Research in Autism Spectrum Disorders

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Who benefits from early intervention in autism spectrum disorders?

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1. Introduction

An important and unresolved question in autism intervention research is what specific child and family factors might be related to treatment outcome. Research in autism spectrum disorders (ASD) described individual differences in response to intervention. As ASD is a complex disorder that affects a myriad of developmental domains, post-intervention progress should be evaluated using various outcome measures (Matson, 2007). Those outcomes might be differentially affected by several pre-intervention variables. Previous studies looked at variables and predictors that might affect outcome in cognitive ability, adaptive skills, language acquisition and improvement in autism symptoms. Eaves and Ho (2004) reported that autism severity at baseline predicted overall cognitive ability outcome. Progress in adaptive socialization skills was predicted by the baseline ASD diagnosis and progress in adaptive communication skills by the baseline language ability (Szatmari, Bryson, Boyle, Streiner, & Duku, 2003). Specific aspects of neurocognitive abilities appeared to be good predictors of outcome in both communication and socializations adaptive skills (Munson, Faja, Meltzoff, Abbott, & Dawson, 2008). Most of the studies focused on verbal abilities outcome. Baseline cognitive ability (Ben Itzchak & Zachor, 2007; Gabriels, Hill, Pierce, Rogers, & Wehner, 2001), non-verbal cognitive level at age 2 (Eaves & Ho, 2004; Thurm, Lord, Lee, & Newschaffer, 2007), baseline social deficits...
communication adaptive skills at age 3 (Thurm et al., 2007) and motor imitation ability (Stone & Yoder, 2001) were found to be good predictors of verbal skills outcome. Change in autism diagnostic classification was predicted by baseline cognitive ability and autism symptoms severity (Turner & Stone, 2007; Zachor, Ben Itzchak, Rabinovitch, & Lahat, 2007), receptive and expressive language scores difference (Ben Itzchak & Zachor, 2009; Chawarska, Klin, Paul, Macari, & Volkmar, 2009), and by baseline non-verbal IQ level (Szatmari et al., 2003).

Since ASD is now diagnosed early before the age of 2 years, understanding of the symptoms expression and the developmental trajectory with intervention is highly important for clinical practice and for research. The use of standardized diagnostic tools for ASD, specifically the recent changes in the autism Diagnostic Observation Schedule (ADOS) that specifies algorithms that include all the behavioral symptoms in ASD for young verbal and non-verbal children allow for better differentiation between different clinical profiles at this young age (Gotham et al., 2008; Gotham, Pickles, & Lord, 2009). In addition, the new calibrated autism severity metric measure based on ADOS raw totals offers a method of quantifying ASD severity with relative independence from individual characteristics such as age and verbal IQ (Gotham et al., 2009). Although previous research has examined cognitive outcome in ASD, only a paucity of studies focused on predictors of cognitive and adaptive skills outcomes. It is important to expand our understanding of who benefits from early intervention in these developmental realms. In the current research we focus on identifying child and parental characteristics at baseline that might predict acquisition of better cognitive gains and outcomes in adaptive skills.

2. Methods

Participants: 78 (71 boys and 7 girls) aged 15–35 months were included in the current study. The diagnostic process included a clinical evaluation by a neurodevelopmental pediatrician, and the use of two standardized autism diagnostic tools, the Autism Diagnosis Interview-Revised (ADI-R) (Lord, Rutter, & LeCouteur, 1994) and the Autism Diagnostic Observation Schedule (ADOS) (Lord, Rutter, DiLavore, & Risi, 1999). All the professionals involved in the diagnosis process established reliability as required. All the participants met criteria for autism based on DSM-IV (APA, 1994) and the cut-off points on the ADI-R and the ADOS. After receiving a diagnosis of autism all the children were referred to either an applied behavior analysis (ABA) or eclectic (integration of several treatment approaches) center-based intervention programs. A detailed and comprehensive description of the treatment approaches was provided in our previous intervention study (Zachor & Ben Itzchak, 2010).

3. Measures

3.1. Autism Diagnostic Interview-Revised (ADI-R)

A semi-structured interview administered to parents was designed to make a diagnosis of autism according to both DSM-IV (Lord et al., 1994) criteria.

3.2. Autism Diagnosis Observation Schedule (ADOS)

A semi-structured, interactive schedule designed to assess social and communicative functioning. The new ADOS diagnostic algorithm that classifies children into categories of autism, ASD or non-spectrum was used (Gotham et al., 2008; Lord et al., 1999). For the severity of ASD the ADOS standardized measure of severity was used (Gotham et al., 2009).

3.3. Vineland Adaptive Behavior Scales

The test assesses functioning in four adaptive skills domains: Communication, Daily Living skills, Socialization and Motor skills (Sparrow, Balla, & Cicchetti, 1984). Vineland composite standard scores were used for the statistical analyses.

3.4. Mullen Scales of Early Learning

The test evaluates cognitive abilities in visual reception, fine motor, expressive language and language comprehension domains. We defined a non-verbal cognitive measure composed of visual reception plus fine motor standard scores [both domains were highly correlated (r = .63, p < .001)], and a verbal measure composed of expressive plus receptive language standard scores [both domains were highly correlated (r = .70, p < .001)] (Mullen, 1995).

4. Procedure

Children underwent comprehensive evaluations at pre-intervention (T1) and after one year of intervention (T2). Of the 78 children who completed the ADOS at T1, 71 had the Vineland and the Mullen. At T2, 77 children completed the ADOS, of whom 75 had the Vineland and 69 the Mullen. Data on paternal and maternal ages (M = 36.5 years, SD = 6.1; M = 33.2 years, SD = 5.1) and educational attainment (Paternal M = 14.6, SD = 2.9; Maternal M = 14.6, SD = 2.4)
were obtained from the medical chart of each participant. Informed consent was obtained from all parents for use of data from their child’s chart in accordance with the institutional Helsinki committee at Assaf Harofeh Medical Center.

5. Results

In our previous study, we compared outcomes in cognitive, language and adaptive skills and in change in autism severity of two intervention groups, one based on behavioral principles (ABA) and the second received integration of several treatment approaches (eclectic). The results of this comparison revealed no significant differences between the two intervention approaches. Therefore, in the current study we treated both intervention groups as one group in all the analyses.

We examined treatment outcome after one year of intervention in adaptive skills (Vineland) and in autism severity (ADOS severity scores) using two ANOVAs, and treatment outcome in verbal and non-verbal skills (MSEL) using MANOVA with repeated measures over time. The analyses yielded significant time-effect for outcome in verbal skills (MSEL) and in autism severity (ADOS severity scores) (Table 1). After one year of intervention children improved significantly in their verbal ability and their autism severity was reduced.

5.1. Predictors of intervention outcome

The objective of this study was to identify child and parental variables at T1 that might explain the variance in intervention outcome at T2. For this purpose two hierarchical multiple regression analyses were conducted. The first analysis examined predictors for outcome in adaptive skills and used Vineland composite score at T2 as the dependent variable. T1 verbal MSEL and non-verbal T1 MSEL scores were entered in the first step, T1 ADOS severity scale scores in the second step and maternal education and maternal age in the third step. Since maternal and paternal education were highly correlated (r = .632, p < .001; r = .778, p < .01, respectively) only the maternal education was entered to the regression analysis. In addition interactions of the above variables were entered. As shown in Table 2 the child’s cognitive ability (MSEL) at T1 in the first step explained 40% of the variance in the Vineland composite score at T2, meaning that higher cognitive level at baseline resulted in better adaptive skills at T2. Only the verbal cognitive ability contributes significantly to the adaptive skills scores after one year of intervention. Autism severity at the second step and child’s age at the third step did not contribute significantly to the total explained variance. Maternal education and age at the forth step contributed 4% to the explained variance, however only maternal age contribution was significant. The older the mother was, the better the adaptive skills outcome was achieved. Interaction of T1 verbal MSEL and ADOS autism severity at the fifth stage was significant and contributed 5% to the explained variance. Altogether, the model explained 49% of the variance.

To explain the significant interaction that was found in the regression analysis, the sample was divided into two groups: a high autism severity group (autism severity scores = 8–10) and a low autism severity group (scores = 6–7). In each group correlation between the T2 Vineland scores and the T1 verbal MSEL scores was performed. The correlation was significant for the high autism severity group (n = 52, r = .672, p < .001) but not for the low autism severity group (n = 15, r = .075, p > .05). Only for children with severe autism symptoms, higher verbal abilities at pre-intervention time correlated with better adaptive skills outcome.

In the second analysis we looked for predictors of better cognitive gains with intervention. Therefore, we calculated the difference between T2 and T1 MSEL and used it as the dependent variable. For this analysis we used the following independent variables: in the first step the T1 ADOS severity score, in the second step the child’s age, and in the third step the maternal education and maternal age. As shown in Table 3, T1 autism severity explained 13% of the sample variance, meaning that cognitive gains were more pronounced in children with less severe autism symptoms at pre-intervention time.

Child’s age in the second step contributed 3% to the explained variance. The additional explained variance was almost significant (p < .1) at the second step and reached significance at the third step (p < .05), meaning that younger children had better chance to gain from intervention. Maternal education and maternal age in the third stage contributed 14% to the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Verbal and non-verbal MSEL scores, Vineland adaptive composite scores.</th>
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<tbody>
<tr>
<td></td>
<td>T1</td>
</tr>
<tr>
<td>Verbal MSEL (n = 63)</td>
<td>60.9 (24.4)</td>
</tr>
<tr>
<td>Nonverbal MSEL (n = 63)</td>
<td>73.9 (23.7)</td>
</tr>
<tr>
<td>Vineland (n = 65)</td>
<td>67.4 (6.4)</td>
</tr>
<tr>
<td>ADOS new algorithm (n = 78)</td>
<td>20.5 (4.4)</td>
</tr>
<tr>
<td>ADOS severity score (n = 78)</td>
<td>8.4 (2.0)</td>
</tr>
</tbody>
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* df = 77–62,

_ p < .05

*** p < .001.
explained variance. Children who had older and more educated mothers had better cognitive gains with intervention. Overall, the model explained 29% of the variance in this analysis.

6. Discussion

The study aim was to identify child and parental variables prior to implementation of early intervention that predict outcome and best response to intervention. Outcome in adaptive skills after one year of intervention was best predicted by the baseline verbal ability. More specifically, only for children with severe autism symptoms at baseline, the verbal ability correlated with outcome. It is possible that in severe autism the verbal ability is a more crucial factor that enables the child to compensate for the significant social-communicative deficits with intervention. The predictive value of the baseline cognitive level has been noted in previous intervention studies, although intervention measures varied widely between
studies (Gabriels et al., 2001; Harris & Handleman, 2000; Magiati, Charman, & Howlin, 2007; Turner & Stone, 2007). Several studies noted that the severity of the child's baseline social deficits was related to a change in autism diagnostic category and to language outcome, but did not examine progress in adaptive skills (Ben Itzchak & Zachor, 2007; Turner & Stone, 2007). In the current study, autism severity at baseline did not predict outcome, although a high correlation was found between autism severity and outcome in adaptive skills. It is possible that the high correlation between cognitive scores and the ADOS measures masked the contribution of last measure. Of the examined maternal characteristics only maternal age predicted outcome in adaptive skills. Advanced maternal age resulted in better outcome. It is possible that more experienced and mature mothers may enable better implementation of their children's potential in daily living skills.

Several variables predicted gains in cognitive ability in response to intervention: autism severity, child's age, and maternal age and education. Autism severity at baseline had the best predictive value, children with less severe autism symptoms showed better gains in cognitive abilities with intervention. Only a few studies looked at the predictive value of baseline autism severity on developmental gains following early intervention. The current study used autism severity as a predictor as only recently can this measure be quantified by standardized diagnostic tools. Magiati et al. (2007) reported that autism severity measured by the ADI total raw scores at baseline predicted “total progress rank” scores (magnitude of gains in cognitive, language, adaptive and autism severity domains). Turner and Stone (2007) found that the ADOS algorithm scores at baseline are associated with change in autism diagnostic category after two years. Charman and colleagues reported that non-verbal IQ, language, and autism symptom severity (ADI-R) at age 3 but not at age 2 were associated at age 7 with the same domains of functioning and with measures of symptom severity and adaptive behavior scores (Vineland) (Charman et al., 2005). For the first time, we found in our study that autism severity measured by the ADOS severity scale is a good predictor of cognitive gains with intervention.

Child's age was another significant predictor of cognitive gains in response to intervention, suggesting that the younger the child at the start of early intervention, the better the response in the cognitive domain. This finding is in accordance with previous studies that found that it is important to initiate intervention at a very young age when brain plasticity enables changes in central nervous system circuits (Harris & Handleman, 2000; Lovaa, 1987; Luise, Cannon, Ellis, & Sisson, 2000; Turner & Stone, 2007). Our study population consisted of very young children and the age range was quite narrow (15–35 months), therefore our finding strongly emphasizes the importance of early intervention in very young age in ASD.

Maternal parameters of age and education predicted rate of cognitive gains in response to intervention. The older and more educated the mother was, the more accelerated was the cognitive gain with intervention. Other intervention studies in ASD found no effect of parental years of education and ages on progress with intervention (Magiati et al., 2007; Turner & Stone, 2007). Maternal education has long been known to be the single best predictor of child development outcome (DiPietro, 2000). The mechanisms through which maternal education affects the child's IQ and other outcomes are not well known, although biological influences as well as experiential ones are likely (DiPietro, Costigan, Shupe, Pressman, & Johnson, 1998). Regarding the impact of maternal age on cognitive gains as mentioned before, it is possible that older mothers are more experienced in raising children. The impact of parental age on the outcome of young children with ASD has not been previously addressed.

The current study suggests that both biological and environmental factors affect the response to intervention in very young children with ASD. Biological factors including age, language abilities and autism severity and environmental factors including maternal age and education, impact the ability to benefit from early intervention in ASD.

There are several important clinical implications of these results. First, it is important to diagnose ASD and start intervention as early as possible. Second, the results offer the clinicians the ability to convey prognosis of future outcome based on construct of several major measures at baseline. This study encourages researchers to continue with investigation of other strong predictors of outcome in ASD.

References

American Psychiatric Association. (1994). Diagnostic and Statistical Manual of Mental Disorders DSM-IV.


