Autism Spectrum Disorders: Early Intervention & Brain Development

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International Conference on Positive Behavior Support
Hyatt Regency Chicago
March 28, 2008

CORE FEATURES OF AUTISM

- Lack of social awareness or empathy
- Communicative dysfunction
- Repetitive, fixed or compulsive routines

MAJOR AUTISM SUB-TYPES

Complex autism
- Have subtle dysmorphia
- Have lower IQs (P<0.006)
- More seizures (P=0.0008)
- More abnormal EEGs (46% vs. 30%)
- More brain abnormalities by MRI (28% vs. 13%)
- All identifiable syndromes were in the complex group.

Essential autism
- Higher IQs (P=0.02)
- Fewer seizures (P=0.0008)
- Higher sibling recurrence
- More relatives with autism (20% vs. 9%)
- Higher male to female ratio (6.5:1 vs. 3.2:1)
- More regressive onset (43% vs. 23%, P=0.02)


Implications of Sub-Types

- Autism subtypes have major implications for understanding effects of early intervention, to which we will return later…
- People with ASDs tend NOT to look at faces, in particular eyes.
- How does that affect brain development?

Face Processing & Gaze-Fixation in Autism

- Disproportionate attention to the mouth versus eyes, (Klin et al., 2002; Schultz et al., 2002).
- Tendency not to show the face inversion effect, (Hobson, Ouston & Lee, 1998).
- More detailed, less specialized rather than a more specialized configural process, (Joseph & Tanaka, 2003).

Amygdala is involved in gaze fixation & facial emotions

Amygdala lesions impair recognition of emotional facial expressions
Amygdala lesions produce diminished eye-fixation
fMRI: Amygdala is activated by emotional facial expressions esp. eyes
Assigning mental states to eyes-only facial stimuli usually activates amygdala, cingulate and frontal brain regions, but NOT among Individuals with high functioning ASDs.

Abnormal amygdala response to fearful faces in people with Asperger’s syndrome

Experimental stimuli: Faces expressing variable intensities of fear

Normal amygdala activation

Attenuated amygdala activation in autism

Attenuated orbitofrontal activation in autism

Neuroanatomy of Face Perception: The Fusiform Face Area (FFA)

Are these the SAME or DIFFERENT person?

Activating the Fusiform Face Area

Are these the SAME or DIFFERENT object?

The Fusiform Face Area

When comparing faces to objects, individuals with autism show less brain activation in the FFA than those without autism (area inside green rectangle).

Eye and Facial Processing Deficits

- As early as 6 months children who are later diagnosed with an ASD fail to look at eyes
- There is little or no amygdala (green spheres) and prefrontal cortex activation to eyes
Fusiform Gyrus and Mirror Neuron Dysfunction

- Fusiform “Face Area” Under Temporal Lobe Does Not Activate to Faces
- Mirror Neuron System Required for Understanding Gestures is Dysfunctional

Are These Deficits Remediable?

- It Appears It May be Possible to Overcome Some of These Deficits by Promoting Synapse Formation Through Early Intervention i.e. synaptogenesis

Synapse Formation As a Function of Age

Huttenlocher & Courten (1987)

Though Neuroplasticity Peaks Between 10-18 months of Age It Occurs Throughout Our Lives

Thank Goodness!!
But the MAGNITUDE of Gains Appears Smaller & Effort to PRODUCE those Gains Appear to Be Much Greater in Later Life

Lovaas (1987)

Intensive Individual Behavior Therapy for 19 children with ASD from 2-5 years of age; 40 Hrs per week
Comparison Children Had 10 Hours Per Week in Preschool Setting Using Some Behavior Therapy Methods.
After 3 Years 11 of Children with ASD in IEBT Group Were Mainstreamed in School with IQs in the typical range
None of the Children in the Preschool 10 Hr Per week group achieved similar outcomes

Educating Young Children with Autism (Lord & McGee, 2001)

- “In sum, it appears that a majority of children participating in comprehensive behavioral interventions made significant progress in at least some developmental domains, although methodological limitations preclude definitive attributions of that progress to specific intervention procedures” page 172
Assessment & Intervention Planning:
Assessment of Basic Language & Learning Skills (ABLLS)

25 Scales Categorized Into:
- Communication & Social Behavior
- Academic Skills Development
- Self-Help Skills
- Motor Skills

Each Sub-Scale Broken Into From 6-52 Teachable Component Skills

James Partington’s (2007)
The Assessment of Basic Language and Learning Skills-R
Pleasant Hill, CA: Behavior Analysts, Inc.

ABLLS-R is used to track changes over time:
- Blue = Baseline
- Red = Six Months Assessment

Intervention Tactics

- Communication and social skills primary targets; Play and cognitive skill development are secondary targets; Repetitive-stereotyped behavior diminishes as communication and social skills increase.
- Begin with discrete trial except in higher functioning children where Incidental Teaching is used.
- Alternate short intervention periods (5-10 minutes) with play and socialization; Increase duration as child tolerates longer periods.
- Transition to Incidental Teaching as child develops skills.
- Incorporate siblings and peers into instruction/therapy.
- Once behavior is under some control, begin generalizing to other settings (friend’s house, playground, YMCA, shopping mall).
- Tantrums, aggression and self injury are treated based on a functional assessment of circumstances giving rise to, and maintaining problem behavior…seldom a significant problem with 2-4 year olds.

Wisconsin Early Intervention Study (Sallows and Graupner, 2005)

- 23 children diagnosed with Autistic Disorder 2-3 yrs old.
- Children fell into two dichotomous categories either exhibiting rapid learning or slow learning with no overlap between the distribution of changes in full scale IQ over 4 years.
- Pre-Post ADI-R scores revealed that in all three diagnostic domains, the Rapid Learners showed dramatic improvements and the slow learners exhibited little improvements over 4 years of IEBT. Outcomes were dichotomous.

Why Do Some Children Do Very Well Within 12-18 Months and Some (30-40%) Profit Much Less From the Same Intensity and Longer Duration of IEBT?

Sallows and Graupner, 2005
AJMR
Predictors of Response to Treatment Among Rapid Learners

- The best single predictor of improvement was motor or verbal imitation at baseline, with a correlation of .90 with ADI-R Social Scale improvement scores.
- Motor imitation is mediated by the Mirror Neuron brain system. There is evidence of mirror neuron dysfunctionality in ASDs.

Social Predictors of Response to Treatment

- ADI-R Low Social Interest, Unresponsiveness to Other’s Approach, Lack of Shared Attention and baseline IQ yielded a negative multiple correlation with Post-Test IQ of .83.
- These skills require intact amygdala, cingulate and orbitofrontal cortical function.
- These differences appear to be present in the first year of life (Zwaigenbaum et. al) suggesting that typical early parenting has been insufficient to overcome these deficits.

Rapid & Slow Learners

- The Rapid Learners appear to be a heritable subtype similar to Miles et.al. (2005) Essential Autism.
- The Slow Learners are a different subtype (Complex Autism) who may have damage to some of the same brain structures due to a different mechanism. They are not influenced by environmental factors to the same degree.

Residual Characteristics

These and Other Data Indicate Approximately Half of Children with ASD Receiving IEBT End Up Being Successfully Integrated in Elementary School

Residual Effects in “Rapid Learners” With ASD Include
- 36% with Social Anxiety & Inattention Features & 36% With Limited Communication & Social Skills.
- 9% Were Seen as Isolated and Not Well Liked; However, they Functioned Sufficiently Well to be Integrated in General Education Elementary Classrooms.

Examples of Brain Structure & Function & Corresponding ABLLS Curriculum & Items

- Early Intervention methods that specifically enlist activity in brain structures that are dysfunctional are more likely to produce lasting effects. The qualitative features of intervention matter. Not all interventions are equally effective.
- Intensity is very likely critical to outcome, depending on the subtype, as recently cogently argued by Warren, Fey and Yoder (2007)
Orbito-Frontal Cortex Required for Social Judgment & Planning

- ABLLS Scales and Items
  - B5. Sort non-identical items into categories
  - B6. Block designs on picture cards
  - B7. Block designs from pictures
  - B8. Sequence pattern to match visual model
  - B15. Delayed replication of a sequence
  - B16. Delayed finding a sample
  - B18. Replicate simple 3-dimensional object
  - B19. Seriation
  - B20. Picture sequences

Epigenetic Influences

- **Epigenetics** refers to changes in gene function that occur without a change in genetic makeup. These changes may occur spontaneously, in response to environmental factors, or in response to the presence of another gene.

Epigenetic Influences on Autism Subtypes

- Autism Subtypes appear to be differentially affected by experiential factors creating degrees of expression of the narrower or broad autism phenotype.
- Zwaigenbaum, Szatmari and colleagues have shown these features present in first year of life in children later diagnosed with ASDs and among siblings of children with autism.
  - Lack of looking at eyes
  - Lack of gesture or response to gesture
  - Lack of receptive language
  - Lack of joint attention

Early Intervention as Epigenetic Variable

- **Hypothesis:** Early Intervention is an experiential epigenetic influence on the expression of genes required for the development of these brain structures and behavioral, emotional and cognitive features.
- EI is a more specialized and intense form of experiences that promotes synapse formation in the amygdala, orbitofrontal cortex, language cortex, caudate and mirror neuron system in the brain of children who inherited genes predisposing them to having autism.

Early Intervention & Autism Subtypes

- Individuals described as having the Broad Autism Phenotype are sufficiently responsive to typical social influences that they only exhibit residual differences
- Those exhibiting autism features within the clinical range have not responded to typical experiential influences sufficient to ameliorate their symptoms.

Conclusions

- Autism symptoms are correlated with specific brain dysfunctions, yielding subtypes varying in severity of expression
- There appears to be an interaction between severity of the autism subtype and experiential factors influencing its expression
- Early intervention can serve as a tool to ameliorate synaptic deficits in approximately half of children with autistic disorder (Essential Autism)
- Much more work is needed to identify underlying mechanisms responsible for deficits in slow learners (Complex Autism) so those needs can be addressed more effectively.
Book Signing at 1:00pm  Paul H. Brookes Table

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Thank You For Your Attention