

Moving Upstream: Social Determinants of Health

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Outline

- Unique vulnerability of children
- Examples of environmental influences:
 - on brain development; on asthma
- Impacts of social factors
- Interactions among multiple factors
- Conclusions

HEALTH

environment

Poverty

Stress

Access to health
care

Social support systems

Nurturing environment

Diet

Air, water

Toxic chemicals

Radiation

Infections

Physical agents

genes

Genes and environment
are in continuous
conversation

Environmental factors
can directly impact
cells, tissues, organs

Environmental factors can alter
gene function, gene expression

The vulnerability of developing children

- Increased exposure to many environmental contaminants
- Increased susceptibility to environmental factors
- Children have more time to develop environmentally triggered diseases with long latency periods

Disproportionate exposure of children

- Pound for pound, children take in more air, food, and water than adults
- Gastrointestinal tract is more permeable to nutrients and contaminants, e.g. calcium, lead
- Children's activities and environment differ from adults

Disproportionate susceptibility of children

- Developing tissues generally more vulnerable to environmental factors
- Environmental factors can “program” genetic expression, tissue and organ development in unique and lifelong ways
- Brain, respiratory, gastrointestinal, reproductive, immune system, metabolic systems are not fully developed for days, weeks, months, or years

The developing brain

- Brain development begins early in fetal life and is not complete for years
- Brain develops under control of neurotransmitters, hormones, other neurotrophic chemicals susceptible to alteration by environmental agents
- Vulnerability extends beyond birth into adulthood

Cellular Events in Neurodevelopment

Each of these events is subject to disruption by environmental agents

- Division
- Migration
- Differentiation
- Formation of synapses
- Pruning of synapses
- Apoptosis
- Myelination

Active
throughout
childhood &
adolescence



Alcohol, nicotine

- Recognized as neurodevelopmental toxicants for years
- Alcohol – hyperactivity, cognitive deficits, behavioral problems
- Nicotine – IQ, learning, and attention deficits

Lead

- IQ, learning, attention deficits; hyperactivity, impulsiveness, aggression; failure to complete school, trouble with the law (effects as low as 2.5 ug/dl)

Canfield, et al
NEJM, 2003
348:1517-1526

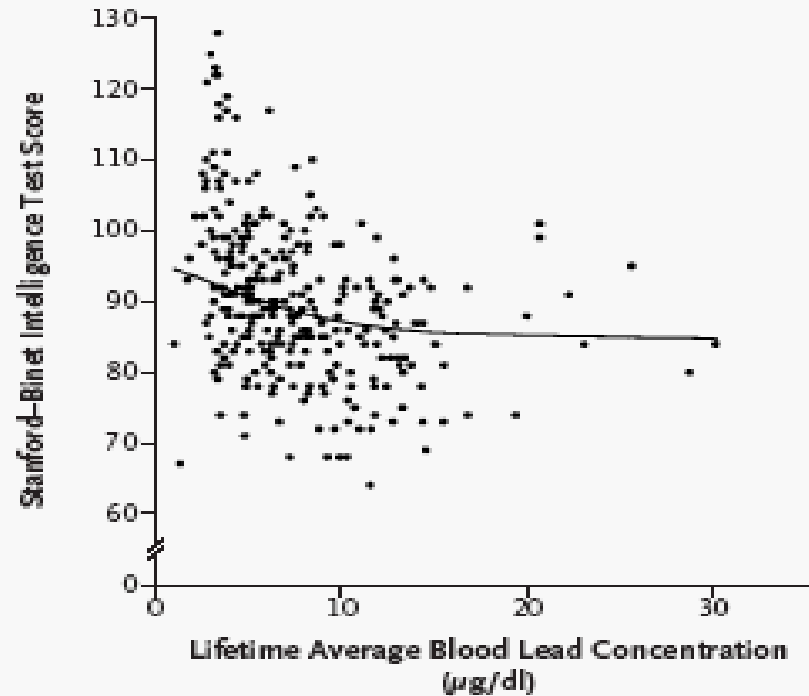


Figure 2. IQ as a Function of Lifetime Average Blood Lead Concentration.

IQ was assessed with use of the Stanford-Binet Intelligence Scale, fourth edition. The line represents the relation between IQ and lifetime average blood lead concentration estimated by the covariate-adjusted penalized-spline mixed model. Individual points are the unadjusted lifetime average blood lead and IQ values. To convert values for lead to micromoles per liter, multiply by 0.0483.

IQ tested at 3 and 5 years; blood lead measured X 7 before age 5

Nutrition and brain development

- All nutrients are important for normal brain growth and development; some more than others
 - Protein, iron, zinc, iodine, selenium, folate, vitamin A, choline, polyunsaturated fatty acids

Iron deficiency and brain development

- Iron deficiency: 10% US toddlers, ↑ poverty, obesity; more common in developing countries
- Iron deficiency > impaired IQ, auditory discrimination, memory
- Iron deficiency and ADHD (53 cases, 27 controls; low ferritin 84% cases, 18% controls) (Konofal, Arch Pediatr Adolesc Med. 2004)

Nutrition and lead absorption: interactions

- Lead absorption increased with:
 - Iron-deficient diet
 - Calcium-deficient diet
 - High fat diet
- Iron deficiency up-regulates iron transporters of Fe into the brain; other heavy metals use those transporters

Socioeconomic status and neurodevelopment

- Adverse socioeconomic conditions independently impair neurodevelopment (this is NOT primarily genetic) (Bradley, Ann R Psych, 2002)
- Lower SES associated with elevated corticosteroid levels in children (the “stress” hormone)
- Lower SES also influences nutritional status, exposures to lead and other neurodevelopmental toxicants, elevates corticosteroid levels (“stress hormone”)

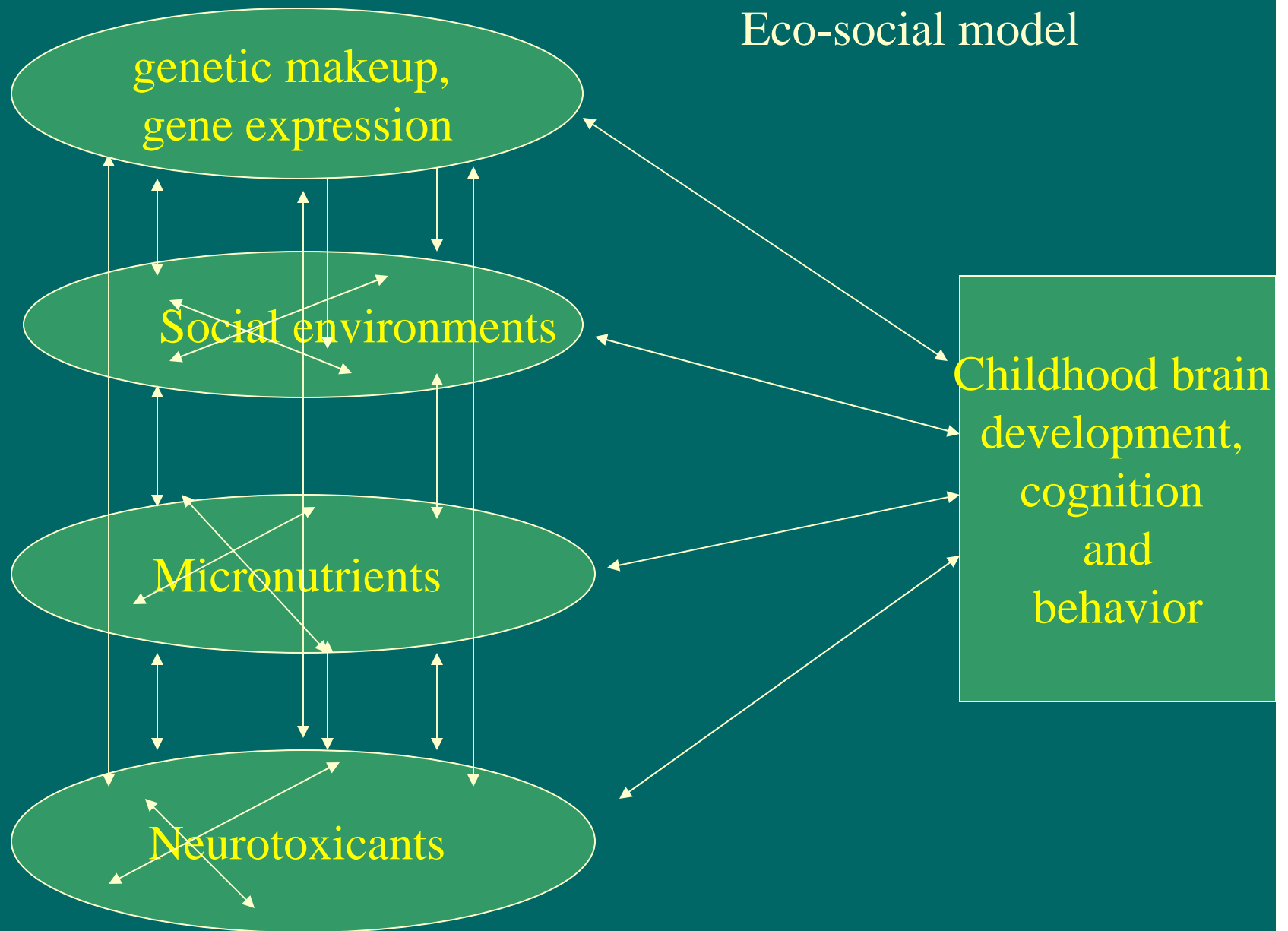
Intervention studies

- Most interventions require addressing lead reduction, iron repletion, improved social circumstances **collectively** in order to have much beneficial effect.

(e.g., Ruff, EHP, 1996)

- BUT, even then, brain vulnerability outweighs plasticity; i.e., “catch-up” with remediation not as effective as primary prevention

Eco-social model



Modified from: Hubbs-Tait et al. Psychological science in the public interest

Neurotoxic pesticides

- Organophosphates
- Pyrethroids/pyrethrins
 - Commonly used
 - Minimal neurodevelopmental toxicity data
- Lindane: (organochlorine)
 - Lowers seizure threshold
 - Reports of infant and child seizures with excess use; occasional infant deaths
- DDT

Organophosphate Pesticide (OP) Effects in Laboratory Animals

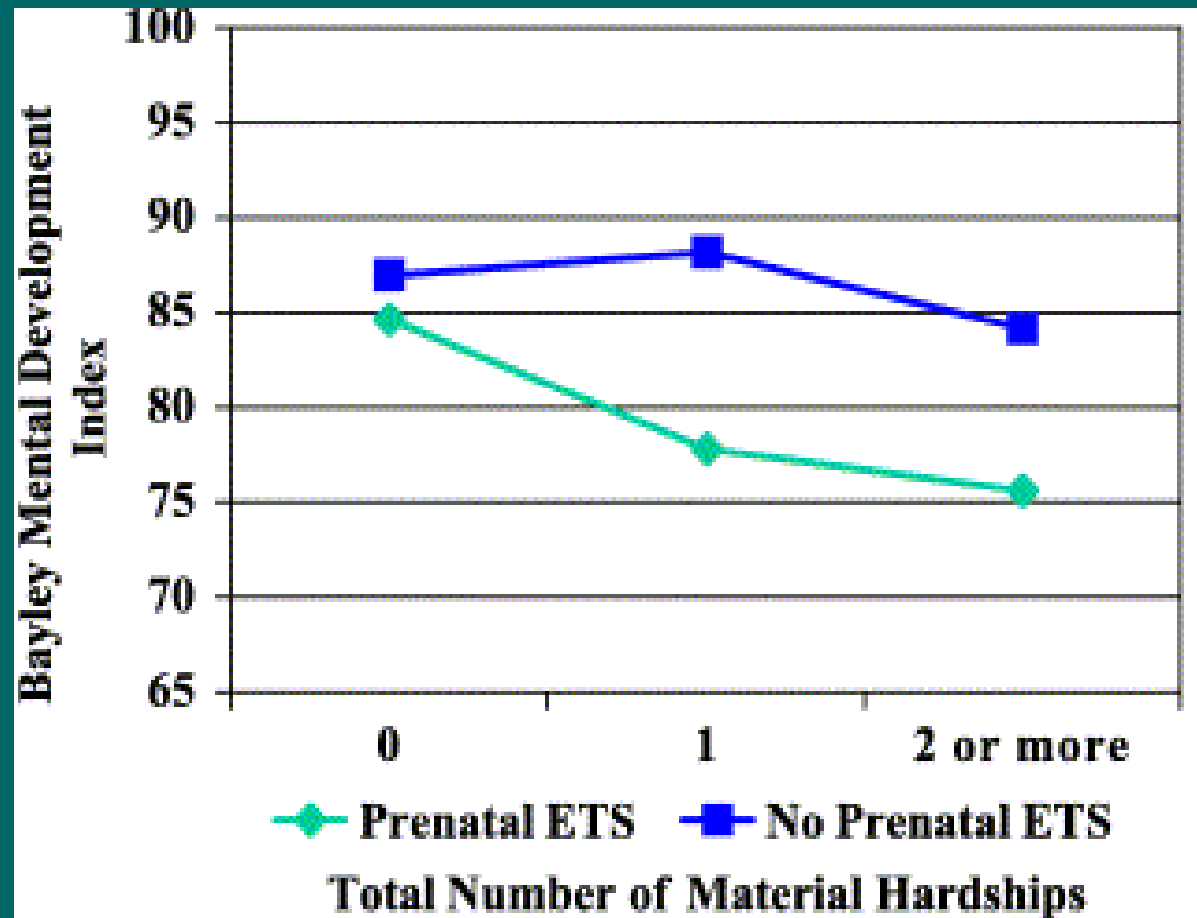
- Small single dose on day 10 (neonatal)
- Permanent changes in brain architecture
- Permanent hyperactivity (Ahlbom, 1995)
- Fetal exposures: coordination and motor disorders, decreased brain weight

Organophosphate effects— human

- Summary from Columbia study:
 - Prenatal chlorpyrifos exposure associated with 3.5-6 point decrease in 36-month development scores (Bayley MDI and PDI); **most marked in a low-income minority sample**
 - This resulted in a 5 fold increased risk of developmental delay
 - Prenatal chlorpyrifos exposure assoc. with increased risk of diagnosis of ADHD, attention problems, and PDD

(Whyatt, et al; in press)

2 yr old MDI; prenatal ETS, material hardships



^aAdjusted for race/ethnicity, gender, gestational age at delivery, age at testing, marital status, maternal age, and level of PAH exposure.

Rauh et al, Neurotox Teratol, 2004

Asthma

- Many indoor and outdoor air pollutants trigger asthma attacks and increase their severity
- Ambient ozone exposures in exercising children increases the incidence of asthma (McConnell, Lancet, 2002)
- Lower SES consistently associated with greater asthma morbidity

Explanations for SES gradient and asthma morbidity

- Greater exposure to asthma triggers—single and cumulative
- Reduced access to health care
- Reduced compliance with medical interventions
- Psychosocial factors

SES, psychological stress, asthma

- N = 76; half with asthma
- Age 13 yrs +/- 2.8
- Associations of SES with stress
- Associations of SES with immune process
- Associations of stress with immune process
- Pathway of SES > stress > immune response indicators (cytokines)

Chen et al. J Allergy Clin Immunol 2006

Results

- Asthma vs. healthy:
 - Mean values: No differences in savings, stress, immune measures (except higher eosinophil count in asthmatics)
- Both groups: Higher SES > lower stress
- Statistical analysis concluded that psychological stress is one pathway that links SES to inflammatory mediators

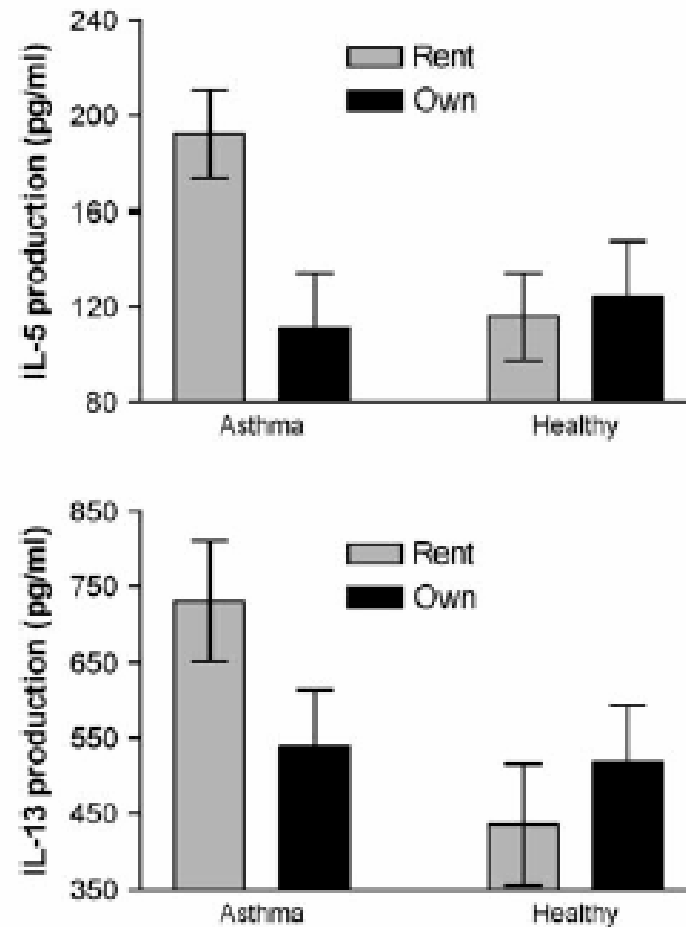


FIG 1. Differences in production of IL-5 and IL-13 for families who rent their homes versus families who own their own home by medical group status.

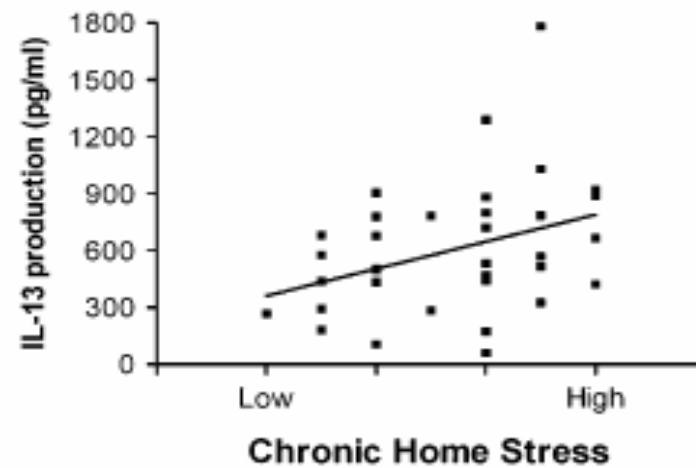
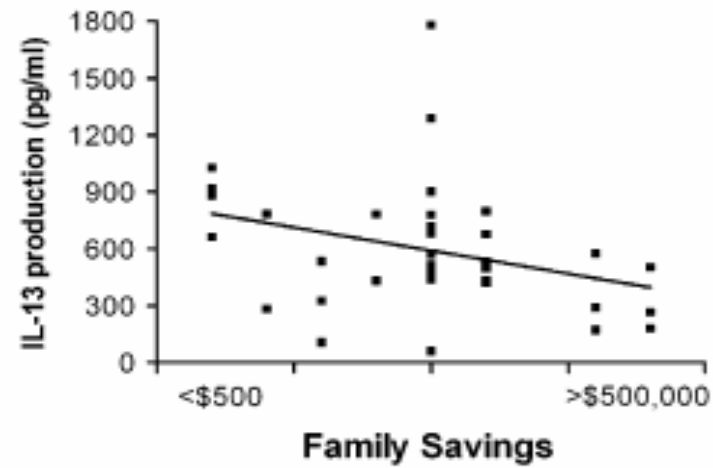


FIG 2. *Top panel*, Association of family savings with production of IL-13 among children with asthma. *Bottom panel*, Association of chronic home stress with production of IL-13 among children with asthma.

Chen, et al

Conclusions

- Developing children more vulnerable to environmental factors
- Toxic chemicals, nutrition, social factors interact in complex ways to influence children's health
- Adverse social circumstances have their own biological impacts AND exacerbate the impacts of toxic chemicals and nutritional deficiencies
- An ecological analysis and interventions that address multiple factors are more likely to provide insight and benefits