes, M. (1985). Handedness and cognitive functions in pervasive developmental disorders. *Journal of Autism and Developmental Disorders*, *15*, 323–333.

Fountain, C., Winter, A., & Beaerman, P. (2012). Six developmental trajectories characterize children with autism. *Pediatrics*, *129*, e1112–e1120.

Helt, M., Kelley, E., Kinsbourne, M., Pandey, J., Boorstein, H., Herbert, M., & Fein, D. (2008). Can children with autism recover? If so, how? *Neuropsychology Review*, *18*, 339–366.

Howard, J.S., Sparkman, C.R., Cohen, H.G., Green, G., & Stanislaw, H. (2005). A comparison of intensive behavior analytic and eclectic treatments for young children with autism. *Research in Developmental Disabilities*, *26*, 359–383.

Howlin, P., Goode, S., Hutton, J., & Rutter, M. (2004). Adult outcome for children with autism. *Journal of Child Psychology and Psychiatry*, *45*, 212–229.

Kelley, E., Fein, D., & Naigles, L. (2006). Residual language deficits in optimal outcome children with a history of autism. *Journal of Autism and Developmental Disorders*, *36*, 807–828.

Kelley, E., Naigles, L., & Fein, D. (2010). An in-depth examination of optimal outcome children with a history of Autism Spectrum Disorders. *Research in Autism Spectrum Disorders*, *4*, 526–538.

Lord, C., Risi, S., Lambrecht, L., Cook,. E.H. Jr, Leventhal, B.L., DiLavore, P.C., & Rutter, M. (2000). The Autism Diagnostic Observation Schedule-Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders*, *30*, 205–223.

Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*, *24*, 659–685.

Lovaas, I.O. (1987). Behavioral treatment and normal educational and intellectual functioning in young autistic children. *Journal of Consulting and Clinical Psychology*, *55*, 3–9.

Luyster, R., Richler, J., Risi, S., Hsu, W., Dawson, G., Bernier, R., … & Lord, C. (2005). Early regression in social communication in Autism Spectrum Disorders: A CPEA Study. *Developmental Neuropsychology*, *27*, 311–336.

Mraz, K.D., Dixon, J., Dumont-Mathieu, T., & Fein, D. (2009). Accelerated head and body growth in infants later diagnosed with autism spectrum disorders: A comparative study of optimal outcome children. *Journal of Child Neurology*, *24*, 833–845.

Mundy, P. (1993). Normal versus high-functioning status in children with autism. *American Journal on Mental Retardation*, *97*, 381–384.

Oldfield, R.C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsycholollgia*, *9*, 97–113.

Piven, J., Harper, J., Palmer, P., & Arndt, S. (1996). Course of behavioral change in autism: A retrospective study of high-IQ adolescents and adults. *Journal of the American Academy of Child & Adolescent Psychiatry*, *35*, 523–529.

Rutter, M. (1970). Autistic children: Infancy to adulthood. *Seminars in Psychiatry*, *2*, 435–450.

Sallows, G.O., & Graupner, T.D. (2005). Intensive behavioral treatment for children with autism: Four-year outcome and predictors. *American Journal on Mental Retardation*, *110*, 417–438.

Saulnier, C.A., & Klin, A. (2007). Brief report: Social and communication abilities and disabilities in higher functioning individuals with autism and Asperger syndrome. *Journal of Autism and Developmental Disorders*, *37*, 788–793.

Seltzer, M., Shattuck, P., Abbeduto, L., & Greenberg, J.S. (2004). Trajectory of development in adolescents and adults with autism. *Mental Retardation and Developmental Disabilities Research Reviews*, *10*, 234–247.

Semel, E., Wiig, E.H., & Secord, W.A.. (2003). Clinical Evaluation of Language Fundamentals (4th edn.). San Antonio, TX: Harcourt Assessment.

Sigman, M., Ruskin, E., Arbeile, S., Corona, R., Dissanayake, C., Espinosa, M., & Zierhut, C. (1999). Continuity and change in the social competence of children with autism, Down syndrome, and developmental delays. *Monographs of the Society for Research in Child Development*, *64*, 1–114.

Sparrow, S.S., Balla, D.A., & Cicchetti, D.V.. (1985). *Vineland Adaptive Behavior Scales (Interview Edn.*). Circle Pines, MN: American Guidance Service.

Sutera, S., Pandey, J., Esser, E., Rosenthal, M., Wilson, L., Barton, M., & Fein, D. (2007). Predictors of optimal outcome in toddlers diagnosed with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *37*, 98–107.

Szatmari, P., Bartolucci, G., & Bremner, R. (1989). Asperger's syndrome and autism: Comparison of early history and

outcome. *Developmental Medicine and Child Neurology*, *31*, 709–720.

Turner, L.M., & Stone, W.L. (2007). Variability in outcome for children with an ASD diagnosis at age 2. *Journal of Child Psychology and Psychiatry*, *48*, 793–802.

Venter, A., Lord, C., & Schopler, E. (1992). A follow-up study of high functioning autistic children. *Journal of Child Psychology and Psychiatry*, *33*, 489–507.

Watt, N., Wetherby, A.M., Barber, A., & Morgan, L. (2008). Repetitive and stereotyped behaviors in children with autism spectrum disorders in the second year of life. *Journal of Autism and Developmental Disorders*, *38*, 1518–1533.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI)*. New York, NY: The Psychological Corporation.

Zappella, M. (1999). Familial complex tics and autistic behaviour with favourable outcome: A dysmaturational disorder. *Infanto-Revista de Neuropsiquiatria da Infancia e Adolescentia*, *7*, 61–66.

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