Optimal Outcome in Children with Autism

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Background (see Helt et al, 2008 review in Neuropsychology Review)

• Most longitudinal studies report 3-25% no longer meet criteria for autism on follow-up
• Most individuals no longer meeting criteria for ASD still show significant impairment in social and/or language functioning (e.g., Piven, 1996; Turner and Stone, 2007)
Lovaas, 1987

- 9/19 in the experimental group (40 hours a week Applied Behavior Analysis - ABA) successfully completed regular first grade in a public school and had an average or better score on IQ tests.
- Attempts at replication generally report some children reaching this outcome, but not as many as Lovaas.
• Mundy (1993) pointed out that normal IQ and functioning in regular education is possible in high-functioning autism and does not by itself constitute losing the diagnosis.
Purpose of our “optimal outcome” studies

• To document the phenomenon in which children with a clear history of ASD no longer meet criteria for ASD, and in whom there are no significant social or language problems

• To explore residual problems that may illuminate core deficits or suggest additional remediation or support needed

• To explore mechanisms of “optimal outcome” by tracking intervention and structural and functional imaging differences
Background

- 73 children dx’d with ASD at age 2 followed to age 4
- 13 (18%) lost dx
DSM-Symptoms

![Graph showing changes in DSM Symptoms at Time 1 and Time 2 for different ASD and NON categories.]

- **ASD-to-NON**
- **ASD-to-ASD**
- **NON-to-NON**
Vineland Communication

![Graph showing communication levels for different scenarios. The x-axis represents Vine.Comm.1 and Vine.Comm.2, and the y-axis ranges from 40 to 100. Three lines are depicted, each representing a different scenario:
- Blue line: asd to non asd
- Pink line: asd to asd
- Yellow line: non asd to non asd]
Vineland Motor

![Graph showing the comparison of motor performances between VINEMOTOR1 and VINEMOTOR2. The graph includes three lines: one for 'asd to non asd', another for 'asd to asd', and a third for 'non asd to non asd'. The x-axis represents VINEMOTOR1 and VINEMOTOR2, while the y-axis represents the performance levels ranging from 50 to 95.]

We predicted that the optimal outcome children would have more typical head circumference findings.
Mean HC z-score group differences

**Figure 2.** Mean HC z-scores for ASD-S, ASD-OO, and control groups
Current Study: Acknowledgements

• Funding: NIMH (NIH R01 MH076189)

• Collaborators:
  – Bob Schultz, Children’s Hosp. of Philadelphia
  – Mike Stevens, Institute of Living, Hartford
  – Letty Naigles, Marianne Barton, Inge-Marie Eigsti, University of Connecticut

• Recruitment: Lynn Brennan, Harriet Levin

• Graduate students: Dr. Mike Rosenthal, Katherine Tyson, Eva Troyb, Alyssa Orinstein, Molly Helt
Inclusion criteria

• All subjects:
  – Verbal, nonverbal, and full-scale IQ standard scores greater than 77
  – No major psychopathology (e.g., active psychotic disorder) that would impede full participation
  – No severe visual or hearing impairments
  – No seizure disorder
  – No Fragile X syndrome
  – no significant head trauma with loss of consciousness
Inclusion criteria for OO s’s

• Participants had a documented ASD diagnosis made by a physician or psychologist specializing in autism before the age of 5
• Early language delay (no words by 18 months or no phrases by 24 months)
• Report (without information on diagnosis, summary, and recommendations) was reviewed by clinician blind to group, mixed in with foils
• No current ASD as per ADOS and expert clinical judgment
• Vineland Communication and Socialization >77
• Full inclusion in regular education with no aide, no social skills services
Inclusion criteria for HFA

- 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.
Inclusion criteria for TD

- No ASD at any point in their development, by parent report
- No first-degree relative with an ASD diagnosis
- No current diagnostic criteria for an ASD on the ADOS, or by clinical judgment
- Vineland Communication and Socialization domains >77
Domains of Data Collection

- Cognitive functioning
- Social functioning
- Executive functioning
- Language functioning
- Academic functioning
- Psychiatric functioning
- Intervention, medical, developmental history
- Structural and functional imaging
- 4 experimental tasks (top-down processing, categorical induction, tone discrimination, dual task performance)

<table>
<thead>
<tr>
<th></th>
<th>HFA (n=44)</th>
<th>OO (n=34)</th>
<th>TD (n=34)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td>40 M; 4 F</td>
<td>27 M; 7 F</td>
<td>31 M; 3 F</td>
<td>.23</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>13.9 (2.7)</td>
<td>12.8 (3.5)</td>
<td>13.9 (2.6)</td>
<td>.20</td>
</tr>
<tr>
<td><strong>VIQ</strong></td>
<td>105.4 (14.4)</td>
<td>112.7 (13.7)</td>
<td>112.0 (11.2)</td>
<td>.03</td>
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<tr>
<td><strong>NVIQ</strong></td>
<td>110.2 (12.8)</td>
<td>110.3 (15.1)</td>
<td>112.8 (11.3)</td>
<td>.64</td>
</tr>
</tbody>
</table>
ADOS Algorithm Totals

Mean Score

Communication
- HFA: 3.50
- OO: 0.47
- TD: 0.41

Social
- HFA: 6.77
- OO: 1.09
- TD: 0.50
<table>
<thead>
<tr>
<th></th>
<th>N=34</th>
<th>N=30</th>
<th>N=32</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>HFA</td>
<td>22.65 (6.15)</td>
<td>17.10 (6.68)</td>
<td>1.50 (1.24)</td>
<td>&lt;.001 HFA &gt; OO &gt; TD</td>
</tr>
<tr>
<td></td>
<td>HFA</td>
<td>OO</td>
<td>F</td>
<td>p</td>
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<tr>
<td>-------------------------</td>
<td>----------</td>
<td>----------</td>
<td>-----</td>
<td>--------</td>
</tr>
<tr>
<td>N</td>
<td>44</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Socialization</td>
<td>20.30</td>
<td>15.24</td>
<td>14.05</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>(5.33)</td>
<td>(6.43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Communication</td>
<td>15.51</td>
<td>14.30</td>
<td>1.12</td>
<td>.29</td>
</tr>
<tr>
<td></td>
<td>(5.07)</td>
<td>(4.73)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repetitive Behaviors</td>
<td>6.19</td>
<td>5.85</td>
<td>0.40</td>
<td>.53</td>
</tr>
<tr>
<td></td>
<td>(2.30)</td>
<td>(2.33)</td>
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</table>
## Vineland Adaptive Behavior

<table>
<thead>
<tr>
<th></th>
<th>HFA</th>
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<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commun.</td>
<td>82.70</td>
<td>98.30</td>
<td>93.44</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>(13.86)</td>
<td>(12.66)</td>
<td>(9.12)</td>
<td></td>
</tr>
<tr>
<td>Socializ.</td>
<td>75.51</td>
<td>102.03</td>
<td>101.74</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>(16.02)</td>
<td>(8.44)</td>
<td>(8.56)</td>
<td></td>
</tr>
<tr>
<td>Daily Living</td>
<td>75.40</td>
<td>92.30</td>
<td>88.76</td>
<td>&lt;.001</td>
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<tr>
<td></td>
<td>(14.26)</td>
<td>(15.88)</td>
<td>(9.26)</td>
<td></td>
</tr>
</tbody>
</table>

For all comparisons, OO, TD > HFA
### Benton Face Recognition

<table>
<thead>
<tr>
<th></th>
<th>HFA</th>
<th>OO</th>
<th>TD</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>40</td>
<td>33</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Benton z-score</td>
<td>( z = -0.49 )</td>
<td>( z = -0.02 )</td>
<td>( z = 0.27 )</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>(1.25)</td>
<td>(1.19)</td>
<td>(0.79)</td>
<td>TD&gt;HFA</td>
</tr>
</tbody>
</table>


Academic Skills (Troyb et al, in press, Autism: The International Journal)

• Measures of decoding, passage comprehension, written expression, and math problem solving
• All three groups performed in the average range on all subtests
• No significant differences between OO and TD groups. The HFA group scored significantly lower on reading comprehension and math problem solving.
Psychiatric Co-Morbidity

• Most common co-morbidities reported for ASD:
  – Anxiety (esp. specific and social phobias)
  – OCD
  – Tics
  – Depression
  – ADHD
  – ODD

• As much as 70% of ASD individuals have one co-morbid condition and 41% have 2 (Simons et al, 2008)
<table>
<thead>
<tr>
<th>Disorder</th>
<th>TD</th>
<th>HFA</th>
<th>Optimal outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific phobia</td>
<td>0</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>ADHD</td>
<td>0</td>
<td>40</td>
<td>21</td>
</tr>
<tr>
<td>Tics</td>
<td>0</td>
<td>20</td>
<td>7</td>
</tr>
</tbody>
</table>
Summary

- OO group show no obvious social, language or cognitive difference from TD group
- Predictors of OO are similar to predictors of good outcome in general (higher cognitive and motor functioning, milder social symptoms)
- High rates of repetitive behavior do not preclude OO
- OO group does not show head circumference growth different from persisting ASD
- Above average IQ in OO group
- Residual deficits or vulnerabilities in the OO group (anxiety, attention)
Some Open Questions

• What percent of ASD children can reach this outcome?
• Is behavioral intervention necessary to produce this outcome?
• Do the children with OO potential have a distinctive set of etiologies?
• Are the OO participants arriving at overt behavior through different means (fMRI may illuminate)
Possible Mechanisms of Loss of Symptoms and Diagnosis

- The early clinical picture represented a transient developmental delay
- Behavioral intervention bypasses intrinsic motivation
- Neurologically based deficit in social orienting is prevented from disrupting further neurological development (Mundy & Crosson)
• Pairing social contact with primary reinforcers results in social contact developing secondary reinforcing value (Dawson) (but how does the connection become autonomous?)

• Suppressing interfering behaviors, especially stimulatory and repetitive behaviors

• Forcing attention to the environment rather than the internal world

• Teaching alternative routes to the same skills (fMRI may illuminate)
Future Directions

• Increase geographic and demographic diversity
• Adult outcome
• Biological differences between ASD-stable and Optimal Outcome individuals:
  – Genetic findings
  – Family history
  – Early growth parameters
  – Imaging findings
• Long term follow-up of children we diagnosed at age 2 to estimate % Optimal Outcome and identify predictors
• Follow children moving into OO to track reduction in symptoms
• Intervention histories
Setting the record straight...

• Children do not generally ‘grow out of’ autism

• These findings are not an argument for less early detection and intervention, but for more
Thank you
Screened N=267

Excluded before group assignment (N=110): Decided not to participate (n=31); Below age 8 (n=16); Unable to participate in MRI (claustrophobic, braces) (n=7); Made initial contact but unable to contact further (n=5)

Potential TD: History of seizures (N=2)

Potential OO: Early documentation insufficient for confirmation of diagnosis (n=11); Extensive support services still in place (n=3)

Potential HFA: Functioning level below study criteria (n=21); No history of language delay (n=12); History of seizures (N=2)

Excluded (N=15): Unable to contact further (n=12), decided not to participate (n=3)

Qualified for Evaluation N=157

Evaluated N=142

Excluded (N=30):

Potential TD: Marked features of ASD (n=2); Did not complete testing (n=4); Functioning level below study criteria (n=2); Excluded because sibling included in the study (n=1)

Potential OO: Did not complete testing (n=1); Excluded because sibling included in the study (n=2)

Potential HFA: Did not meet criteria for ASD (n=10); Functioning level below study criteria (n=6); Did not complete testing (n=2)

Included in Final Sample N=112
Predictors of Better Outcome

- higher initial IQ
- better receptive language
- imitation
- better motor skills*
- better pretend play
- less repetitive behavior
- milder overall severity
- better overall adaptive skills
- earlier diagnosis
- earlier treatment
- diagnosis of PDD-NOS rather than Autistic Disorder
Background

• Piven et al (1996) followed 38 high-IQ individuals with ASD from age 5 to age 13-28
• Majority showed improvement in social behavior and communication, but only half in repetitive behaviors
• 5 lost the ASD diagnosis, but all had persistent significant impairments in social interaction and/or repetitive behavior

• 18 children lost the diagnosis
  – milder social symptoms
  – higher cognitive functioning
  – were younger at initial diagnosis
  – tended to have persisting language problems
Specific Phobias

- HFA: crowds, babies, dogs,
- OO: dark, stink bugs, ants and bees, loud noises, crowds, elevators, ketchup, germs, dogs, crying, boats/water, heights
- TD: dogs, forests, snakes
Interpretations of the autistic to ADHD clinical picture

• Comorbid ASD/ADHD; autism resolves, leaving the ADHD clinical picture

• The children are a severe subtype of ADHD that presents as autism in the early years

• Attention impairment is part of ASD; when social, behavioral, and communication impairments subside, attention impairments remain
Mechanisms of Co-Morbidity

- Reactive disorder because of stress
- Overlapping symptoms with different causes
- Common underlying pathophysiology
- Misdiagnosis (avoidant anxious children may meet ADOS criteria for ASD)
- Subtypes of ASD that include other symptoms