First Principles

- Biologically driven behaviors / traits
  - Occur irrespective of environmental contingencies
  - Do not serve a function
  - Specific behaviors / traits are tied to specific neurotransmitters / brain systems

- Socially driven behaviors
  - Occur in response to environmental contingencies
  - Serve a function
    - Attention
    - Access to desired objects or activities
    - Escape from undesired activities
    - [Anxiety reduction]

- Intervention: Often requires biological (i.e. pharmacologic) as well as environmentally-based measures

Outline

Neuropsychological Deficits in persons with ASD
- Cognitive Rigidity
- Dysregulation of attention
- Dysregulation of arousal
- Dysregulation of mood
- Psychopharmacology for the non-physician
- Behaviorism: Its utility and its limits

Mental Illness in persons with ASD: The Elephant in the Room
- Co-Morbidity, Continuum, or Metamorphosis?
  - Case Histories
  - Epidemiology
  - Laboratory Data
  - Where do we go from here?

Summary
Abnormal regulation of arousal
Abnormal regulation of attention
Abnormal regulation of sleep
Abnormal Sensory Processing

Cognitive Rigidity

Rainman, 1988

Cognitive Rigidity: Changes in Routine / Unmet Expectations

Cognitive Rigidity [difficulty shifting mental sets] ➔ Anxiety ➔ Disruptive Behavior

“Our son experiences extreme anxiety when what he anticipates isn’t what happens...When we know a change is coming we can prepare him, but those we can’t anticipate are still very upsetting for him...The switch flips in his mind, and it’s out of his control.”

6 y.o. boy with ASD, anxiety, and normal nonverbal IQ

Cognitive Rigidity (Difficulty shifting mental sets)

- "Externalizing Behaviors"
  - Insistently repetitious behavior
  - Difficulty with unmet expectations
  - Perfectionism
  - Compulsions
  - (Aggression, SIB)

- "Internalizing Behaviors"
  - Perfectionism
  - Obsessions
  - (Anxiety / Depression)
IDEA, Section 614(d)(2)(B)

(B) Consideration of special factors.--The IEP Team shall--

(i) in the case of a child whose behavior impedes the child's learning or that of others, consider the use of positive behavioral interventions and supports, and other strategies, to address that behavior.

Comment: A few commenters recommended that Sec. 300.324(a)(2)(i) refer specifically to children with internalizing and externalizing behaviors.

Discussion: We do not believe it is necessary to make the recommended change because Sec. 300.324(a)(2)(i) is written broadly enough to include children with internalizing and externalizing behaviors.

Changes: None.

IDEA

As a practical matter, however:
– “Behavior” is tacitly interpreted to mean “Externalizing” behavior
– “Impedes Learning” is equated with academic failure
– Assessment is in the hands of BCBAs (who disregard internalizing behavior)
Perfectionism

Compulsions

Joseph F: 15 y.o. boy Asperger Syndrome

Anxiety

RM: 9 y.o. boy: ASD, normal IQ, anxiety d/o, disruptive behavior. Mother: Anxiety D/O; PGM hoarding & OCD

Anxiety

RD. 7 y.o. F, nl IQ, PDD-NOS & Anxiety. Father: GAD

Anxiety

RD. 7 y.o. F, nl IQ, PDD-NOS & Anxiety. Father: GAD

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Anxiety

RD. 7 y.o. F, nl IQ, PDD-NOS & Anxiety. Father: GAD

"The house is on fire and we are running for our life."

A.W.: 9 year old boy with PDD-NOS and normal IQ

Depression

"Standing in the Atlantic Ocean. The ocean has a very high surface, up to their mouth, so they can't breathe." Six year old boy with ASD and Anxiety.

KO: 10 yr old female, PDD-NOS, normal IQ

Depression

"Draw a picture of your family, with everybody in the picture doing something."

IB: 12 yr old male, Mild ASD, Superior IQ
Depression

“Draw a picture of your family, with everybody in the picture doing something.”

IB: 12 yr old male, Mild ASD, Superior IQ

IB: 12 yr old male, Mild ASD, normal IQ

Depression ( & Perseveration)

Standard Score: 123

IB: 12 yr old male, Mild ASD, normal IQ

Anxiety, Perfectionism, and Self-Injurious Behavior

Standard Score: 138

A.D. : 9 y.o. girl with ASD (my MRN: 06-0227)

Throughout the session, “Alice” delivered a steady stream of self-deprecating comments, calling herself “stupid,” or perseveratively asking if she was “fat.” During the Bender, she anxiously and angrily twisted the eraser off the tip of the pencil, while declaring “Why do I keep making stupid mistakes?” As her stress level rose, she escalated to slapping herself, and then punching herself in the face.

Unaddressed internalizing behavior often comes out as externalizing behavior

How do you kill a blue elephant?

Shoot it with a blue elephant gun.
How do you kill a pink elephant?

Hold it by the trunk until it turns blue, then shoot it with a blue elephant gun.

Positive Behavior Support Plan for Internalizing Behavior

- Staff Awareness
- Visual Schedules
  - What am I supposed to be doing now?
  - What am I supposed to do next?
- Relaxation Techniques
  - Mental Imagery
  - Isometrics
  - Deep Breathing
  - “Break” cards
- Cognitive Behavioral Therapy (CBT)
- SSRIs

Disrespectful
Non-compliant
Unmotivated
Stubborn
Aggressive
Disruptive
Impulsive
Inattentive
Could do better if only he tried harder

J.B. Watson
Psychology as the behaviorist sees it. (1913)

- “The behavior of animals can be investigated without appeal to consciousness.”
- Limits psychology to the study of outwardly visible (i.e. externalizing) behavior.
Behaviorism’s Blind Spot

- Behavior Analysis fails to address internalizing behavior (ex: Sometimes the function of task-avoidant behavior is anxiety reduction, not escape from task per se).

Not seeing the vase (ignoring internalizing behavior)

“We caution against the use of the word “stubborn” to characterize Ryan’s classroom behavior. Ryan’s task avoidance and non-adherence to teacher instruction reflect cognitive rigidity and anxiety, rather than “stubborn” behavior. Re-framing his actions will lead to more appropriate intervention, placing the focus on anxiety management and cognitive flexibility, rather than “compliance.”

www.drcoplan.com

Not seeing the vase (recognizing internalizing behavior)

<table>
<thead>
<tr>
<th>Antecedents</th>
<th>Behaviors</th>
<th>Consequences</th>
<th>Perceived Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiousness</td>
<td>Tantrums</td>
<td>Temporary reduction in anxiety via task avoidance</td>
<td>Avoidance of self-blame for not completing the task perfectly</td>
</tr>
<tr>
<td>Perfectionism</td>
<td>Eloping</td>
<td>Task Refusal</td>
<td></td>
</tr>
<tr>
<td>Fear of Failure</td>
<td>Task Refusal</td>
<td></td>
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</tr>
</tbody>
</table>

Seeing the vase (recognizing internalizing behavior)

<table>
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</tr>
<tr>
<td>Fear of Failure</td>
<td>Task Refusal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Story of Billy’s Box - 1
(or, why it’s important to ID internalizing behavior)

- 8 y.o. boy with ASD and normal Nonverbal IQ
- Severe tantrums at school
- Antecedents: – TRANSITIONS
- Function? – Not attention, escape, access – “Biological” (i.e. “just part of his ASD”)?

The Story of Billy’s Box - 2
(or, why it’s important to ID internalizing behavior)

Q: “Billy – You’re always getting in trouble at school. What’s going on?”

A: “I'm afraid that if I hand in my work, I'll never get a chance to go back and make it perfect.”
The Story of Billy’s Box - 3
(or, why it’s important to ID internalizing behavior)

“Put your papers in the box, and we promise you will be able to go back later and work on them some more, if you want to.”

Visual Schedules

Positive Behavior Support Plan for Internalizing Behavior

- Staff Awareness
- Visual Schedules
  - What am I supposed to be doing now?
  - What am I supposed to do next?
- Relaxation Techniques
  - Mental Imagery
  - Isometrics
  - Deep Breathing
  - “Break” cards
- Cognitive Behavioral Therapy (CBT)
- SSRIs

www.drcoplan.com
Positive Behavior Support Plan for Internalizing Behavior

- Staff Awareness
- Visual Schedules
  - What am I supposed to be doing now?
  - What am I supposed to do next?
- Relaxation Techniques
  - Mental Imagery
  - Isometrics
  - Deep Breathing
  - “Break” cards
- Cognitive Behavioral Therapy (CBT)
- SSRIs

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Primary targets
  - Cognitive Rigidity
    - Anxiety
    - Obsessions (thoughts)
    - Compulsions (behavior)
    - Perfectionism
  - Depression
  - Stereotypies: Probably not
- “Downstream” benefit:
  - Disruptive Behavior
  - Quality of Life

Nestler, Molecular Neuropharmacology, Fig 9.3
Serotonin (5 HT) Pathways

SSRIs in ASDs
- Side Effects
  - Activation
    - Hyperactivity
    - Irritability
    - Insomnia
    - Agitation
  - Uncommon or irrelevant
    - GI dysfunction
    - Sexual dysfunction
    - "Black Box" warning (suicidal mentation)

Selective Serotonin Reuptake Inhibitors (SSRIs)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>Prozac</td>
<td>The first selective SRI</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Luvox</td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td>Zoloft</td>
<td>May be less activating</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Celexa</td>
<td>Prolonged QT interval</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Lexapro</td>
<td>Prolonged QT interval</td>
</tr>
<tr>
<td>And others...</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pharmacotherapy for anxiety disorders in children and adolescents
- Studies reviewed: 22 RCTs/ 2,519 participants
  - Short-term (average 11 wks)
  - Mean age 12 yrs
  - Drugs studied (versus placebo)
    - SSRIs: 15 (fluoxetine 6, fluvoxamine 2, paroxetine 3, sertraline 4)
    - SNRIs: 5 (clomipramine 3), venlafaxine 2)
    - Benzodiazepines: 2 (alprazolam 1, clonazepam 1)
    - Tricyclic antidepressants: 1 (desipramine)
- Meta-analysis
  - Response rate: Medication 59%; Placebo 31%
  - 7.3% of subjects treated with SSRIs withdrew bec/o side effects
  - "The overwhelming majority of evidence of efficacy was for the SSRIs, with the most evidence in paediatric OCD"
Anxiety

A.W.: 9 year old boy with PDD-NOS and normal IQ (MRN 11-07710)

"The house is on fire and we are running for our life."

Fluoxetine 10 mg/d

A.W.: 9 year old boy with PDD-NOS and normal IQ (MRN 11-07710)

Anxiety, Perfectionism, and Self-Injurious Behavior

Sent: Thursday, May 31, 2012
To: James Coplan
Subject: amazing shift in A.D.

Dr. Coplan,

I "know" that it takes several weeks for SSRIs to "kick in" but the child I saw in my office today is simply a different child and the improvements are being noted across settings by multiple adults. There was NO self abuse, NO negative self statements, an availability for interventions, just a complete transformation. We "fixed" mistakes, "re-did" errors, told jokes, and played together. The "core" Autistic symptoms are obviously still there - perseveration on bras, drawing, etc - but mood-wise there is no question that A. is already benefitting from the Sertraline... Impossible perhaps but really visibly clear...

Thank you very much.

S.S. Ph.D.

After one week on Sertraline

Abnormal regulation of arousal

Abnormal regulation of attention

- (Perseveration)
  - (Inattention)

Cognitive Rigidity

Rigidity

Abnormal sensory processing

Agitation

Agitation

Abnormal regulation of sleep

Abnormal regulation of food

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Rigid
Regulation of Attention

Let go &
Shift

Attend to
stimulus #1

Attend to
stimulus #2

Abnormal Regulation of Attention - 1

- Perseveration
  - Inability to “Let go and shift”
  - Gets “stuck”
  - “Overattention Deficit Disorder”
- Compounds the effects of cognitive rigidity

Abnormal Regulation of Attention - 2

Perseveration

Interventions
- Verbal preparation for transitions
- Visual Schedules
- SSRIs (OCD: Proven; ASD: likely)
Abnormal Regulation of Attention - 2

- Inattention
  - Inability to focus
  - Impulsive
  - Distractible

Inattention

- Interventions
  - Limited stimuli
  - Short work periods
  - Medication
    - Stimulants (may ↑ anxiety / rigidity / agitation)
    - alpha-2 agonists

Noradrenergic pathways (Norepinephrine)

Locus Ceruleus ('blue spot'): Principal noradrenergic source in brain.
Neuler, Molecular Neuropharmacology, Fig 8.5

Insufficient activation of frontal cortex →→→ Inattention
Stahl, Essential Psychopharmacology, fig 12.1
**Noradrenergic pathways (Norepinephrine)**

Noradrenergic pathways are involved in several cognitive functions, including attention and vigilance. Norepinephrine plays a role in the modulation of cognitive processes, such as working memory and the speed of information processing. Alpha-2 adrenergic receptors may be important in transmitting presynaptic signals regulating attention and vigilance.

Stahl, Essential Psychopharmacology, fig 5.25

**Stimulants (Dopaminergic; Noradrenergic; Sympathomimetic)**

Stimulants are medications that increase the levels of dopamine and norepinephrine in the brain, affecting attention and cognitive function. They are used to treat attention deficit hyperactivity disorder (ADHD) and other conditions associated with hyperactivity and impulsivity.

Stahl, Essential Psychopharmacology, fig 5.25

**Stimulants, NRI’s**

<table>
<thead>
<tr>
<th>Generic Name(s)</th>
<th>Brand Name(s)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td></td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td></td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Dextroamphetamine + amphetamine</td>
<td>Adderall</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>Concerta, Ritalin, Metadate</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Dexmethylphenidate</td>
<td>Focalin</td>
<td>FDA Schedule II</td>
</tr>
<tr>
<td>Atomoxetine, Attention Strattera</td>
<td>Norepinephrine reuptake inhibitor (NRI), not FDA Schedule II</td>
<td></td>
</tr>
</tbody>
</table>

**Alpha-2 Agonists**

Alpha-2 agonists, such as clonidine and guanfacine, are used to treat ADHD and other conditions associated with hyperactivity and impulsivity. They work by blocking presynaptic alpha-2 receptors in the brain.

Stahl, Essential Psychopharmacology, fig 12.6

**Alpha-2 Agonists**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name(s)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonidine</td>
<td>Catapres</td>
<td>More sedating than guanfacine</td>
</tr>
<tr>
<td>Guanfacine</td>
<td>Tenex, Intuniv</td>
<td></td>
</tr>
</tbody>
</table>

- Frontal cortex / Locus Ceruleus: post-synaptic alpha-2 receptors
- Sympathetic outflow (autonomic nervous system): Pre-synaptic autoreceptors

Stahl, Essential Psychopharmacology, fig 12.6
**Alpha-2 Agonists**

**Benefits**
- ↓ Agitation
- ↓ Hyperactivity
- ↑ Attention Span
- No exacerbation of anxiety / rigidity

**Side Effects**
- Sleepiness: Common
- Emotional Lability (crying) - occasional
- Hypotension (low BP) - rare

---

**Clinical Pearl**

- **Beware of Cognitive Rigidity masquerading as ADHD**
  - Perseveration on inner stimuli: “Inattentive”
  - Perfectionism:
    - “Problems w. task completion”
    - (Or: Task avoidance!)
  - Anxiety:
    - “Rushes through work”
    - “Out of seat behavior”

---

**Regulation of Arousal**

<table>
<thead>
<tr>
<th>Hypoarousal</th>
<th>Calm &amp; Relaxed</th>
<th>Fight or Flight Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lethargic</td>
<td></td>
<td>“Red Alert” Adrenaline Heart Rate Resp. Rate Combative</td>
</tr>
</tbody>
</table>

“He is so hard to calm down when he gets upset….His emotional thermostat doesn’t work”

Parent of an 8 year old with ASD
Abnormal regulation of arousal

Abnormal regulation of attention

- Perseveration
- Inattention

Cognitive Rigidity

Abnormal regulation of sleep

- Hypo-arousal
- Hyper-arousal

Routines
- Stereotypies
- Agitation
- Aggression
- Self-injurious behavior (SIB)
- Impulsivity
- Hyperactivity

Atypical neuroleptics
- D2 antagonists
- GABA-ergic drugs

Impulsive + Agitated / Disruptive

Rigid + Perseverative

Abnormal sensory processing

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Dopamine

(Dopaminergic; Noradrenergic; Sympathomimetic)

www.drcoplan.com

Atypical Neuroleptics

(Generic Name)  |  (Brand Name)  |  Comment
---|---|---
Aripiprazole  |  Abilify  |  - Relatively less risk of weight gain
  |  |  - FDA approved for Rx of ASD
Clozapine  |  Clozaril  |  - Bone marrow suppression
Olanzapine  |  Zyprexa  |  - Greater risk of weight gain
Quetiapine  |  Seroquel  |  - Greater sedation
Risperidone  |  Risperdal  |  - Greater risk of weight gain
  |  |  - FDA approved for Rx of ASD
Ziprasidone  |  Geodon  |  - Relatively less risk of weight gain

Anger (mood)

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Side Effects
- Sleepiness (initially)
- Weight Gain (common)
- Diabetes (uncommon)
- Movement Disorder (rare)
Regulation of Sleep - 1

- Melatonin
  - Brain hormone
  - ↓ Metabolic rate (Heart, Temp)
  - “You’re sleepy now”
- Suppressed by light
  - 24 hr cycle
  - Seasonal cycle

Regulation of Sleep - 2

- Abnormal melatonin cycling
  - Primary disorders of sleep
  - Blindness
  - ASD
- Symptoms
  - Delayed onset of sleep
  - Shortened duration / frequent wakening

Regulation of Sleep - 3

- Shared genetic control
  - Regulation of sleep
  - Regulation of arousal
- Family history of sleep disorder
Sensory Processing

- Subjective Properties
  - Familiar / Unfamiliar
  - Pleasant / Unpleasant
  - Strong / Weak
  - Internal / External
- Sensory Input ➔ Self-awareness
- Mirror Neurons ➔ Empathy


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Mirror Neurons: The Missing Link?

“The observation of actions done by another individual activates, besides visual areas, also areas that have motor properties.”

Rizzolatti & Fabbri-Destro; Exp Brain Res 2010

The whole is greater than the sum of its parts

Max Wertheimer

Abnormal regulation of arousal

Abnormal regulation of attention

- (Perseveration)
- (Inattention)

Cognitive Rigidity

Abnormal regulation of sleep

Abnormal Sensory Threshold

Sensory Overload

Abnormal regulation of arousal

Impulsivity

Impulsive + Agitated / Disruptive

Stimulants

Atypical neuroleptics

-2 agonists

SSRIs

Disordered Sleep

Melatonin

Sensory Dysfunction

Rigid + Perseverative

Sensory Seeking

Agitation

Hyperactivity

Impulsivity

Hyperactivity

Disruptive

Routines

Stereotypies

Sensory Seeking

Agitation

Impulsivity

Hyperactivity

Disruptive

Summary

• Why this child?
  – What is this child’s developmental level?
  • Is this stage-appropriate behavior?
  – Does the behavior serve a social function?
  • Escape, access, attention
  – Is the classroom placement appropriate?
  • Language level?
  – Does this behavior occur in other settings?
  • Family factors?
    – Parents consistent at home?
    – Parental psychopathology? (Anxiety, Depression, Alcohol)
  – Neuropsychological factors?
    • Cognitive Rigidity
    • Dysregulation of attention
    • Dysregulation of arousal
    • Sensory Seeking / Sensory Overload

• Behavioral Intervention – Usually
  – FBA’s usually disregard internalizing behavior

• Change in classroom setting – sometimes
  – Shift from rote to inferential learning (2nd - 3rd grade): challenge

• Medication: Often
• Family mental health intervention: Often

An ounce of prevention….

• Identify internalizing behaviors before they lead to externalizing behaviors
  – Positive Behavior Support Plan that proactively addresses internalizing behaviors (anxiety, perfectionism, obsessive mentation, depression, e.g.)

More on IDEA and FBAs here:
http://www.wrightslaw.com/info/discipl.index.htm
http://www.pent.ca.gov/lgl/addressingbehaviorIDEA.pdf

Outline

Neuropsychological Deficits in persons with ASD
• Cognitive Rigidity
• Dysregulation of attention
• Dysregulation of arousal
• Dysregulation of mood
• Psychopharmacology for the non-physician
• Behaviorism: Its utility and its limits

Mental Illness in persons with ASD: The Elephant in the Room
• Losing the Diagnosis does not equal “cured”
• Co-Morbidity, Continuum, or Metamorphosis?
• Case Histories
• Epidemiology
• Laboratory Data
• Where do we go from here?

Summary

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BREAK
Atypical features improve over time…

But society is raising the bar.

Transition to Middle School

“Friendship is getting more complex and he is falling further behind his peers... We think he may be lonely.”

Parent of a 10 y.o. boy with ASD and normal IQ

Transition to Middle School

Now that he’s 10, he’s less cute. It was cute when he was 5; not when he’s 10.

Transition to Adulthood

Our son turned 13 last year. We are noticing that...the world interacts very differently to an autistic child vs. an autistic man.

Transition to Adulthood

Sometimes he is so average. Sometimes he is so autistic.

Mother of a 16 y.o. boy with ASD and uneven cognitive development
Long-Term Outcome

- “Losing the diagnosis” does not mean “cured”
- Persistence of
  - Cognitive patterns
  - Behavioral patterns
  - Emotional patterns
- Symptoms ⇒ Quirks ⇒ Traits
- Non-ASD neuropsychiatric disorders

“Losing the Diagnosis” does not equal “Cured”

Cognitive Rigidity
- Difficulty changing mental sets
- Routines
- Transitions
- Repetitious behaviors
- Perfectionism

Atypicality
- Social:
  - Theory of Mind
- Language:
  - Pragmatics
  - Prosody
- Cognitive
  - Central Coherence
- Sensory/Motor:
  - Aversions / Attractions
  - Clumsiness

Anxiety
- Generalized Anx. D/O
- OCD
- Depression
- Bipolar D/O

Presentation in Childhood

Extended Family

ASD (Autism, PDD-NOS, AS)

NLD, SPLD

Broad Autism Phenotype

- Social Impairment
- Communication Impairment
- Restricted, repetitive behaviors & interests

- Anxiety Disorders
- Obsessive-Compulsive Disorder
- Depression, Bipolar Disorder
- Alcoholism

Non-ASD Psych D/O

Outcome for children with High Functioning ASD

Adult Outcomes

NLD, SPLD

Non-ASD Psych D/O

- Social Impairment
- Communication Impairment
- Restricted, repetitive behaviors & interests

- Anxiety Disorders
- Obsessive-Compulsive Disorder
- Depression, Bipolar Disorder
- Alcoholism

NLD: Non-Verbal LD, SPLD: Semantic-Pragmatic Lang. Disorder

ASD and Mental Illness: The Myth

ASD

Mental Illness

ASD and Mental Illness: Reality

- Comorbidity
- Continuum
- Metamorphosis
ASD and Mental Illness: Reality

- Comorbidity,
- Continuum, or
- Metamorphosis?

Comorbidity:
“ASD and Mental Illness are different entities that sometimes co-exist”

Continuum:
“ASD shades into Mental Illness, with no ‘bright line’ of separation.”

Metamorphosis:
“Over time, ASD is evolves into Mental Illness.”
An example…

- **DB** (MRN 08-0543)
  - 1st visit: Age 6 ½
    - Occasional ophthalmologic eye contact
    - Pedantic, overly precise, adult-like speech
    - Mild verbal perseveration
    - Preference for routines
    - Sensory issues
    - “Likely” Dx of AS on the ASDS (mom as reporter)

- **FH**
  - Mother: Anxiety D/O, OCD traits
    - 12 page typewritten single spaced note attached to PQ

“Draw anything you want”
(DB, age 10)

“Draw anything you want”
(DB, age 12)

Neuropsychological Deficits in Children with ASD

- Abnormal regulation of arousal
- Abnormal regulation of attention
- Abnormal Sensory Processing
- Abnormal regulation of sleep
- Cognitive Rigidity
Children with ASDs, age 10+:
Neuropsychiatric co-morbidity

<table>
<thead>
<tr>
<th></th>
<th>Autism</th>
<th>PDG+HOS</th>
<th>Aspergers</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>AD/ADD</td>
<td>66%</td>
<td>61%</td>
<td>33%</td>
<td>33%</td>
</tr>
<tr>
<td>ADHD</td>
<td>46%</td>
<td>21%</td>
<td>19%</td>
<td>20%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>23%</td>
<td>29%</td>
<td>22%</td>
<td>23%</td>
</tr>
<tr>
<td>Depression</td>
<td>22%</td>
<td>24%</td>
<td>17%</td>
<td>17%</td>
</tr>
<tr>
<td>Bipolar D/O</td>
<td>9%</td>
<td>4%</td>
<td>6%</td>
<td>5%</td>
</tr>
</tbody>
</table>

IAN Research Report #1 - May 2007
http://www.iancommunity.org/ian_research_reports/adults_on_the_autism_spectrum_september_2009

Adults with ASD – Online Survey

It’s a family affair…

Adult outcomes for children who “lose the diagnosis”
(Coplan, J. Making Sense of Autistic Spectrum Disorders, fig. 5.8)

Causes of ASD

- Prenatal
  - Genetic: Nearly all cases of ASD with a known etiology
  - Teratogenic (rare; rubella, valproate)
  - Associations: Parental Age; Infertility, ?ART

- Perinatal:
  - Associations: (extreme prematurity), but no proven causes

- Postnatal:
  - Some associations, but no proven causes
  - No proof: Diet, immunizations

TS, Anxiety, ASD

Generalized Anxiety D/O Obsessive Traits
ASD with normal NV IQ Tourette Syndrome

www.drcoplan.com
info@drcoplan.com
Anxiety, OCD, ASD

OCD
[Assault rifle]

Anxiety

ASD Anxiety

SK, MRN 12-0824

Anxiety, Depression, ASD, Agitation

Anxiety / Agoraphobia

Depression

Suicidal Mentation

ASD Anxiety

Agitated behavior

ASD Anxiety

Agitated behavior

MRN 12-0810
MRN 13-0876

BPD, OCD, Anxiety, AS

Bipolar Disorder

OCD

Anxiety

Asperger Syndrome

Anxiety

Speech Delay

“Processing Disorder”

C.A.; MRN 12-0811

3

2

TS, Anxiety, Depression, Bipolar D/O, ASD, ADHD

Depression

Bipolar D/O

Generalized Anxiety D/O w. Panic Attacks

ASD

TS

ADHD

AH, MRN 13-0887

Parents & Siblings of Children with ASDs:
Issues of Attention and Mood
(self-report survey)

Epidemiologic Evidence

- ADHD
- Anxiety
- ASD
- Bipolar D/O
- Schizophrenia

Parents & Siblings of Children with ASDs:
Issues of Attention and Mood
(self-report survey)

www.drcoplan.com
info@drcoplan.com

IAN Research Report #1 - May 2007
http://www.iancommunity.org/ian_research_reports
Comorbidity Clusters in Autism Spectrum Disorders: An Electronic Health Record Time-Series Analysis  
Doshi-Velez et al, Pediatrics, Volume 133, Number 1, January 2014

- Electronic health record review  
- 4,934 children (78% boys), at least 15 years old  
- Empirically observed clusters:  
  - 1: Seizures: N=120  
  - 2: Multisystem (GI, ENT, other): N=197  
  - 3: Psychiatric D/O: N=212  
  - 4: No associated morbidity: N=4316

Prevalence of associated diagnoses in subgroup 3, over the first 15 years of life.

Examine the comorbidity of bipolar disorder and autism spectrum disorders: a large controlled analysis of phenotypic and familial correlates in a referred population of youth with bipolar I disorder with and without autism spectrum disorders.  

- Subjects & Methods:  
  - Secondary analysis of data from a family study of youth with Bipolar I D/O (probands = 157, relatives = 487)  
- Results  
  - 30% (47/155) of Bipolar I probands met criteria for ASD  
  - Onset of Bipolar I occurred earlier in the presence of ASD (4.7±2.9 y vs 6.3±3.7 y; p=.01)

“Is Schizophrenia on the Autism Spectrum?”  
King & Lord, 2011

- “Schizotypal Personality” is distinguished by “unusual preoccupations, unusual perceptual experiences, odd thinking and speech (e.g., overelaborate, or stereotyped), inappropriate or constricted affect, behavior or appearance that is odd, eccentric, or peculiar; lack of close friends or confidants other than first-degree relatives, and social anxiety…”  
- c/w Wing’s “Active but odd” ASD phenotype

“Is Schizophrenia on the Autism Spectrum?”  
King & Lord, 2011

- “What arguably distinguishes schizophrenia spectrum from autism spectrum in two individuals who otherwise share all of these symptoms is the presence of paranoid ideation…”  
- “Given the degree of overlap, one might reasonably ask if paranoid thinking could be a logical downstream consequence of a common underlying difficulty in the perception of social communication”
**ASD & Schizophrenia: Epidemiology**

- **Prevalence**
  - ASD ~ 1/100
  - SCZ ~ 1/100 (lifetime risk)

- **Joint occurrence of ASD and SCZ**
  - Predicted (if independent): 1/10,000
  - Observed (small samples, ascertainment bias):
    1. Outcome studies, children w. ASD: How many develop SCZ?
       - Howlin 2004 (n=49; none developed SCZ; underpowered)
       - Rapoport et al 2009, Unenge & Hallerback 2012
    2. Adults with ASD: 7-35% meet criteria for SCZ
       - Howlin 2000, Stahlberg 2004, Mouridsen 2008a, b
    3. Adults with SCZ: Unknown how many meet criteria for ASD

Refs: King & Lord 2011; deLacy & King 2013

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**Laboratory Evidence**

- ADHD
- Anxiety
- ASD
- Bipolar D/O
- Schizophrenia

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**Developmental brain dysfunction: revival and expansion of old concepts based on new genetic evidence**

Andrea Monique De Luca*, Scott H. Wymann†, Thomas D. Ruddle‡, Niall M. Dowell*, David H. Evans, David H. Liedbetter


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**Table 1: Variable expression in selected microdeletion syndromes**

<table>
<thead>
<tr>
<th>Microdeletion</th>
<th>Frequency in clinical cohort</th>
<th>Intellectual disability or developmental delay</th>
<th>Autism spectrum disorder</th>
<th>Schizophrenia</th>
<th>Epilepsy</th>
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<tr>
<td>17q11.2</td>
<td>1 in 150</td>
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<td>✗</td>
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<td>15q11.2</td>
<td>1 in 241</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td>15q13</td>
<td>1 in 375</td>
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</table>

*Frequency is individual referred for chromosome microarray testing. Common indications for testing include neurodevelopmental disorders and multiple congenital anomalies. 2

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**What’s happening in this picture?**

“Two strangers got into the house and are handing out newspapers.”

---

**“Childhood Onset ASD”**

- Up to 50%
  - Child. Onset SCZ
- Most
  - Adults with ASD
  - 7-35% (+) for CSZ
- Adults with SCZ
Network Topologies and Convergent Aetiologies Arising from Deletions and Duplications Observed in Individuals with Autism
PLOS Genetics, June 6 2013
http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1003523

- 192 genes form an interconnected cluster
- Patients with copy number variations within this cluster possess on average, 3 CNV’s
- Many of these genes are implicated in psychiatric disorders in humans (anxiety, e.g.), and/or behavioral abnormalities in animal models (abnormal nurturing behavior, e.g.)

The Real Elephant in the Room
Child w. ASD + Parent with MH D/O =

Family Mental Health
(“We give our children roots and wings” — Hodding Carter)
Family Mental Health is a key ingredient in outcome for all children, but especially for the child with developmental disability, who is less able to work around obstacles arising from family dysfunction than a child with normal development.

Signs of Family Mental Health
- Cognitive, Emotional, and Tactical Flexibility
  - Shifting alliances (adults vs. kids, “boys vs. girls,” etc.)
  - Shifting roles (role of “hero” or “in the doghouse”)
  - Shifting solutions (one size does not fit all; “equitable” vs. “equal”)
  - Shifting combinations for activities. All legitimate combinations should come up once in a while.
- Sense of humor / playfulness / resilience

Individual Mental Health as a contributor to family mental health
- Parents of children with ASD:
  - High frequency of neuropsychiatric disorders (esp. anxiety, depression)
  - Decreased Theory of Mind skills
  - Limits adult’s ability to respond in a flexible manner to the extraordinary demands from child w. ASD
Danger Signs

- Inflexibility
  - Fixed roles
  - Fixed solutions
- Hypervigilance
  - Lack of trust in care providers
- Social Isolation
  - “Circle the wagons” mentality
  - “Nobody helps us!”

Vignette #1

- “Obedience is very important to me.”
  - Father of 10 y.o. boy with ASD
  - Father has untreated anxiety d/o
  - Works in law enforcement
  - Keeps unsecured firearms in the home
  - Perceives his son with ASD as “a predator,” because “everything is all about him”

Vignette #2

- “Nobody helps us.”
  - Mother of 14 y.o. boy with ASD
  - Family has no social supports
  - Child is on homebound instruction
  - Spends hours / day watching violent video games
  - Threatens to “kill” the examiner during home visit
  - Mother has untreated Anxiety D/O

Anxiety, OCD, ASD

- OCD [Assault rifle]
- Anxiety
- ASD

Adam Lanza: What We Think We Know About the Apparent Newtown Shooter

http://www.examiner.com/article/ryan-lanza-reveals-brother-adam-lanza-was-autistic-have-personality-disorder
http://www.theatlanticwire.com/national/2012/12/adam-lanza-bio/60018/
Does ASD predispose to violent crime?

FOR EVERY COMPLEX PROBLEM THERE IS A SIMPLE SOLUTION... AND IT IS WRONG

H. L. Mencken

Autism Canada's Statement On The Sandy Hook Elementary School Tragedy 12/17/2012

- It has been reported that the shooter at Sandy Hook Elementary School had autism. In the weeks and months to come there will be much more information about his condition, but today it has never been more important to understand that autism / Asperger's is not a mental health condition. Autism is a neurological condition.....

Autism Society of America Statement 12/17/2012

- No evidence exists to link autism and premeditated violence...
- Individuals with autism who act aggressively typically do so because they are reacting to a situation...
- Many of the individuals with Asperger’s syndrome who have committed crimes had co-existing psychiatric disorders...

People want immediate or simple answers when an unimaginable tragedy like this occurs. Autism did not cause this horror...


ARI Statement on the Newtown, CT Tragedy

The staff at the Autism Research Institute is deeply saddened by yesterday’s tragic events at Sandy Hook Elementary School in Newtown, Connecticut...

Some public comments have drawn potentially inaccurate and stigmatizing conclusions about a link between the diagnosis [of autism] and a propensity for violence and lack of empathy...

Autism is not a mental health disorder - it is a neurodevelopmental disorder....
We have a problem here…

- ASD and MH are not mutually exclusive, separable entities
- Shifting responsibility onto “Mental Health Disorders”:
  1. Stigmatizes the MH population, and
  2. Ignores the MH needs of the ASD population

Emerging Perspectives on Adolescents and Young Adults With High-Functioning Autism Spectrum Disorders, Violence, and Criminal Law
Lerner, M et al; J. Am Acad of Psychiatry and the Law Online, 4/2012

- “Link between ASD and violent crime is inconclusive and is supported by only 11 of 147 studies on the subject

Asperger’s syndrome in forensic settings
Murrie DC, Warren JI, and Kristiansson M
Int J Forensic Ment Health 1:59–70, 2002

Case Series of adult males referred for forensic evaluation
Charges:
- Arson (1)
- Sexual assault (4)
- Attempted murder (1)

Asperger’s syndrome in forensic settings
Murrie DC, Warren JI, and Kristiansson M
Int J Forensic Ment Health 1:59–70, 2002

Case History
AB: 31 y.o. male, arrested for arson
Referred for forensic psychiatric evaluation after 11 episodes
No prior criminal history or clinical diagnosis

His parents described a developmental history in which he was generally shy and quiet and considered “peculiar” by teachers. In school, he had some concentration difficulties due to being extremely careful about details. His parents described a series of special interests, to which AB devoted extensive research time….His parents also described a strict adherence to routines. For example, they described meals as “ceremonies” in which every part was to be performed in a certain order. When his parents tried to make changes in his routines, AB became very irritated….

Asperger’s syndrome in forensic settings
Murrie DC, Warren JI, and Kristiansson M
Int J Forensic Ment Health 1:59–70, 2002

Often, he left jobs after conflicts with supervisors or other staff. His boss described AB as so wedded to routines that he was unable to be flexible or cope with unanticipated changes.

Socially, he had some friendships, but these occurred one at a time. He was reportedly bullied, or at least showed an over-sensitivity to behaviors by peers. For example, years later, he reported being unable to forget incidents such as being shot at with a water gun.

AB lived with his parents and had no sexual or romantic relationships. But, he explained that if he could just afford a large apartment, he would immediately be married.
According to his parents, about one year before the crimes AB became increasingly irritable and verbally aggressive. During this time, he tended to isolate himself more often, to purchase numerous pornographic magazines, and to ruminate about episodes during his childhood in which he believed schoolmates mistreated him.

During evaluation, AB described the year prior to his offense as a period in which he became increasingly preoccupied with those who had wronged him and increasingly convinced that he needed to avenge himself. He reportedly considered burglary for revenge, but later began to fantasize about firesetting. When AB saw an arson report on the news, he decided that firesetting was the best way to solve his problems.

AB was referred for forensic evaluation after he was charged with 11 cases of arson. For two months, he broke into summer homes in his neighborhood, dousing them with gasoline and setting them ablaze.

When apprehended by police, he immediately confessed to the crimes and explained that they were a means of revenge against schoolmates who had harassed him during his youth. Investigation revealed that there was actually no relationship between the summer homes and the schoolmates, but AB described small details of the houses that had reminded him of peers who had harassed him. He reported feeling satisfied and calm after the fires.

CD, a 27 year-old male, was referred for evaluation after a sexual offense involving a teenage male. At the time of the evaluation CD carried an Asperger’s diagnosis based on adult functioning and early history. In kindergarten, for example, he was described as “oblivious to everyone around him.” Mental health records from his adulthood also noted his marked social impairments and deficits in nonverbal communication. CD graduated high school with a mediocre academic record, and worked for several years as a fast-food worker with limited customer contact.

Although he was intensely preoccupied with having intercourse, his efforts to find partners tended to be rather passive and naive. CD summarized his courtship strategy as “hanging around” a woman “until sex happened.”

… His first contact with the legal system and our subsequent evaluation occurred after CD had repeated sexual contact with a 15-year-old male over a period of several days. CD met the young man, who reportedly had no place to stay at the time, in their apartment complex laundromat and the two subsequently went to CD’s home. Over the ensuing days, CD bought the young man a variety of presents, gave him money, and had an active sexual relationship with him.

The contact ended when CD was no longer willing to give the youth money. The youth left CD’s home, taking his stereo. When CD went to the police station to report this theft, he was subsequently arrested for sexual assault against a minor.

Common Themes

- Deficient Empathy: Each of the four men charged with a sex offense, as well as the man who attempted murder, seemed genuinely unaware of the harm they caused their victims. Likewise, the arsonist appeared untroubled that he destroyed property belonging to strangers, rather than to those against whom he sought revenge.

- Interpersonal Naiveté: A naïve and often impoverished understanding of human relationships…not only leaves Asperger’s syndrome patients vulnerable to mistreatment by others, but also may lead them to seek interpersonal contact in misguided ways…CD maintained a sexual relationship with a teenage male and demonstrated his ignorance of the inappropriateness of this relationship by going to the police to complain that the youth took his stereo when the relationship ended.
Common Themes
• Immediate Confession: At least four of the six men were quick to confess to the police. This could reflect a variety of traits ranging from deficient shame, poor judgment, lack of experience, or an impaired appreciation of the social and legal consequences of a confession, to simple forthrightness, rule-abiding behavior or honesty. This warrants additional research, as it would be of considerable significance if such confessions were not fully competent or voluntary.

Asperger’s syndrome in forensic settings
Murrie DC, Warren JI, and Kristiansson M
Int J Forensic Ment Health 1:59–70, 2002

Common Themes
• Sexual Frustration: At least five of the six men had sexual problems, and four were quite harmful to others when acting upon their sexual drive, highlighting the quandary faced by men who are interpersonally less equipped to initiate or sustain the types of intimate relationships commonly associated with consensual sexual contact…Clinicians working with Asperger’s syndrome patients should recognize that social impairments combined with a desire for attachment or sexual experience could lead to illegal behavior…The use of pornography was one socially tolerated way by which several of the men in our sample pursued an impersonal sexual outlet….
August 5, 2009

Will neurodiversity diagnose George Sodini with autism?

Last night….a man entered a gym in the vicinity of Pittsburgh Pennsylvania. He walked into a room where a "Latin impact" aerobics class was being held. He turned out the lights and drew a gun out of his gym bag. He started shooting, killing three women and then killing himself….

... Apparently, the man was frustrated by the fact that he was 48 years old and had not had a girlfriend for a long time. In fact he kept a detailed online diary describing his frustrations and his plan to go out and kill some women at some point; apparently revenge for being rejected so much. Looking at the diary we see his occupation was a software designer, a job that Simon Baron-Cohen, Temple Grandin and others have claimed requires autistic traits....

Sodini had written: ‘The biggest problem of all is not having relationships or friends, but not being able to achieve and acquire what I desire in those or many other areas….Everything stays the same regardless of the effort I put in...' 

Sound familiar? Well, this is someone with computer skills and social impairments who was frustrated by celibacy. Perhaps neurodiversity could diagnose him with autism as they have diagnosed Bill Gates...”

“...Of course, most persons who suffer from loneliness regardless of whether or not they are autistic will not go out on a shooting spree, but it is frustrating. This man was clearly deranged. He may or may not have had an autism spectrum disorder, but I feel in order to be fair neurodiversity should take the bad with the good. If they are going to preach about what a gift autism is and say that Bill Gates, Stephen Spielberg, Einstein, Jefferson, etc. prove that autism is such a gift because these individuals have or had it, why not say that Sodini may have been autistic also.”
What you can do

Cognitive Rigidity
• Difficulty changing mental sets
• Routines
• Transitions
• Repetitious behaviors
• Perfectionism

Anxiety
• Generalized Anx. D/O
• OCD

Depression
• Bipolar D/O

Atypicality
• Social:
  - Theory of Mind
• Language:
  - Pragmatics
  - Prosody
• Cognitive
  - Central Coherence
• Sensory/Motor:
  - Aversions / Attractions
  - Clumsiness

“Losing the Diagnosis” does not equal “Cured”

NASP: School-based Mental Health Services

• “Mental health is directly related to children’s learning and development. It encompasses or intersects with interpersonal relationships, social-emotional skills, behavior, learning, academic motivation, certain disabilities, mental illness (e.g., depression or bipolar disorder), crisis prevention and response, school safety and substance abuse. Each of these issues affects not only the success and well-being of the individual student but also the school climate and outcomes for all students
• “School-Based Health Clinics” where students and their families can come to the school for all medical, social-emotional, and/or behavioral health services

http://www.nasponline.org/advocacy/overview_sbmh.pdf

Progression of Interventions

House Rule #1

• The family is a system ➔ The unit of treatment is the family
• Assess mental health of all players
• Assess relationships among the players
• Fostering the family’s ability to move forward is my #1 goal. The child’s parents & siblings will be involved with my patient long after I have left the stage.

House Rule #1a

• Get both parents to come in for the interview & informing session
  – Have a sofa if possible, and watch the body language
  – “What do you think about what your spouse just said?”
House Rule #2

- No medication unless parents agree to behavioral and MH evaluation for their child and/or themselves, if you deem it necessary

Probe Questions

(In ascending order of intimacy)

- Do you and your partner ever go out as a couple? When was the last time?
- Who else do you have as supports?
- What have you told your other children / parents?
- Tell me a little bit about yourself / how you were raised / your own mental health?

Neurodevelopmental Pediatrics of the Main Line, PC

Psychoactive Medication – Informed Consent Form

Medication cannot cure developmental or behavior problems. However, medication can sometimes alleviate biologically-based symptoms, such as inattention, impulsivity, anxiety, depression, cognitive rigidity, agitation, disruptive, or self-injurious behavior. Medication alone is frequently less effective than medication plus behavioral or mental health services.

Therefore, in addition to administering psychoactive medication to your child, Dr. Coplan may recommend behavioral and/or mental health services as part of your child’s treatment plan as follows: .....

Summary

- ASD has a natural history for improvement over time, insofar as visibly atypical features are concerned
- Cognitive & behavioral patterns persist
- Mental Illness is not “a separate problem.” Rather, impaired MH is another expression of shared neurobiology
- Over time, mental health issues present a progressively greater challenge, that may supersede the ASD

Summary

• ASD in a child is a red flag for developmental and/or mental health disorders in parents / siblings
• Optimal outcome for the child with a disability depends upon addressing the parents’ mental health issues, as well as the child’s developmental and mental health needs

Summary

• To be successful, intervention needs to be multimodal and family-centered
  – Mental health intervention
    • Child: Self-awareness, self-esteem, self-regulation
    • Parents: Address their own MH issues
    • Family: Take a family-system approach
      – Flexibility / Resilience within the family structure
      – Siblings are at high risk for genetically based morbidity, and/or collateral damage because of family system dysfunction
  – Educational / Vocational services
  – Psychotropic Medication - often

Summary

• Need for Adult Services
  – Clinics for “Long-Term Survivors of Childhood ASD” patterned after Long-Term Survivors of Childhood Cancer
    • Mental Health
    • Job coaching
    • Social contact
    • Family / Caregiver support (parents, partners)
    • Developmental screening of offspring

Summary

• Need for Better Research
  – Prevalence of ASD in adults?
  – Psychiatric Comorbidity
  – Obstacles
    • Privacy issues
      – “Informative censoring”
    • Cross-Disciplinary collaboration
      – Child / Adult
      – DD / Mental Health
    – Long-term funding

Resources

• Married with Special Needs Children; A couples’ guide to keeping connected. Marshak LE and Prezant, FP. Woodbine, 2007
• Voices from the spectrum. Parents, grandparents, siblings, people with autism, and professionals share their wisdom. Ariel, CN and Naseef, R (eds). Jessica Kingsley, 2006
• The American Association of Marriage and Family Therapy http://www.aamft.org/iMIS15/AAMFT/
• The Bowen Center: http://www.thebowencenter.org/
Thank you