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This speaker will discuss off-label use of medication but has no conflict of interest to disclose.

Pervasive Developmental Disorders or Autistic Spectrum Disorders

1 in 110/150 kids are “in the spectrum”.
4-5 male to female, but 2:1 female to male who are severely retarded.
40% of children in ASD are non-verbal (CDC).
215 times more likely after 1 child with ASD.
35-50% have seizure disorder by age 20 (Child and Adolescent Psychiatry, 2003).
30-60% of children with ASD are on psychotropic medications (Rosenberg, et al, 2010).

Objectives for presentation
- Participants will be able to:
- Repeat 3 different statistics on autism.
- State the 3 areas of deficits for autism based on DSM-IV criteria.
- State two differences in the proposed new criteria for diagnosis of autism.
- State what therapies are based on evidence base practice (EBP).
- List two medications presenter has found helpful in treatment of children within the autistic spectrum (ASD).

Statistics

Cost of ASD
- Having a child with autism typically decreases a family’s income by $6,200 or 14% of annual income (IACC).
- Both medical and non-medical can cost up to $67,000 (New York Times, 8-29-11).
- Children with autism typically have more medical expenses than those without autism.
- 3.2 million dollars spent over lifetime for care of child with autism (CDC).
**DSM-IV CRITERIA**

- Social deficits
  - Little “affect” use in communication
  - Few friends.
  - Doesn’t share life’s experiences.
  - No social/emotional reciprocity.
    - Doesn’t play with, but next to.

- Communication
  - Late to speak/no speech
  - Unable to start or keep a conversation
  - Echolalia
  - Weird use of language
  - Lack of make believe play

**COMMON CHARACTERISTICS**

- Sensory issues
  - Tags, lights, sounds, tastes, textures

- Trouble with transitions
  - Seasonal
  - Classroom
  - Bedtime

- Concrete interpretation of language
  - “School” example
  - Constantly correcting people

**PROPOSED DSM-V**


**ARRA, 2009**

  - 3 million dollars for research
  - UC Davis Center Children’s Environmental Health (CCEH)
    - Better understand risk and severity factors of ASD
    - ID early markers of susceptibility for ASD
    - Develop mouse models
    - Develop diagnostic tools based on research to ID at risk kids
    - Provide information to community on risk factors (National Institute of Environmental Health-Sciences-National Institutes of Health [NIEHS-NIH]).
Also funded by ARRA

- Early Autism Risk Longitudinal Investigation (EARLI)
  - 3 sites with 1200 total pregnant women who already have a child with autism.
  - Looks at genetics and environment
  - Will follow from the time mom knows until the child is 36 mo old
  - Funded by grant from Autism Speaks (NIEHS-NIH)

New Research

- Center for Children’s Environmental Health (CCEH) out of UC Davis
  - Looking at factors that may be associated with autism
    - Environmental toxins
    - Medical history
    - Lifestyle factors both before and after birth
    - Lipids, amino acids, and sugars
    - Gene activity
    - Immune system function (National Institute of Environmental Health-Sciences-National Institute of Health [NIEHS-NIH]).

Possible Causes

- Not vaccines
    - “Favors rejection of a causal relationship between the MMR vaccine and autism” [Link]
  - Bearman interview, 2009 National Institute of Mental Health (NIMH)
    - Focus of work is autism prevalence at Columbia described reason for increase as:
      - Change in dx criteria 25%
      - ASD and other neuro-developmental disorders, 16%
      - The rest is unknown cause of increase in prevalence, perhaps parent age

Research Based Treatments

- Findings from Effective Health Care Program April, 2011
  - Looked at interventions in
    - Behavioral Treatment
    - Educational
    - Medical
    - Allied health (speech, OT, PT)
    - Complimentary and alternative medicine (CAM) (Agency for Healthcare Research and Quality [AHRQ]).

Possible causes

- Mutation in SHANK2 and SHANK3. These genes impact functioning of synapse (Berkel, et al., 2010).
- Known genetic causes 5-15%. 19% of 996 people studied had abnormalities, with each abnormality in only 1% of the people (Pinto, et al., 2010).
- Gene CNTNAP2 on fMRI had changes in connections to frontal lobe and other parts of brain than those who did not have the gene. Not all children with risk gene had ASD, but all showed abnormalities (Scott-Van Zeeland, et al., 2010).
- All information taken from Interagency autism coordinating committee (IACC) Summary 2010.

AHRQ

- Review based on children 2–12 within the autistic spectrum.
- Medline, PsychINFO, and ERIC
- Excluded
  - Non–English articles
  - Not pertinent to questions
  - Published prior to 2000.
  - Not original research
  - “Did not present aggregated results” p. 4
  - Fewer than 10 participants for all areas other than medical where it was 30
**New research**

- Odom, Boyd, Hall, and Hume (2010) reported of 30 models.
  - Many did not have measureable outcomes these did:
    - Denver Model
    - LEAP (Learning Experiences and Alternative Programs for Preschooler and their Parents
    - UCLA Lovaas Institute
    - May Institute
    - PCDI (Princeton Child Development Institute)
  - ESDM group had
    - 17.6 pt increase in IQ vs 7 pt increase.
    - Increase in adaptive skills versus loss of skills.
    - 7/24 changed to PPD versus 1/24 had a change (Dawson, et al., 2010) From the 2010 IACC Summary.

**Behavioral Studies**

- 78 Behavioral studies
  - The intention is early and intense improve core deficits.
  - Defined as early, intense developmental programs
  - May be helpful for core areas, but;
    - Few Random Controlled Trials (RCT)
    - None compare different treatments
    - “Little evidence of practical effectiveness or feasibility exists”. P 5.
    - Few studies have been published.

**Less intensive Behavioral (AHRQ)**

- Parents interventions
  - Focused on training parents
- Short-term gains
  - Communication
  - Language use
- Lack consistency in
  - Interventions
  - Outcomes
  - Generalization of social skills
- Overall show positive results, but insufficient strength of evidence.

**AHRQ**

- Intense programs have low strength of evidence:
  - UCLA/Lovaas
    - Greater improvement than eclectic approach.
    - Strength of evidence is low.
    - Change in children is not universal.
  - Many children continue with significant impairment.
    - Not all display rapid gains.
  - Early Start Denver Model (ESDM)
    - Positive results reported, but
  - Few studies have been published for any intensive program.

**Educational interventions (AHRQR)**

- 15 studies met criteria
  - Treatment and Education of Autistic and Communication related handicapped Children (TEACCH) program
    - Most of these studies were complete prior to 2000.
    - Improved motor, eye-hand coordination and cognitive.
    - But evidence was insufficient
    - Too few studies
    - Measured outcomes not the same
Other educational

- The National Professional Development Center on Autistic Spectrum Disorders (NPDC on ASD).
  - Website that lists 24 evidence based practices (EBP), not models.
  - What is EBP?
  - Has modules of some of the 24 practices.
    - Free modules
  - An article citing this research was found in IACC summary.

Aripiprazole

- Retrospective study
  - 34 children and adolescents.
  - Mean dose 8.1 mg to 13 mg.
  - 1/3 had much or very improved on CGI.
  - 1/3 minimally improved.
  - 1/3 unchanged or worse.
  - 35.3% stopped medication because ineffective or side effects. (Masi, et al., 2009).

Medical (AHRQ)

- 42 studies, 27 were RCT.
- No treatment for social or communication.
- Aripiprazole and risperidone at least 2 RCT each
  - Do show improvement for repetitive and challenging behavior.
  - Improvement in hyperactivity and non-compliance.
  - Considerable side effects
    - Weight gain
    - Sedation
    - Risk of EPS

Risperidone

- 40 subjects 8–56
  - All DD, 36 with ASD.
  - 22 week crossover study.
  - 24 weeks open after.
  - 58% had better than 50% decrease measured behavior.
  - 88% showed a 25% decrease (Hellings, et al., 2006).

Medical evidence

- High evidence for adverse effects.
- Moderate for risperidone to effect challenging behavior.
- High for aripiprazole effect on challenging behavior (AHRQ).

- Other research
  - 15 charts reviewed, 73% significant improvement in anxiety/mood with citalopram (measured on CGI)

Allied Health (AHRQ)

- 17 studies;
  - Sensory integration and music therapy were poor quality.
  - Auditory integration showed no improvement.
  - Language and communication interventions;
    - Picture Exchange Communication System (PECS) and Education and Prelinguistic Milieu Training (RPMT)
  - Short term improvement.
    - But no effect durability.
  - Need further study.
  - No allied health had adequate research to assess strength of evidence
Not enough evidence to assess.

What are the modifiers of outcome for different treatments?
- Only 2 studies looked at modifiers.
  - Study between 2 communication systems (Picture exchange communication system [PECS] and Responsive education and prelinguistic milieu training [RPMT]).
  - Showed some benefit in joint attention in the RPMT but had restrictions on the benefit.
  - Other looked at using intense program (UCLA/Lovaas) having two different providers (parents at home/clinical setting) showed no difference.
  - Areas of potential, but need more studies.
  - Overall studies failed to show correlates between autism and treatment response.

Early results predict outcome.
- No information about early results that would predict long term outcomes.
End of treatment predict outcome.
- Only 1 study predicted longer range outcomes, outcomes 12 months post intervention.
Generalization of treatment outcomes.
- Behavior studies outside of therapeutic setting.
  - But only reported by parents.
  - Medical studies were seen outside of setting.
  - Collaborated by parents and teachers.

What specific component of treatment influence outcome?
- No studies addressed this.
Treatments for children under 2 at risk for ASD
- One RCT study in ESDM with positive results
  - Adaptive behavior
  - Language
  - Cognitive outcomes
  - Close to 30% of children had shifts in dx shifts, but not in severity of ADOS

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Increased risk of depression and anxiety disorders (Tsai, 2007).
Can be DSM-IV anxiety disorders
Can be different
  - Reactive
  - Irritable
  - Not sure if a part of biology and/or because they don't fit
Non-FDA approved for anxiety
  - Citalopram
  - Fluoxetine (is FDA for children 8 and up)
  - Guanfacine short and long acting
ADHD Symptoms

• DSM-IV prohibits diagnosis in kids with ASD.
• 50% have problems with core symptoms.
• Stimulants can help.
• Have decreased effectiveness.
• Increased adverse reactions (Floyd and McIntosh, 2009).
• Still use stimulants first.
• Have recently found guanfacine long acting very helpful.
  • 1 mg at HS increase as needed/tolerated

Strategies

• No power struggles
• Patience
  • Patience
  • Patience
• Know their interests
• Be very careful with humor
• If you don't want to work with these kids, don't they will know it
• Nursing skills at their best!

Sleep Issues

• Significant sleep issues (Tsai, 2007).
• Study of 167, 86% had 1 sleep problem daily (Liu, Hubbard, Fabes, & Adam, 2006).
• Good sleep hygiene.
• Mood disorders?
  • Medications for sleep;
    • Melatonin
    • Guanfacine short and long acting
    • Clonidine

Other therapies

• Applied Behavioral Analysis Therapy (ABA).
• Sensory therapy.
• Speech therapy.
• Food therapy.
• Social skills.

Atypicals

• Aripiprazole and risperidone FDA approved
• Aripiprazole first, typically better tolerated
• Risperidone for “sex and aggression”
• Quetiapine for severe anxiety and/or sleep problems (non-FDA approved)
  • Have used combination of XR and IR
• Be sure to do lab work
  • FBS, Lipid profile minimally, add CBC and LFT if doing anyway
• Monitor
  • Weight, B/P, and height for BMI

Reference

• Berkel, S., et al. (2010). Mutations in the SHANK2 synaptic scaffolding gene in autism spectrum disorder and mental retardation. Nature Genetics, 42(6), 489-491.
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