

Comorbidity Associated with FASD: A Behavioral Phenotype ?

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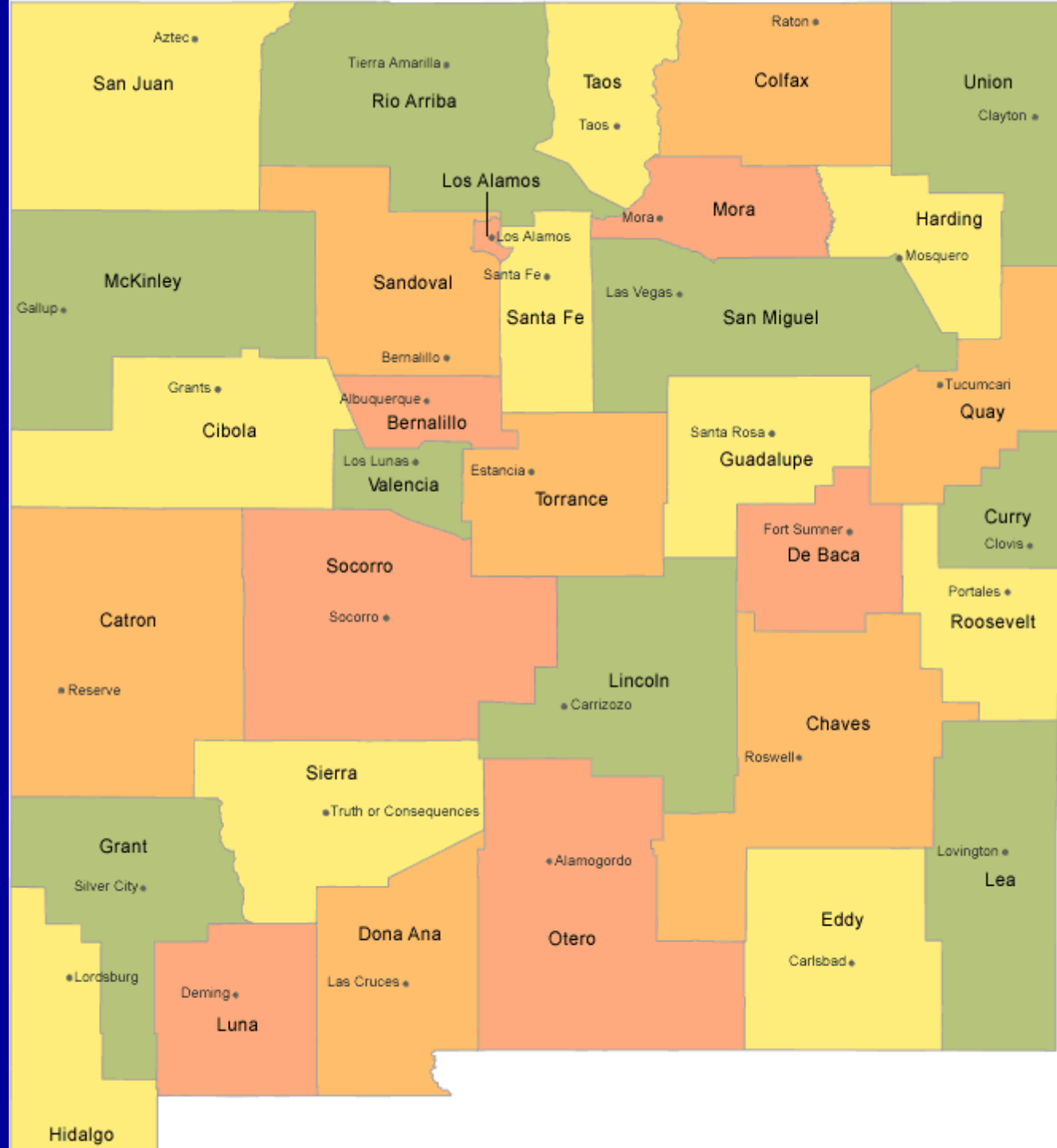
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Significance of the study of comorbid conditions

- Children with prenatal alcohol exposure are often referred for clinical evaluations because of their comorbid conditions (e.g. ADHD, conduct disorder, learning problems)
- If the comorbid conditions associated with FASD are directly linked to alcohol-induced brain damage, the study of those conditions will advance our knowledge of FASD

New Mexico



Diagnoses

- 36 FAS or partial FAS; 39 ARND; 37 Prenatal alcohol exposure
- ADHD (38%), oppositional defiant disorder (5%), conduct disorder (3%), Anxiety (6%), PTSD (16%), Reactive attachment disorder (15%), language disorder (13%), math disorder (1%), reading disorder (2%), intellectual disability (6%), mixed developmental disorder (18%), other (46%)

A Systematic Review and Meta-Analysis (Popova et al., 2016)

- Popova et al. (2016) reviewed 127 articles and found 428 comorbid conditions co-occurring in individuals with FASD
- These investigators found 5 comorbid conditions that had the highest pooled prevalence (between 51% and 91%): disorders involving peripheral nervous system and senses, conduct disorder, receptive language disorder, chronic serous otitis media and expressive language disorders

Neuropsychiatric Disorders

- A number of investigators have reported high rates of neuropsychiatric disorders such as depression and anxiety among children with FASD.
- In a clinically referred sample of children, O'Connor et al. (2002) found 87% met a psychiatric diagnosis.
- The majority of the children (61%) received a mood disorder diagnosis (26% major depression; 35% bipolar disorder); only 13% ADHD.

Neuropsychiatric Disorders

- Fryer et al. (2007) estimated the prevalence of psychiatric problems at 97% in a clinic-referred sample
- 59% of this sample met the criteria for a disruptive behavior disorder: ADHD, conduct disorder, oppositional defiant disorder
- Only 28% met the criteria for mood disorders
- In Europe, investigators such as Steinhausen (1993) have reported a broad range of comorbid conditions in children with FASD

Neuropsychiatric Disorders

- However, fewer comorbid conditions have been observed in community-based studies.
- In a community-based sample in Italy, we found mainly attentional problems, primarily of inattentive type in children with prenatal alcohol exposure (Kodituwakku et al., 2006)
- Researchers have found high prevalence rates of conduct disorder in clinic-referred samples (Roebuck et al., 1999), but Lynch et al. (2003) did not observe high rates of conduct problems in a community sample of alcohol-exposed children

Primary Comorbid Disorders

- Expressive and receptive language disorder
- Conduct disorder and ADHD
- Depression
- Anxiety Disorder
- Otitis Media
- Disorders associated with peripheral nervous system and special senses

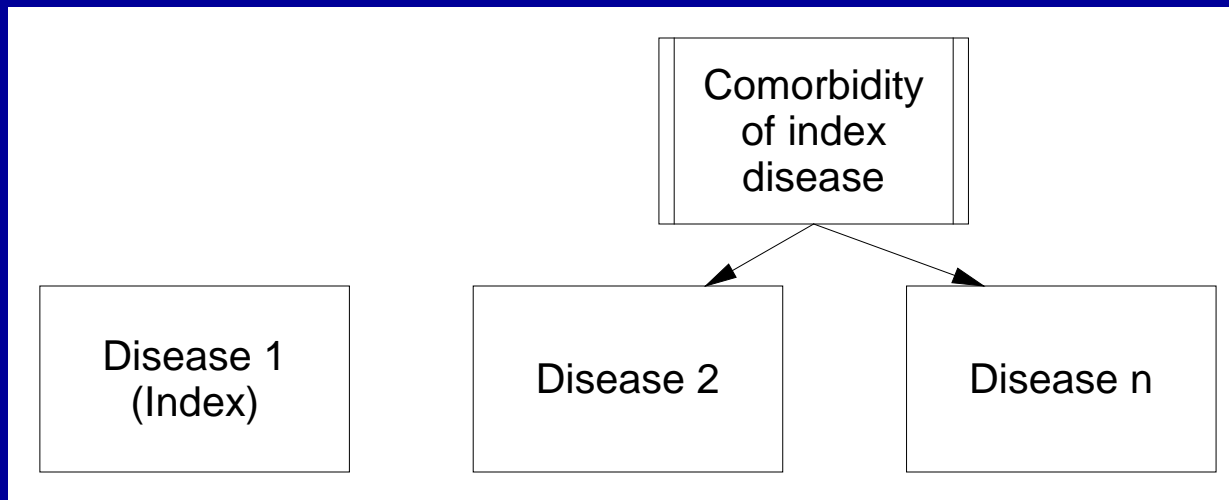
Two Central Questions

- Are these disorders comorbid conditions or multi-morbid conditions?
- If they are comorbid conditions, are they causally linked to prenatal alcohol exposure?

Implication: The comorbid conditions associated with FASD are an integral part of the behavioral phenotype

What is comorbidity?

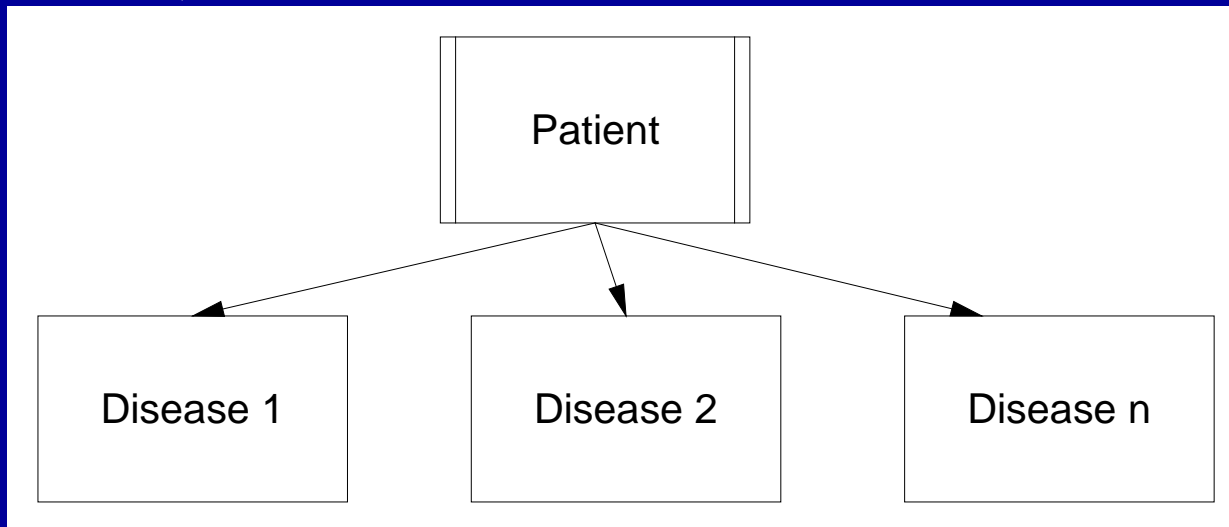
“Any distinct additional entity that has existed or may occur during the clinical course of a patient who has the index disease under study” (Feinstein, 1970)



Adapted from Valderas et al, 2009)

Multimorbidity

“the co-occurrence of multiple chronic or acute diseases and medical conditions within one person” without any reference to an index condition (Bayliss et al. 2008)



Adapted from Valderas et al, 2009)

Behavioral Phenotype

*“A characteristic pattern of motor, cognitive, linguistic and social abnormalities consistently associated with a biological disorder”
(O’Brien and Yule, 1995)*

Behavioral Phenotype

- The term behavioral phenotype is used to describe the unique patterns of behaviors associated with neurogenetic disorders such as Williams syndrome and Angelman's syndrome.
- Can the comorbid conditions associated with FASD be considered linked to one dominant cause?

Single dominant cause

Streissguth et al., (1996, 2004)

Alcohol
exposure



Primary
disabilities
(IQ)



Secondary disabilities
(e.g. substance use)

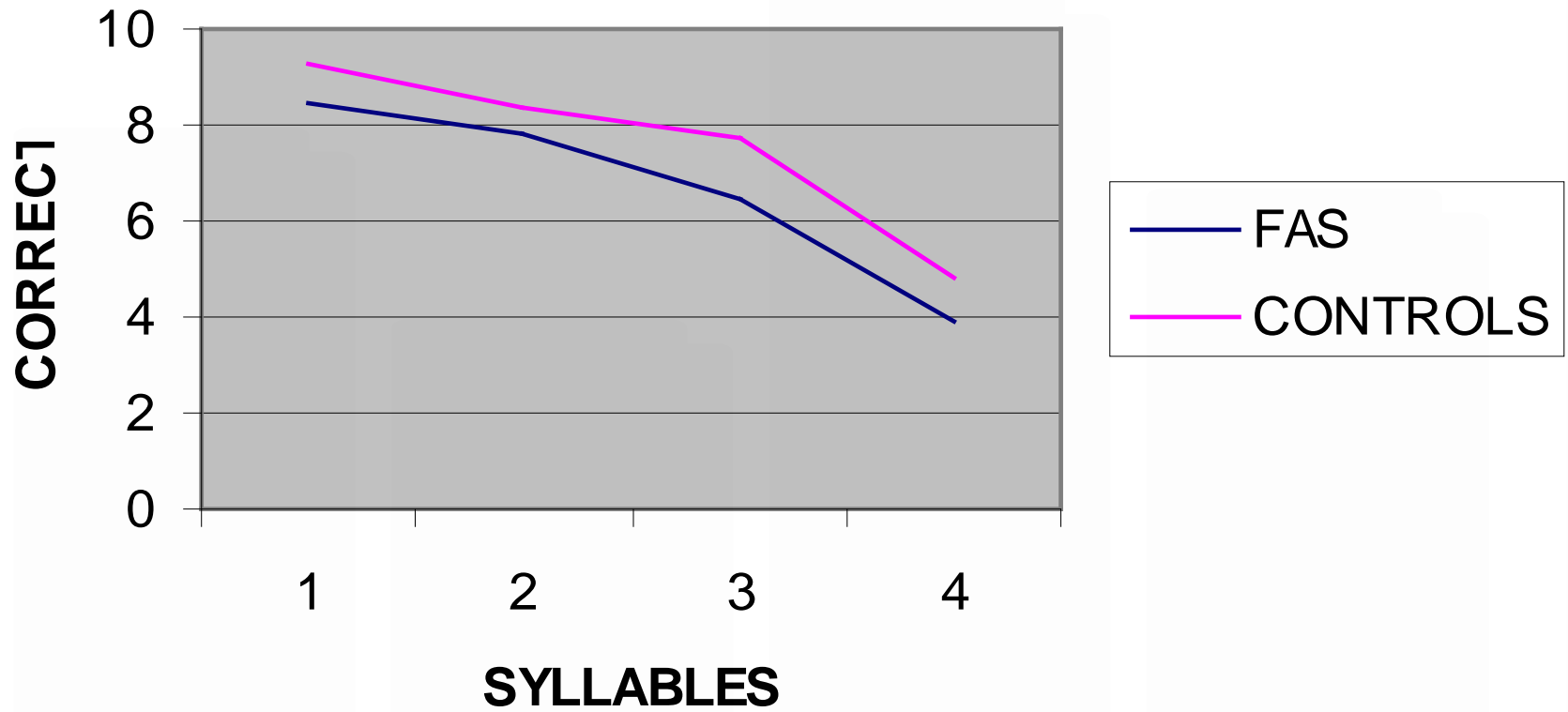
The Single Dominant Cause Hypothesis: Limitations

- Expressive and receptive language disorders
- Neuropsychiatric disorders

Deficits in Expressive and Receptive Language

- Domain-specific hypothesis: there is alcohol-induced damage to the areas that subserve language function (temporal lobe)
- Domain-general hypothesis: general functions that mediate language learning such as intellectual ability are impaired in children with FASD (those with higher IQs learn language better than those with lower IQs)

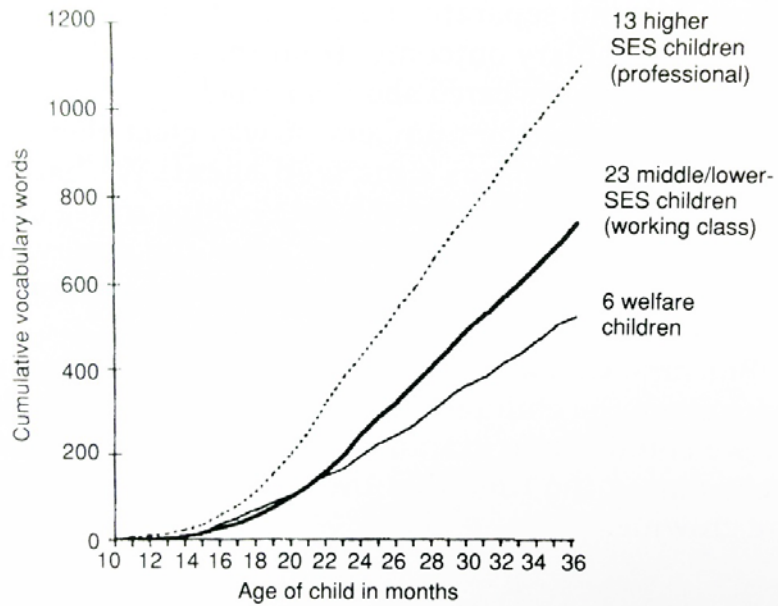
Impaired phonological working memory



Language input plays a key role

- Language input is a robust correlate of language development
- The size of the child's vocabulary is linearly correlated with the amount of language produced by parents (particularly the mother)
- Consequently, there is a significant social class effect on language development

Social Class and Vocabulary Development (Hart and Risley, 1995)



Parents' level of education (percentages)

	Mother's education	Father's education
< 11 th Grade	63	51
High School	29	36
Post High School	8	13

The genetics of language impairments

- A subset of parents dropped out of school because they themselves had learning disabilities, particularly in language-based disabilities
- Some language-based learning disabilities are heritable

Misdiagnosis of language disorders in children with FASD

- A child with substantial prenatal alcohol exposure who had ADHD:
- Low scores on standard measures of reading, writing, and comprehension; so, could have received a diagnosis of language disorder
- However, process-oriented testing revealed that he was able to decode non-words (stree, mest, glack) with ease

Expressive and Receptive Language Disorders- Summary

- Multiple risk factors work together to produce language difficulties in children with FASD
- These include exposure to alcohol and drugs, limited language input, and genetic factors
- Language deficits in this population are often misdiagnosed due to incorrect interpretation of test data

Neuropsychiatric Disorders

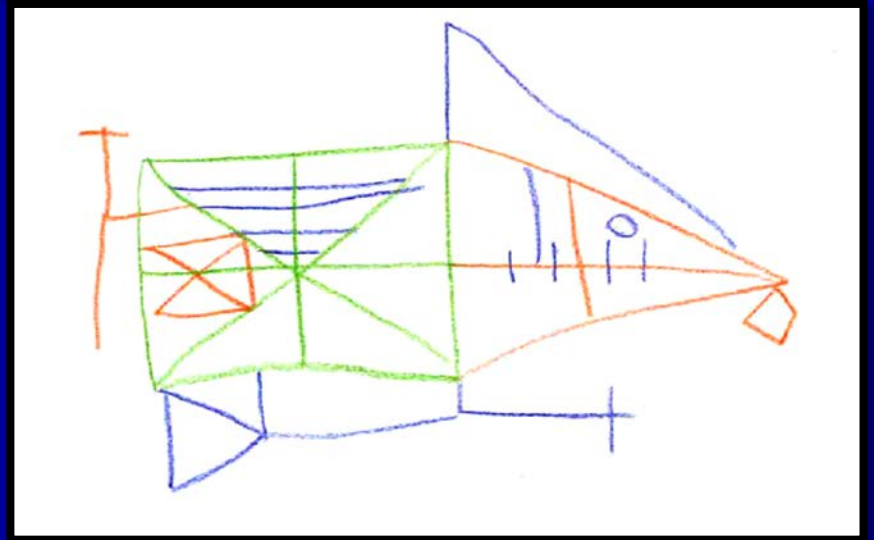
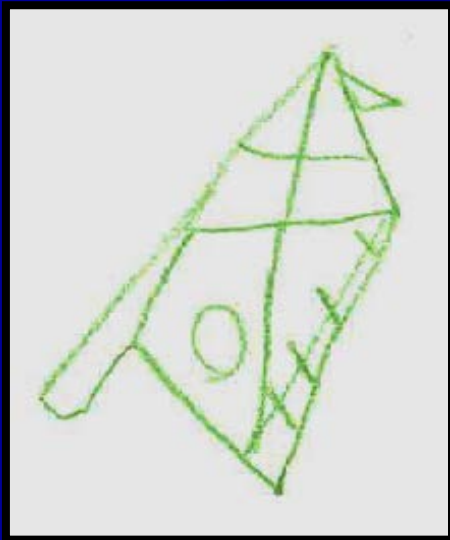
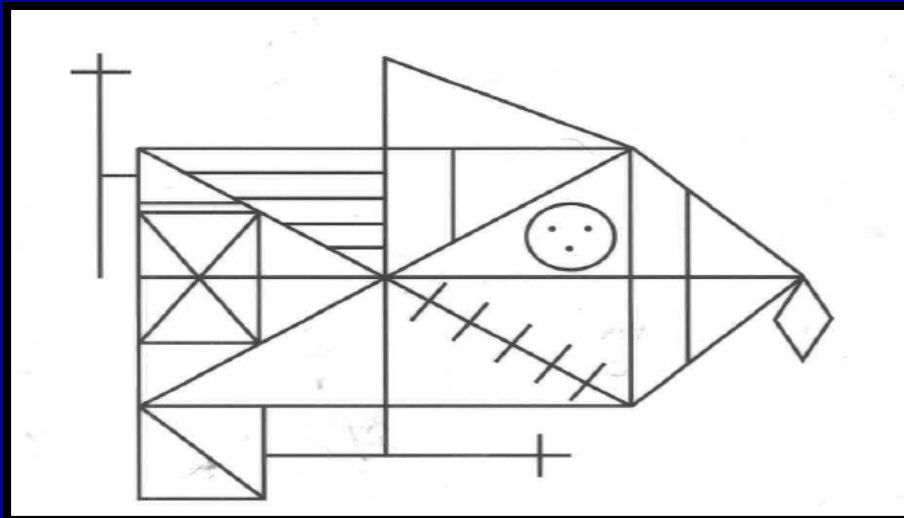
- Animal research has obtained evidence that prenatal alcohol exposure disrupts neurotransmitter systems in the brain (See Valenzuela et al. 2011 review).
- Weinberg and associates (2010, 2011) have shown the alterations of the HPA axis in rodent models and the implications of these alterations for understanding anxiety and depression in alcohol-exposed humans

Genetic influences on neuropsychiatric disorders

- We have identified a group of children with FASD who show a profile of behavioral disturbances notable for pronounced fluctuations of mood and severe attentional problems
- All of these children had a family history of psychiatric problems that is significant for bipolar disorder and alcoholism in mother

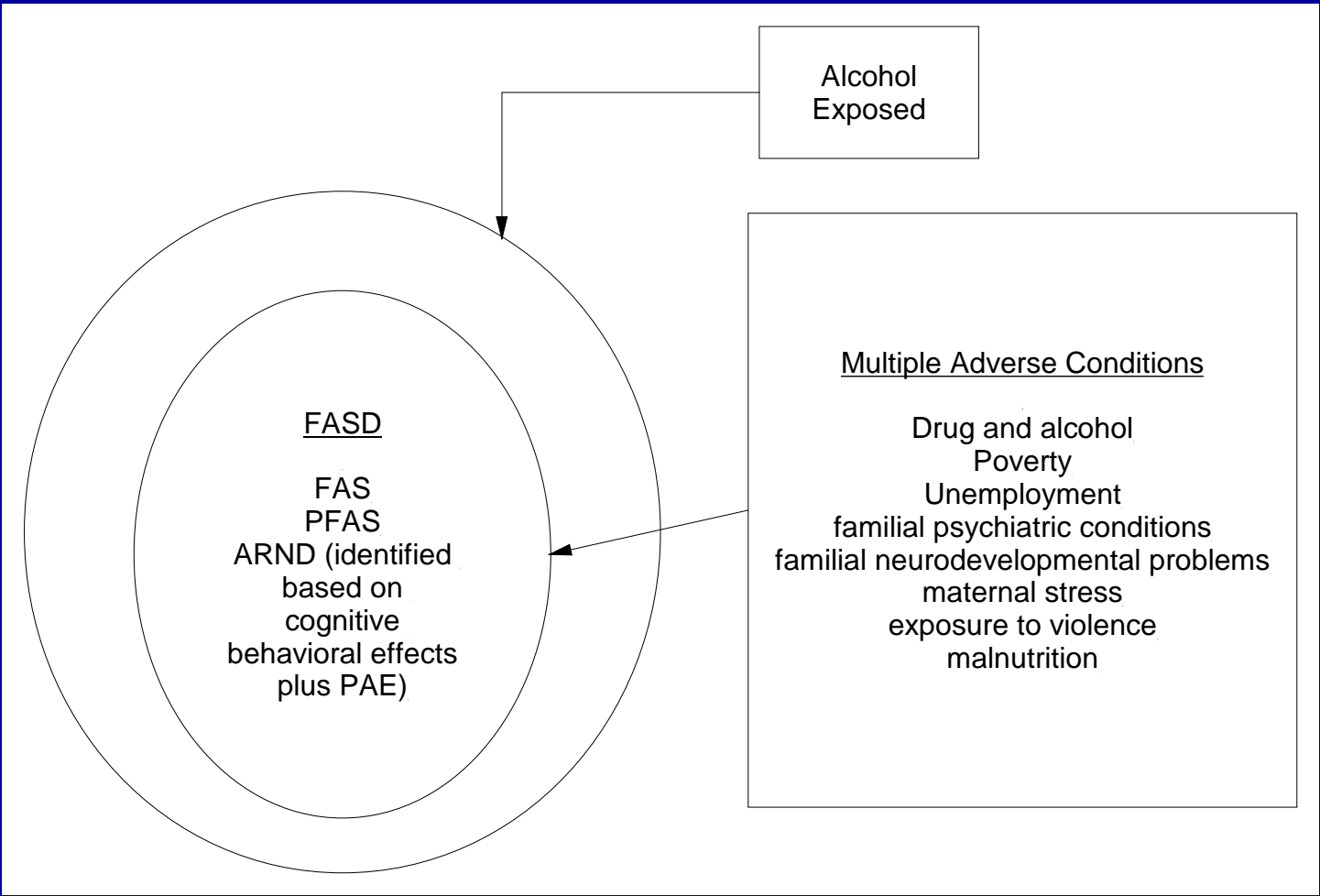
Genetic influences (cont.)

- These children display a unique neuropsychological profile
 - Nonverbal IQ is lower than verbal IQ
 - Difficulty in reading social cues
 - Greater difficulty with math than language-based tasks
 - Difficulty emotional regulation
 - Profound difficulty visual construction and fine motor skills



Environmental Influences on neuropsychiatric disorders

- 84% of the group (N=120) were living in foster care or in adoptive homes; 16% were living with bio parents
- About 40% of the sample had been placed in multiple homes (>3)
- Many of them had experienced toxic stress, including physical abuse (28%), sexual abuse (20%), neglect (45%), exposure to violence (33%)



Summary and Conclusions

- Multiple factors “working together” produce a range of comorbid conditions in children with FASD
- These factors considerably vary in this population
- Consequently, they do not form a unique phenotype
- Based on clusters of risk factors present in a child there are different profiles

Summary and Conclusions

- It is of paramount importance to adopt a “process-oriented approach” to assessment
- Such an assessment will answer not only ‘what score did a child earn on a test?’, but also “why did he or she earn a particular score?”
- This will entail affording a child to perform a task under different condition
- This is different from the administration of a test to a large group of children under the same condition.