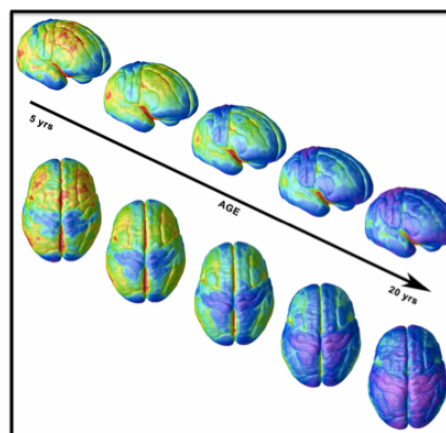
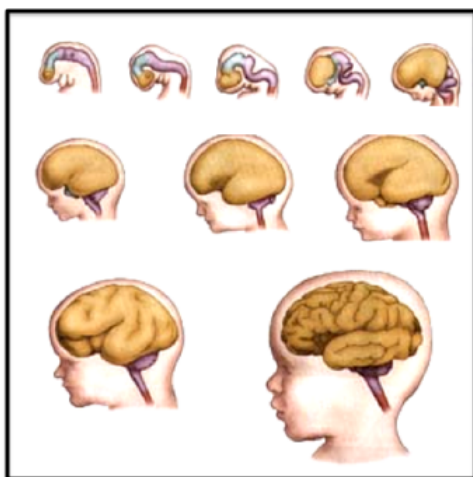


La construcción del cerebro en el neurodesarrollo: "efectos ambientales"



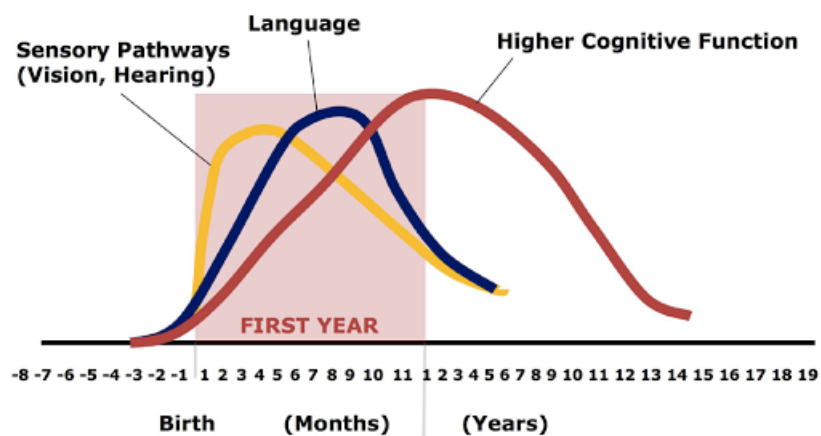
Luis Barbeito

barbeito@pasteur.edu.uy

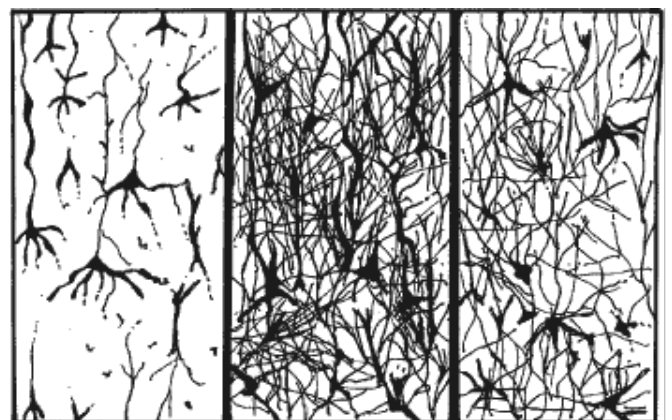
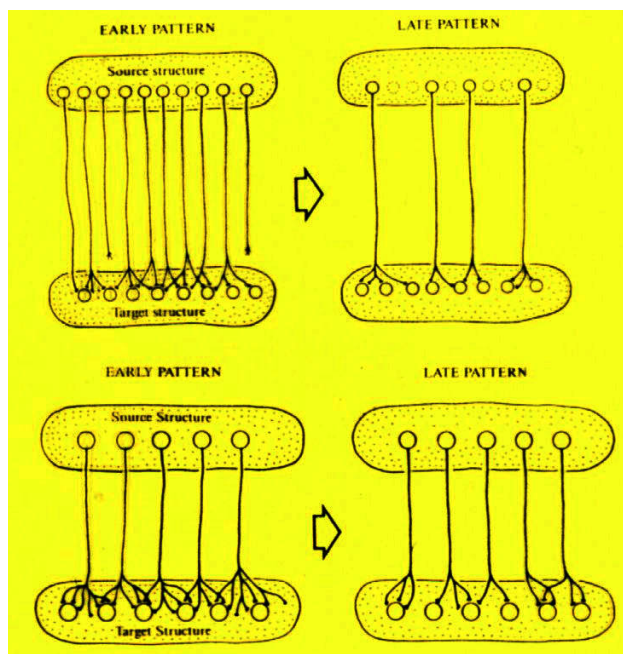
La construcción del cerebro



Human Brain Development Neural Connections for Different Functions Develop Sequentially



Darwinismo neuronal y sináptico



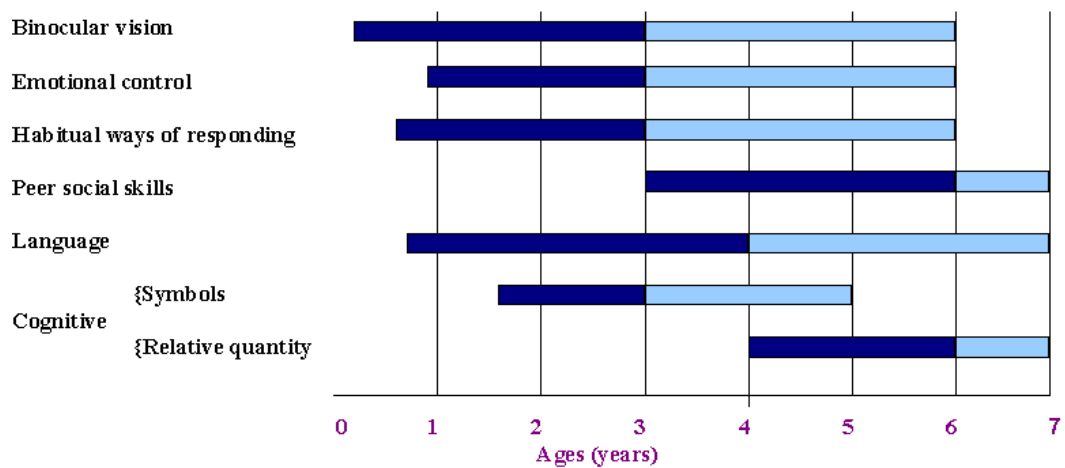
Nacimiento

7 años

15 años

G. Edelman, 1990

Periodos críticos en desarrollo funcional del sistema nervioso central



Source: Eliot, L. (1999). What's going on in there? How the brain and mind develop in the first five years of life. London: Penguin

Consecuencias y Determinantes

CHILD DEVELOPMENT

Child Development, January/February 2010, Volume 81, Number 1, Pages 41-79



Periodo perinatal:

Epigenetics and the Biological Definition of Gene × Environment Interactions

Michael J. Meaney
McGill University

- Rasgos de la personalidad (ej. estrategias defensivas, emoción)
- Conducta reproductiva
- Conducta alimentaria y metabolismo
- Funciones ejecutivas, CI, desempeño educativo
- Salud mental

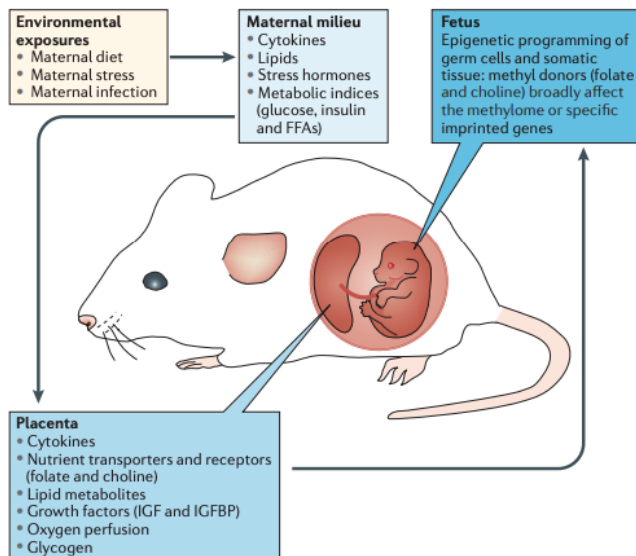
$$\begin{array}{l} \text{Carga} \\ \text{genética} \end{array} + \begin{array}{l} \text{Influencias} \\ \text{ambientales} \\ \text{(epigenética)} \end{array} = \text{Fenotipo}$$

Epigenética: Modificaciones físicas, estructurales del ADN y la cromatina que modulan la expresión génica. Las modificaciones más frecuentes son por agregados de **metilación y acetilación**.

M. Meaney mostró que la metilación en el SNC tiene un impacto en la estructura y función cerebral en la primera infancia.

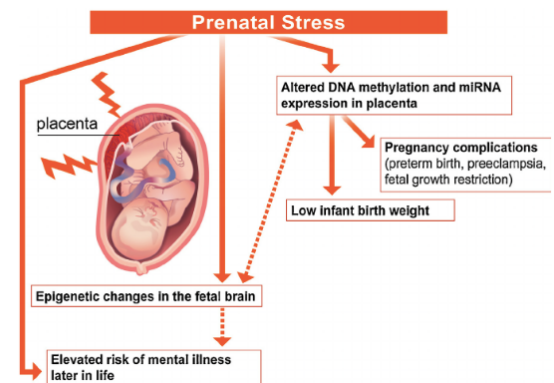
75% de los cambios epigenéticos ocurren in utero, asociados a condiciones maternas (depresión, obesidad, tabaquismo) y fetales.

Influencias prenatales



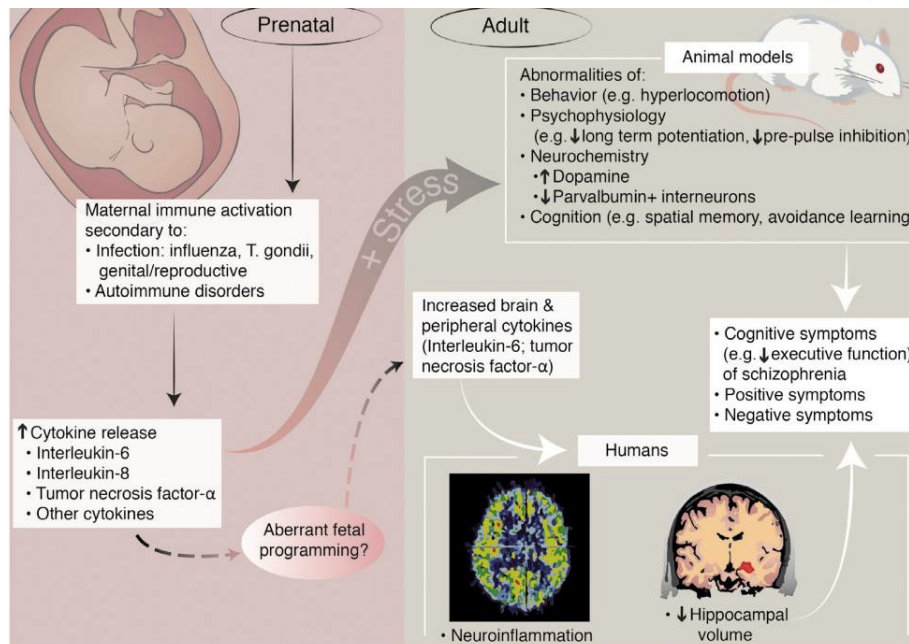
Early environmental influences on the development of children's brain structure and function

PATRÍCIA M MIGUEL^{1,2} | LENIR O PEREIRA^{1,2} | PATRÍCIA P SILVEIRA^{3,4,5} | MICHAEL J MEANEY^{3,4,5,6,7}

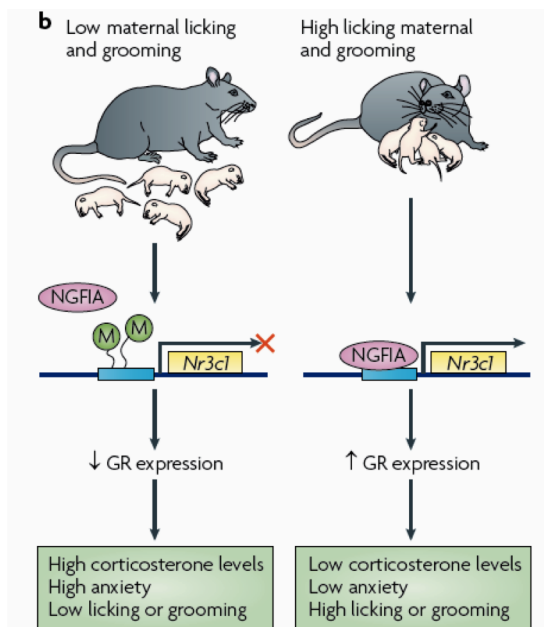


Efecto prenatales de la inflamación materna

The Cytokine Model of Schizophrenia: Emerging Therapeutic Strategies
 Ragy R. Giris^{a,b}, Samhita S. Kumar^{a,b,c} and Alan S. Brown^{a,b,c,*}



Influencias post-natales

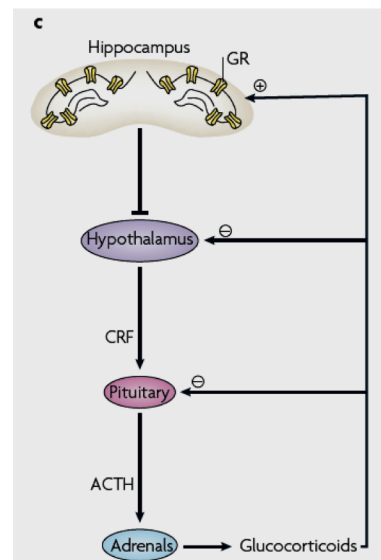


CHILD DEVELOPMENT

Child Development, January/February 2010, Volume 81, Number 1, Pages 41–79

Epigenetics and the Biological Definition of Gene × Environment Interactions

Michael J. Meaney
McGill University

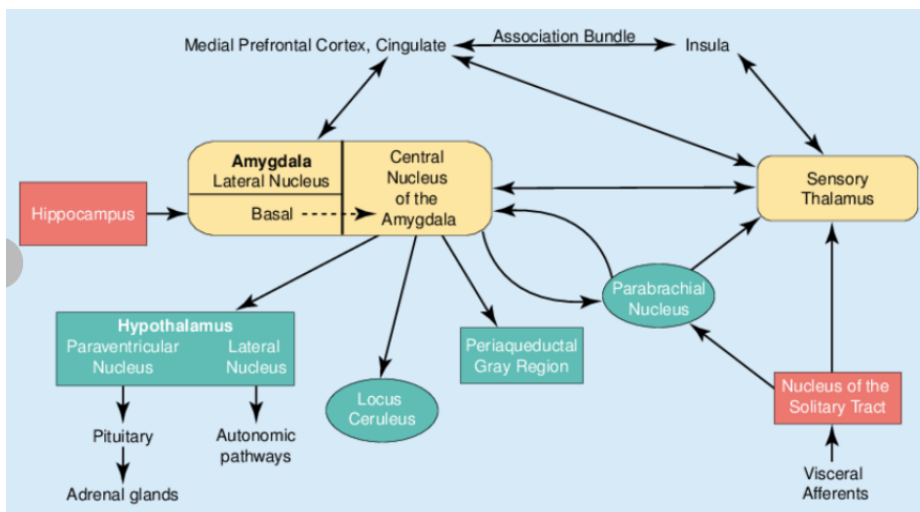


Comunicación intestino-cerebro

Normal gut microbiota modulates brain development and behavior

Rochellys Diaz Heijtz^{a,b,1}, Shugui Wang^c, Farhana Anwar^d, Yu Qian^{a,b}, Britta Björkholm^d, Annika Samuelsson^d, Martin L. Hibberd^e, Hans Forsberg^{a,b}, and Sven Pettersson^{c,d,1}

Departments of ^aNeuroscience, and ^bMicrobiology, Cell and Tumor Biology, Karolinska Institutet, 171 77 Stockholm, Sweden; ^cStockholm Brain Institute, 171 77 Stockholm, Sweden; ^dGenome Institute of Singapore, 02-01 Genome 138672, Singapore; and ^eDepartment of Women's and Children's Health, Karolinska Institutet, 171 76 Stockholm, Sweden
 Edited by Arturo Zychlinsky, Max Planck Institute for Infection Biology, Berlin, Germany, and accepted by the Editorial Board January 4, 2011 (received for review August 11, 2010)

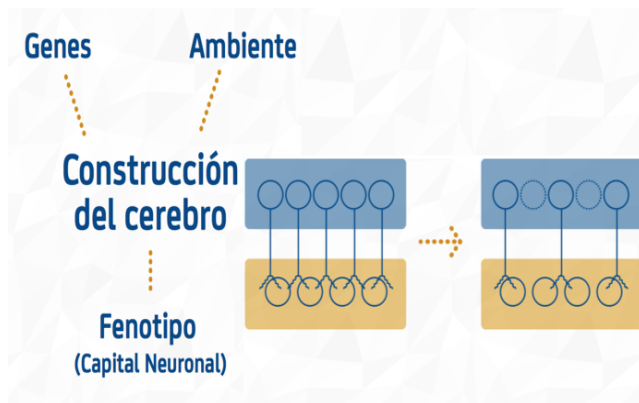


Periodo de vulnerabilidad:

- Lactancia
- Infecciones
- Alteraciones GI

EFEECTO DE LA ADVERSIDAD Y EL ESTRES TOXICO

El “ecosistema” del desarrollo perinatal



- Condiciones del embarazo (depresión, ansiedad, tabaquismo, infecciones)
- Peso al nacer
- Hipoxia-isquemia
- Apoyo parental (lactancia)
- Estimulación sensorial y cognitiva
- Exposición a agentes infecciosos y toxinas
- Estrés

Consecuencias de la adversidad perinatal

Las experiencias tempranas influyen en el desarrollo del cerebro.

El estrés tóxico ejerce toxicidad en el neurodesarrollo.

La adversidad durante el neurodesarrollo puede llevar a vulnerabilidad durante toda la vida.

El neurodesarrollo requiere de relaciones parentales adecuadas.

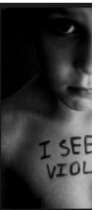
Las intervenciones tempranas permiten la prevención y hasta la reversión de los daños causados.

Traumatic Events and Chronic Stress Undermine Achievement

- Changes in **brain** development and functioning
- Lags in **concentration**, memory, and creativity
- Diminished **social skills** and social judgment
- Reductions in **motivation** and effort
- Increases in **impulsive** behavior and depression

Educational Disparities:

- Miss an average of **18-22** days of school
- Are **3X** more likely to be absent, suspended, or expelled than children with other disabilities
- More likely to **drop out of high school** (44% of youth with diagnosed behavioral illnesses)



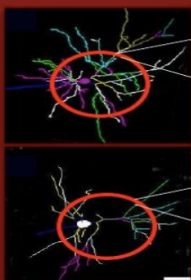
THE IMPACT OF EARLY ADVERSITY ON CHILDREN'S DEVELOPMENT



Center on the Developing Child
HARVARD UNIVERSITY

Toxic Stress Changes Brain Architecture

Normal



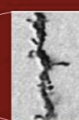
Typical neuron—
many connections



Toxic
stress



Damaged neuron—
fewer connections



Prefrontal Cortex and
Hippocampus

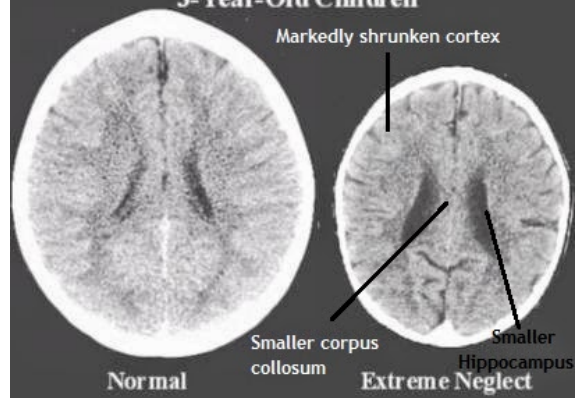
Sokolovo 2011

Sources: Radley et al. (2004); Bock et al. (2005)

22

3-Year-Old Children

Markedly shrunk cortex



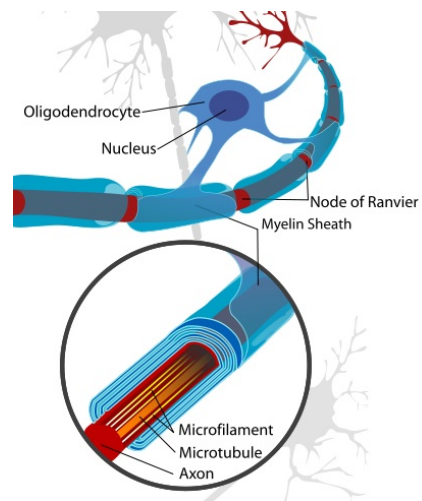
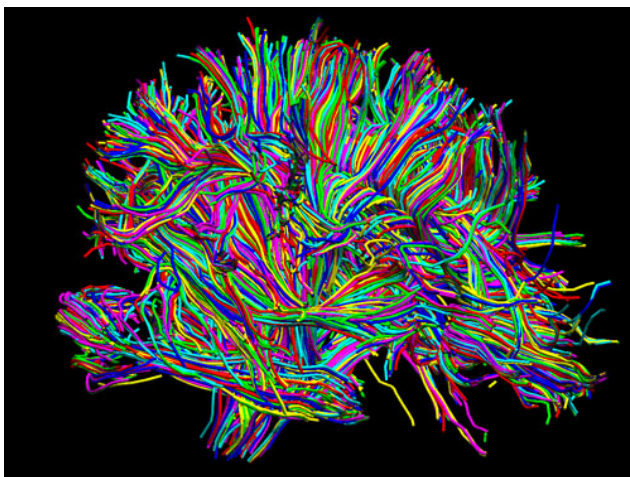
Normal

Smaller corpus
callosum

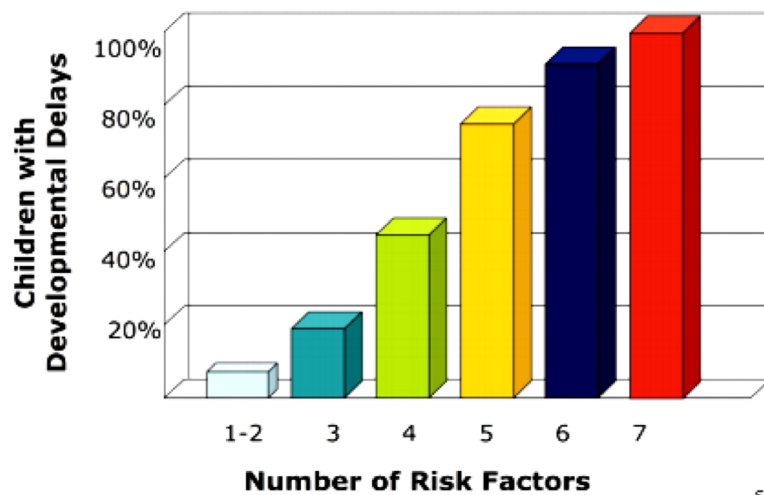
Smaller
Hippocampus

Extreme Neglect

Anemia ferropénica y mielinización durante el desarrollo postnatal

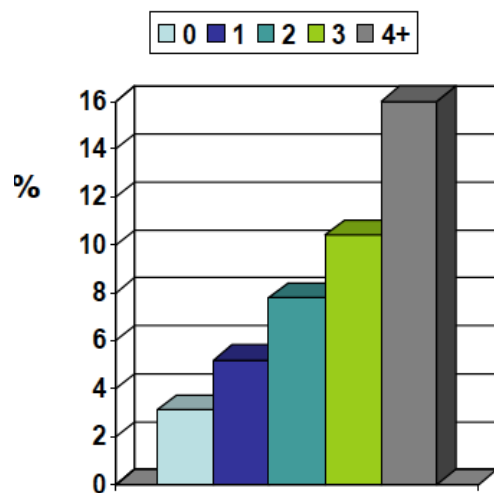


La adversidad se asocia a retardo del desarrollo

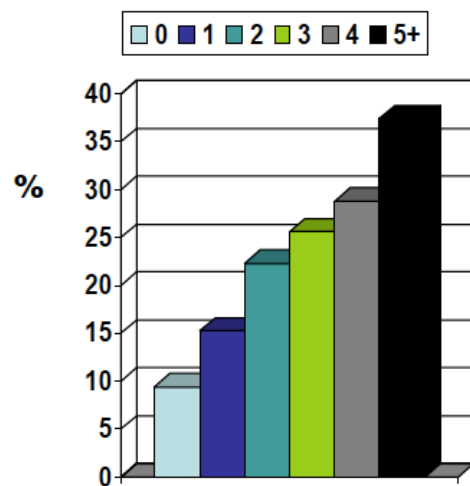


Source: Barth et al. (2008)

La adversidad se asocia a adicción en adultos



Self-Report: Alcoholism
Dube et al, 2002



Self-Report: Illicit Drugs
Dube et al, 2005

El efecto de la exclusión social

SCIENCE AND SOCIETY

Socioeconomic status and the brain: mechanistic insights from human and animal research

Daniel A. Hackman, Martha J. Farah and Michael J. Meaney

Nature Reviews Neuroscience **11**, 651-659 (2010) |

- El desarrollo del sistema nervioso humano ocurre en un contexto social y económico.
- Por lo tanto, el status socioeconómico en la infancia influencia el desarrollo cerebral.
- Los sistemas más afectados son los subyacentes al lenguaje y funciones ejecutivas.

Box 1 | **The role of neuroscience in addressing socioeconomic status-related disparities**

