Mental Health Services for Students with Autism Spectrum Disorders

Raphael Bernier, PhD
Associate Professor
Department of Psychiatry & Behavioral Sciences
Clinical Director, Seattle Children’s Autism Center

Disclosures

No Conflicts of Interest
Funding sources:


Overview

• Mile High Overview of Autism Spectrum Disorders
• Diagnosis and Characterization
• Etiology
• Neuroscience
• Mental Health Services/Intervention
What do we know about ASD?

- Autism is a neurobiological disorder characterized by impairments in social communication and restricted/repetitive behaviors.
- Is diagnosed in males 3-4 more times than females.
- Autism is found in all social class levels and in all racial/ethnic groups.
- Behaviorally based interventions are effective at improving outcomes.
- There are no genetic or biological tests to diagnose autism.
- Autism has a strong genetic component.

State of the Science on Diagnosis of ASD

ASD per the DSM-5

1. Eliminated the separate diagnostic sub-categories within the autism spectrum and subsuming them under a single category of Autism Spectrum Disorder (ASD)
2. Reduced the number of ASD symptom domains from three to two
3. Added specifiers regarding intellectual functioning, language, and associated conditions
4. Added a rating for level of ASD severity
   - Requiring support, requiring substantial support, requiring very substantial support
ASD in the DSM-5

1. Eliminated the separate diagnostic subcategories within the autism spectrum and subsuming them under a single category of Autism Spectrum Disorder (ASD)

WHY?

- Clinicians don’t agree on current subcategories
- Etiological research doesn’t support the current distinctions
- Treatment rec are not based on subcategories
Simons Simplex Collection
- History of including clinical diagnosis in studies of autism within sites (even when blind, reliable diagnoses).
- Examine clinical diagnosis across sites where clinicians reliably use all measures, but haven’t established “clinical diagnosis” prototypes.
- Strict guidelines and reliability measures for evaluative tools:
  - ADI
  - ADOS

Expert clinicians don’t agree
Expert clinicians don’t agree

ASD diagnoses assigned by 12 university-based sites (n = 2,102)


ASD in the DSM-5

2. Reduced the number of ASD symptom domains from three to two

WHY?

- Communication and social behaviors are overlapping and hard to distinguish
- Reduces likelihood of some criteria carrying excessive weight
- Secondary data analysis supports the more streamlined approach in terms of sensitivity and specificity

Diagnostic Process

- Interview of Developmental History
- Intake interview focusing on primary domains of ASD with caregiver (ADI)
- Interaction with individual (ADOS)
- Assessment of language (broadly speaking), cognitive (IQ), and adaptive ability (ABAS, Vineland)
State of the Science on Diagnosis of ASD

Questions?

State of the Science on Etiology of ASD

- Why do we care about etiology?
- How do we know genetics is involved in ASD?
- Advances in the genetics of ASD
- Current thinking on etiology

Why do we care about etiology?
Early Detection

- **Age (years)**
  - 0
  - 1
  - 2
  - 3

- **detect**
- **diagnose**
- **intervene**

Early Detection

- **early detection**
- **early intervention**
- **better outcome?**

Genetic insights inform mechanism and provide treatment options

- **genes**
- **proteins**
- **molecules**
- **mechanism**
- **pharmacological interventions?**
How do we know genetics is involved in ASD?

Twin studies provide powerful tools for examining etiology

Infant siblings inform ASD risk
Advances in the genetics of ASD

A decade and a half of studies

Collaborative Linkage Study of Autism

- 1999
- 2007
- 2011
- 2012
- 2013
- 2014

De Novo Copy Number Variations

Genome-Wide Associations

MIP (molecular inversion probe) Sequencing

Pilot Exome Sequencing

Full Scale Exome Sequencing

CHD8 gene

Collaborative Linkage Study of Autism

Autism risk genes

- Aa
- Bb
- Cc
- dd
- ee

father

mother

Autism risk genes

- aa
- bb
- cc
d
- ee

son

(autism)

son

(autism)

son

(autism)
Collaborative Linkage Study of Autism

- Linkage to chromosome 13
- Linkage to chromosome 7

Barrett, et al, 1999

Genetic Contributors

From Abrahams & Geschwind, 2008

A decade and a half of studies

- Collaborative Linkage Study of Autism
- Genome-Wide Associations
- MIP (molecular inversion probe) Sequencing
- De Novo Copy Number Variations
- Pilot Exome Sequencing
- Full Scale Exome Sequencing
- CHD8 gene

© University of Washington Autism Center
Copy Number Variations

Chromosome 16p11.2

Deletion

Duplication

CNV analysis in SSC

CNV analysis in SSC

A decade and a half of studies

Exome Sequencing in Autism

- Selected 20 individuals
  - No family history of mental illness
  - No BAP in family members
  - Significantly impacted by ASD symptoms
- Identified neurologically expressed gene-disrupting mutations in 4 individuals
- These 4 individuals were more impaired

Ozak et al., 2011, Nature Genetics
A decade and a half of studies

- Collaborative Linkage Study of Autism
- Genome-Wide Associations
- MIP (molecular inversion probe) Sequencing
- De Novo Copy Number Variations
- Pilot Exome Sequencing
- Full Scale Exome Sequencing
- CHD8 gene

Exome Sequencing in Autism

- Replicated exome study in 209 individuals with ASD
- Identified 248 neurologically expressed gene-disrupting mutations in 25% of the sample
- Only 2 genes with recurrence: CHD8 (2 individuals) & NTNG1 (2 individuals)
- Based on this number of mutations, we can estimate there are 384-821 autism risk loci

Ornak et al, 2012, Nature
A decade and a half of studies

1999
Collaborative Linkage Study of Autism

2007
De Novo Copy Number Variations

2009
MIP (molecular inversion probe) Sequencing

2011
Pilot Exome Sequencing

2012
Full Scale Exome Sequencing

2013
Genome-Wide Associations

2014
De Novo Copy Number Variations

MIP Sequencing

- Tested for disruption of the 44 network genes in over 2000 individuals with ASD.
- Identified recurrent mutations to these genes.
- The most common 6 genes in this network account for 1% of ASD.

Ozak et al, 2012, Science
Clinical Characterization

- 87% (13/15) meet strict diagnostic criteria for ASD
- 60% have Intellectual Disability
- 80% have macrocephaly (rapid, early growth)
- 80% tall stature
- Hypertelorism, down-slanted palpebral fissures, prominent forehead, pointed chin
- 80% have gastrointestinal problems (constipation)*
- 67% have significant sleep problems
- 3 of 3 females with precocious puberty (following observation by Talkowski et al, 2012)

Recapitulation in zebrafish
Current thinking on etiology?

Genetic Risk Factors

- Genetic Risk Factors
- Syndromic and other monogenic disorders
  - Fragile X (FMR1), Rett (MeCP2), CNTN3/4, NLGN1/3, SHANK2/3, UBE3A...
- 16p11.2
- Recurrent chromosomal abnormalities
  - 15q11-13, 22q11...
- Private, de novo CNVs
- CHD8
- De novo LGD mutations

What about the environment?

- Genes don't always act alone
Potential Environmental Risk Factors

- Toxic exposures during pregnancy:
  - valproic acid (seizure/mood stabilizer)
  - prenatal rubella
  - misoprostol (ulcer treatment)
  - Chlorpyrifos (insecticide)
  - Pollution (proximity to freeways, amt of traffic)
  - Agricultural pesticides
- Increased paternal age
- Interaction between exposures and genetic background

Maternal infection in utero

Reported infectious illnesses and observed copy number variants (CNVs) in probands (N=1971)

Infections and CNVs
Conclusion

- Tremendous behavioral and causal heterogeneity in ASD.
- Genetically defined individuals reveal subtle but real behavioral subtypes in ASD.
- Interactions between genotype and exposures early in development likely contributing.
- By identifying causal mechanisms we can detect autism earlier, develop targeted treatments (at multiple levels), inform course and prognosis, identify individualized interventions.

State of the Science on Etiology of ASD

Questions?

State of the Science on Neuroscience of ASD

- Current theories on neurophysiology of ASD
- Imitation, Mirror Neurons, and ASD
The brain in ASD

- Autopsy, neuropsych testing, imaging, EEG, MEG, TMS, etc all show differential activity in the brain in ASD.
- 3 current theories:
  - Connectivity hypothesis
  - Social information processing hypothesis
  - Social Motivation hypothesis

Connectivity Hypothesis

- Due to poor long range connectivity, simple, local processing is intact while complex, distributed information processing is impaired.
- The nature of the information processed is relevant only insofar as it requires distributed brain function.
- Because social interaction tends to be complex, these theories suggest that it is particularly vulnerable to disruption due to underconnectivity.

Underconnectivity

Kana et al, 2014
Support for Connectivity

- Imaging study results vary: showing overconnectivity, underconnectivity, and typical connectivity in ASD.
- Movement artifact in MRI actually causes increased close connectivity and decreased long range connectivity: blow to connectivity theories.
- Behavioral correlates are proposed: improved visual-spatial, splinter skills, etc.
- Connectivity unlikely to be universal.

Social Motivation Hypothesis

- Disruption of brain structures related to assignment of reward that result in the cascade of impairments observed in ASD
  - Amygdala, ventral striatum, orbitofrontal and ventromedial prefrontal cortex
- Reduced reward value placed on social stimuli.
- Reduced reward value leads to decreased attention (behaviorally/neurologically) to social, increased to non-social.
- Decreased attention results in decreased experience (and therefore decreased skill and ability) in social cognition.

Social Motivation

Scott-Van Zeeland et al, 2010
Support for Social Motivation

- Imaging study results suggest differential activation in response to social vs nonsocial rewards.
- Eye tracking studies provide strong support for differential attention to social stimuli.
- Design limitations temper conclusions (e.g., faulty comparisons between smiling faces and money; how motivation defined).
- Promising avenue for future work.

Social Information Processing Hypothesis

- Disruption of brain structures in the social brain that result in the impairments observed in ASD.
- Brothers (1990) proposed a collection of brain regions to be responsible for social information processing and interpretation.
- Non-human primate studies: lesions of brain regions impacted social functioning.
- In Humans, different approaches used.

Social Brain Circuitry Implicated in ASD

- Anterior Cingulate (Mundy, 2003)
- Hippocampus (Bauman & Kemper, 2005)
- Orbital Frontal Cortex (Rolls, 2000)
- Superior Temporal Sulcus (Pelphrey & Carter, 2008)
- Fusiform Gyrus (Schulte et al, 2000)
- Medial Prefrontal Cortex (Dawson et al, 1998)
- Amygdala (Baron-Cohen et al, 2000)
- Inferior Frontal Gyrus; Inferior Parietal Lobe (Dapretto et al, 2006)
- Cerebellum (Courchesne, 1997)
Social Brain Circuitry Implicated in ASD

Imitation Impairments in Autism
- Symbolic meaning hypothesis
  - (Baron-Cohen, 1988; Rogers et al, 1996)
- Executive functioning hypothesis
  - (Ozonoff, Pennington & Rogers, 1991; Rogers et al, 1996)
- Poor social motivation to attempt tasks
  - (Trevathan & Aitken, 2001)
- Dyspraxia or motor dysfunction
  - (Jones & Pryor, 1985)
- Deficit in Self-Other mapping
  - (Rogers & Pennington, 1991; Williams et al, 2001)

Imitation and Self-Other Mapping
- Class of visuomotor neurons that activate when an individual is both performing an action and observing a similar action
- Potentially serve as neurological substrate for self other mapping
**Mirror Neurons: non-human primates**

- Mirror neurons activate during the execution AND observation of actions.
- First identified in area F5 of monkeys.
- Proposed to mediate action understanding.

(from Ramachandran & Oberman, 2006)

**Mirror Neurons: Humans**

- In humans, also appears to be an execution/observation system.
- Proposed to be the mirror neuron system—limited direct evidence (e.g., fMRI and EEG).

**Mirror Neuron Regions**

- Inferior Frontal Gyrus
- Inferior Parietal Lobe
- Related regions?
  - Superior Temporal Sulcus
  - Insula
  - Anterior Cingulate

Rizzolatti & Arbib, 1998
Mirror Neurons: Humans

- In humans, area 44 (Inferior Frontal Gyrus) is activated when observing, executing, and imitating movement.
  - Iacoboni et al, 1999

- Only species specific actions result in MNS activation.
  - Buccino et al, 2004

- Activation occurs
  - With intransitive movements (emotional expressions)
  - Actions that are in behavioral repertoire (lip reading vs barking)
  - Seems to serve a wider role.
  - Provide the ability to understand others’ actions and emotions through internal representation without reflection.
  - Hypothesized to underlie imitation, empathy, theory of mind, metaphor, and evolution of language.
  - How best to study non-invasively with individuals with autism?
Electroencephalography and Mirror Neurons

EEG Mu rhythm reflects execution/observation matching system

EEGs and Mirror Neurons

Mu rhythm is neuronal activity recorded from central channels over motor cortex in ~8-13 Hz frequency band

- At rest = synchronous
- Execution and observation of movement = asynchronous → reducing mu amplitude
Research Questions

- Observed deficits in social cognition in ASD.
- Proposed role of MNS in social cognition.

- Is there disruption of the MNS in autism?
- Is there a correlation between imitation ability and MNS functioning?

Procedure

Imitation battery

Tasks:
- Single step facial expressions
- Sequenced facial expressions
- Single step hand gestures
- Sequenced hand gestures
- Complex two hand gestures
- Meaningless hand movements
- Actions on objects (gentle or harsh style)
Imitation Task Models

Single Face Expression Example

Sequenced Hand Gesture Example

Results

Condition X Group: p<.05

Ratio of mu power by condition

Condition

Ratio of mu power (condition/resting)

execute observe

control autism

Bernier et al 2007

Results

Mu suppression and face summary score in the observe condition

Bernier et al 2007
Conclusions

- Adults with ASD show less attenuation of the mu rhythm in response to the observation of actions. Suggests dysfunction of the mirror neuron system.
- Continued impairments in behavioral imitation skills.
- Mu wave attenuation when observing actions correlates with facial imitation skills. Suggests the EEG mu rhythm may reflect underlying neurological activity related to imitation ability.

Mu rhythm in children with ASD

Bernier et al, 2013

Conclusions

- Children with ASD on average do not show mu wave attenuation differences from typical children.
- Continued impairments in behavioral imitation skills.
- Mu wave attenuation when observing actions correlates with imitation skills. Suggests the EEG mu rhythm may reflect underlying neurological activity related to imitation ability.
- Variability in findings may be due to variability in imitation ability, not presence of ASD per se.
Mu rhythm in ASD

- Conflicting results in literature:
  - Between group differences:
    - Oberman et al., 2005
    - Bernier et al., 2007
    - Martineau et al., 2008
    - Oberman et al., 2008
    - Dumas et al., 2014
  - No differences between groups
    - Raymaekers et al., 2009
    - Fan et al., 2010
    - Bernier et al., 2013
    - Ruysschaert et al., 2014
- Due to Sample differences:
  - Diagnostic presentation, variability in ASD related abilities (e.g., imitation), etiological contribution

Question: How does etiology contribute?

- Complete exome sequencing in ASD sample
  - All ASD individuals meet strict ADI, ADOS, clinical criteria
  - Participants in Simons Simplex Collection or SAGE Study
- Identify individuals with Likely Gene Disrupting (LGD) mutations in interactive protein network playing a contributory role in ASD
- Re-contact and invite for visit for comprehensive follow up
- LGD events: CHD8 (2), OSCAM, DYRK1A (3), GRIN2B, KDM6B, SCN2A, SETBP
- Identify comparison groups: age & gender matched
  - “idiopathic ASD” and typical group
- Hypothesis: ASD group is comprised of many etiologies each contributing distinctly to neural structure/function leading to variable findings.

Dynamic Stimuli
ASD vs TYP

- No group X condition interaction: $F(1,7023) = .94, p = .33$.
- Both exhibit more mu attenuation for social vs. nonsocial.

ASD vs LGD vs TYP

- Group X condition interaction: $F(1,7031) = 30.93, p < .0001$.
  - ASD-LGD and TYP groups exhibited more mu attenuation for social than nonsocial stimuli, respectively, $t = 5.39$ and $t = 6.09, p < .0001$.
  - ASD-NON group did not exhibit mu attenuation condition differences, $t = 2.49, p = .19$.

ASD subtypes

- No social discrimination (Social ~ NonSocial)
Conclusions

- Conflicting brain findings in ASD.
- Our results demonstrate that distinct etiologies may contribute differentially to imaging findings.
- Given, ASD is genetically heterogeneous, neglecting etiology introduces variability and obscures true relationships between genotype; protein expression; neural development; structure, function; and behavior.

Questions?

State of the Science on Mental Health Services/Intervention Approaches

- Interventions for ASD
- What does science tell us about interventions for ASD
- How to think about interventions for ASD
### Interventions for ASD

- No known cure. Focus is on educational and behavioral approaches to:
  - Improve skills in core deficit areas
  - Optimize functional outcomes:
    - Independence
    - Acceptance
    - Productivity
  - Treatments needs can be lifelong
  - Lifetime costs of caring for an individual with autism is estimated at $3.5 to 5 million.
  - Early Intervention is critical

<table>
<thead>
<tr>
<th>Interventions for Autism Spectrum Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Behavioral Interventions</strong></td>
</tr>
<tr>
<td>EARLY START DENVER MODEL (ESDM)</td>
</tr>
<tr>
<td>PIVOTAL RESPONSE TRAINING (PRT)</td>
</tr>
<tr>
<td>DISCRETE TRIAL TRAINING (DTT)</td>
</tr>
<tr>
<td>SOCIAL STORIES</td>
</tr>
<tr>
<td>SOCIAL SKILLS TRAINING</td>
</tr>
<tr>
<td>SOCIAL GROUPS</td>
</tr>
<tr>
<td>INTEGRATED PLAY THERAPY</td>
</tr>
<tr>
<td><strong>Educational and Integrated Services</strong></td>
</tr>
<tr>
<td>TEACCH</td>
</tr>
<tr>
<td>DAILY LIFE THERAPY</td>
</tr>
<tr>
<td>DAILY LIFE THERAPY</td>
</tr>
<tr>
<td>DAY LIFE THERAPY</td>
</tr>
<tr>
<td>DAY LIFE THERAPY</td>
</tr>
<tr>
<td>DAY LIFE THERAPY</td>
</tr>
<tr>
<td><strong>Medical Procedures</strong></td>
</tr>
<tr>
<td>CHELATION</td>
</tr>
<tr>
<td>HYPERBARIC OXYGEN THERAPY</td>
</tr>
<tr>
<td>ELECTROCONVULSIVE THERAPY</td>
</tr>
<tr>
<td><strong>Diet and Supplements</strong></td>
</tr>
<tr>
<td>DIETARY INTERVENTION (E.G. GLUTEN-FREE, CASEIN-FREE, YEAST FREE, KETOGENIC)</td>
</tr>
<tr>
<td><strong>Complementary</strong></td>
</tr>
<tr>
<td>HOMEOPATHY</td>
</tr>
<tr>
<td>VITAMIN THERAPY</td>
</tr>
<tr>
<td>SECRETIN</td>
</tr>
<tr>
<td>MELATONIN</td>
</tr>
<tr>
<td><strong>Animal based</strong></td>
</tr>
<tr>
<td>CANINE COMPANION</td>
</tr>
<tr>
<td>DOLPHIN THERAPY</td>
</tr>
<tr>
<td>HIPPO THERAPY</td>
</tr>
<tr>
<td>THERAPEUTIC HORSEBACK RIDING</td>
</tr>
<tr>
<td><strong>Spirituality based</strong></td>
</tr>
<tr>
<td>PRAYER</td>
</tr>
<tr>
<td>ENERGY HEALING</td>
</tr>
<tr>
<td><strong>Tech based</strong></td>
</tr>
<tr>
<td>ASSISTIVE TECHNOLOGY</td>
</tr>
<tr>
<td>TEACHTOWN</td>
</tr>
<tr>
<td>FAST FORWORD</td>
</tr>
<tr>
<td><strong>Psycho-Pharmacological</strong></td>
</tr>
<tr>
<td>ANTI-CONVULSANTS</td>
</tr>
<tr>
<td>ANTI-DEPRESSANTS</td>
</tr>
<tr>
<td>ANTI-FUNGALS</td>
</tr>
<tr>
<td>ANTI-HYPERTENSIVES</td>
</tr>
<tr>
<td>ANTI-PYSCHOTICS</td>
</tr>
<tr>
<td>ANXIOLYTIKS</td>
</tr>
<tr>
<td>MOOD STABILIZERS</td>
</tr>
<tr>
<td>SEDATIVES</td>
</tr>
<tr>
<td>STIMULANTS</td>
</tr>
</tbody>
</table>

- **Interventions for Autism Spectrum Disorders**

- **Educational and Integrated Services**
  - TEACCH
  - DAILY LIFE THERAPY
  - VITAMIN THERAPY
  - SECRETIN
  - MELATONIN
- **Animal based**
  - CANINE COMPANION
  - DOLPHIN THERAPY
  - HIPPO THERAPY
  - THERAPEUTIC HORSEBACK RIDING
- **Psychological based**
  - PRAYER
  - ENERGY HEALING
- **Tech based**
  - ASSISTIVE TECHNOLOGY
  - TEACHTOWN
  - FAST FORWORD
- **Psycho-pharmacological**
  - ANTI-CONVULSANTS
  - ANTI-DEPRESSANTS
  - ANTI-FUNGALS
  - ANTI-HYPERTENSIVES
  - ANTI-PYSCHOTICS
  - ANXIOLYTIKS
  - MOOD STABILIZERS
  - SEDATIVES
  - STIMULANTS
Interventions for Autism Spectrum Disorders

**Psychosocial Educational**
- Music therapy
- Speech therapy
- Pivotal response training
- Social skills training
- Early intensive behavioral intervention (EIBI)
- Early Start Denver Model (ESDM)

**Complementary**
- Complementary and alternative medicine (CAM)
- Pharmacological
- Pharmacological interventions, including:
  - Antiepileptic
  - Antidepressants
  - Antipsychotics
  - Antihistamines
  - Antianxiety, sedatives, stimulants among others.

Interventions in ASD:
- Many different models of autism intervention
- Many common terms represent multiple approaches
- Applied Behavioral Analysis (ABA)
- Discrete Trial Training (DTT) or Lovaas method
- Early Intensive Behavioral Intervention (EIBI)
- Early Start Denver Model (ESDM)
- Pivotal Response Training (PRT)
- Social skills training
- Complementary and alternative medicine (CAM)
- Pharmacological

Differences between ASD treatments
- **Scope** (skill-focused vs. comprehensive)
- **Targeted outcomes** (language, behavior)
- **Setting** (clinic, home, school)
- **Intensity** (hours per week)
- **Duration** (weeks, months, years)
- **Recipient** (child, caregivers)
- **Methodology** (behavioral vs. developmental)
Some comprehensive models

DTT
- Breaking a skill into smaller parts
- Teaching one subskill at a time
- Prompt fading and shaping of appropriate behaviors until mastered
- Data collection

ESDM
- Focuses on developmentally appropriate skill learning
- Particular focus on child’s affect, attention, and arousal.
- Data collection

PRT
- Focus on two pivotal behaviors: motivation and responsivity to multiple cues
- The thinking is by changing these behaviors, improves everything else
- Data collection

TEACCH model
- TEACCH: Treatment and Education of Autistic and related Communication Handicapped Children
- Started by Eric Schopler at UNC in 1966.
- Physical modification of space, providing visual cues, schedules, and structure to help accommodate needs of those with ASD.

Social skills training
- Multiple settings: clinic, home, school
- Multiple formats: dyad, group
- Multiple approaches: therapist-led, peer-led
- In general:
  - Therapist/trained peer role:
    - Teach skill
    - Provide concrete reinforcement for all attempts
    - Highlight natural contingencies
  - Fun activities:
    - Developing rules that are clear, concrete and appropriate
    - Conversation Pong and Conversation Bridge
    - Emotional Charades
## Complementary and Alternative Medicines (CAM)

<table>
<thead>
<tr>
<th>Animal based CAMS</th>
<th>Relationship based Interventions</th>
<th>Physiological Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANINE COMPANION</td>
<td>FLOOR TREATMENT</td>
<td>CHIROPRACTIC</td>
</tr>
<tr>
<td>DOLPHIN THERAPY</td>
<td>GENTLE TEACHING</td>
<td>ACUPUNCTURE AND ACUPRESSURE</td>
</tr>
<tr>
<td>HIPPO THERAPY</td>
<td>HOLDING THERAPY</td>
<td>YOGA</td>
</tr>
<tr>
<td>THERAPEUTIC HORSEBACK RIDING</td>
<td>RELATIONSHIP DEVELOPMENT</td>
<td>THERAPEUTIC MASSAGE</td>
</tr>
<tr>
<td>Spiritually based CAMS</td>
<td>INDIVIDUALIZED</td>
<td>PATTERNING THERAPIES</td>
</tr>
<tr>
<td>FLOWER THERAPY</td>
<td>PEER MENTORING</td>
<td>MILLER METHOD</td>
</tr>
<tr>
<td>ENERGY HEALING</td>
<td>RELATIONSHIP DEVELOPMENT</td>
<td>AUDITORY INTEGRATION THERAPY</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dietary and Supplements</th>
<th>Water: small sips</th>
<th>IMMOBILIZATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASEIN-FREE</td>
<td>FLOWER THERAPY</td>
<td>RAPID PROMPTING</td>
</tr>
<tr>
<td>YEAST FREE</td>
<td>IMMUNOTHERAPY</td>
<td>TECHNOLOGY</td>
</tr>
<tr>
<td>DIET</td>
<td>HOMEOPATHY</td>
<td>THERAPY</td>
</tr>
<tr>
<td>GLUTEN-FREE</td>
<td>VITAMIN THERAPY</td>
<td>TECHNOLOGY</td>
</tr>
<tr>
<td>GFCF DIET</td>
<td>IMMOBILIZATION</td>
<td>INTRODUCTION</td>
</tr>
<tr>
<td>HOMEO</td>
<td>HOMEOPATHY</td>
<td>SENSORY INTEGRATION THERAPY</td>
</tr>
<tr>
<td>IMMUNOTHERAPY</td>
<td>HOMEO</td>
<td>TOMPHT METHOD</td>
</tr>
<tr>
<td>VITAMIN THERAPY</td>
<td>HOMEOPATHY</td>
<td>TRICKS THERAPY</td>
</tr>
<tr>
<td>WATER</td>
<td>HOMEOPATHY</td>
<td>VISION THERAPY</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical Procedures</th>
<th>Wi-Fi: limited use</th>
<th>BORIS SENSORY AND NEUROFEEDBACK</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHELATION</td>
<td>ELECTROCONVULSIVE THERAPY</td>
<td>AQUA THERAPY</td>
</tr>
<tr>
<td>HYPERBARIC OXYGEN THERAPY</td>
<td>ELECTROCONVULSIVE THERAPY</td>
<td>AQUA THERAPY</td>
</tr>
</tbody>
</table>

## Pharmacological

- Antipsychotics (risperidone): aggressive behavior
- SSRI’s: anxiety, depression, OCD, aggression
- Naltrexone: hyperactivity, inattention
- Stimulants: hyperactivity, impulsiveness, inattention
- Mood Stabilizers: mood lability
- Treats issues not autism itself!

## What does science tell us?
Early intensive behavioral intervention (EIBI) is very effective for some children. A substantial proportion of children are able to attend regular education classes. Children with higher IQs are likely to respond better. Gains are stable into adolescence. Early intervention is cost-effective.

**What we know about Early Intervention**

- Early intensive behavioral intervention (EIBI) is very effective for some children.
- A substantial proportion of children are able to attend regular education classes.
- Children with higher IQs are likely to respond better.
- Gains are stable into adolescence.
- Early intervention is cost-effective.

**Elements of successful EIBI program:**

- **EIBI:**
  - Comprehensive curriculum addressing attention, imitation, language, play, and social interaction.
  - Sensitivity to normal developmental sequence.
  - Highly supportive teaching strategies (based on ABA).
  - Behavioral strategies for disruptive behaviors.
  - Parent involvement.
  - Gradual, careful transition from highly supportive to naturalistic environment.
  - Intensive intervention of about 25 hours per week for 2 years.
  - Onset of intervention around 2-4 years.
Review Study

- Systematic review of studies conducted between 2000 to 2010.
- Included studies published in English, with >30 participants, and relevant to ASD.
- 159 unique studies: 13 good quality, 56 fair, 90 poor.
  - Risperidone & aripiprazole improves challenging behaviors, but have side effects. Do not address social-communication impairments.
  - Early Intensive Behavioral Intervention (Lovaas model or Early Start Denver Model) improves cognition, language skills, & adaptive behavior.
  - Cognitive Behavior Therapy shows promise for social communication & challenging behaviors (e.g., anxiety).
  - Parent training augments treatment outcomes.
  - TEACCH model shows improvements in cognition.
  - Little empirical support for any other treatments (including any CAM treatments).

Warren et al, 2011

Current Status of Intervention Research in ASD

- Most intervention research has been conducted with children over the age of 3 years.
- Few randomized, controlled trials have been conducted.
- Even fewer interventions have been studied in community settings.
- There is support for both behavioral and developmental approaches.
- Most interventions are associated with improvements for SOME children. No interventions show improvement for ALL children.

Understanding individual differences in treatment response

- Key Research Questions:
  - Which interventions are more effective for which children (and which skills)?
  - What are the characteristics of treatment responders (e.g. joint attention, imitation, object play)?
  - How can we match children to the most appropriate interventions for them?
CAM Use for SSC participants

- 74% of SSC participants report using a CAM approach to address behavior.
- CAM use is related to child characteristics.
- Families twice as likely to use CAM if child also had intellectual disability.

What to expect in the near future

- Parent focused intervention
- Examination/evaluation of CAM
- Use of technology in intervention
- Interventions tied to specific gene functions and disrupted proteins

Considering Intervention Options
Thinking about interventions

**Effectiveness:**
- Limited or inconclusive evidence
- Evidence in support

**Safety:**
- Evidence in support
- Limited or inconclusive evidence

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerate; use caution; closely monitor for effectiveness</td>
<td>Evidence in support</td>
</tr>
<tr>
<td>Avoid and Discourage</td>
<td>Limited or inconclusive evidence</td>
</tr>
</tbody>
</table>

Cohen & Eisenberg, 2002

Questions to Ask regarding a Specific Treatment

- Will the treatment result in harm?
- Is the treatment developmentally appropriate?
- How will failure of the treatment affect the family?
- Has the treatment been validated scientifically?
- How will the treatment be integrated into the child’s current program?

Freeman, Journal of Autism & Dev. Disorders, 27(6), 1997

Guidelines for Evaluating Treatments

- Approach any treatment with hopeful skepticism
- BEWARE any treatment which states: "appropriate for every person with autism"
- BEWARE any treatment which thwarts individualization
- Be AWARE that any one treatment represents one of several options

Freeman, Journal of Autism & Dev. Disorders, 27(6), 1997
Guidelines for Evaluating Treatments

- Be AWARE any treatment should depend on independent assessment of the child which points the intervention as appropriate for the child
- Be AWARE that no treatment should be started until the proponents identify what assessments are needed to determine that it is the appropriate intervention for that child
- Be AWARE that debates over treatment can sometimes develop into superficial arguments
- Be AWARE that often new treatments have not been validated scientifically

Freeman, Journal of Autism & Dev. Disorders, 27(6), 1997

State of the Science on Intervention Approaches

Questions?