Ethical issues in etiological and biological research into autism

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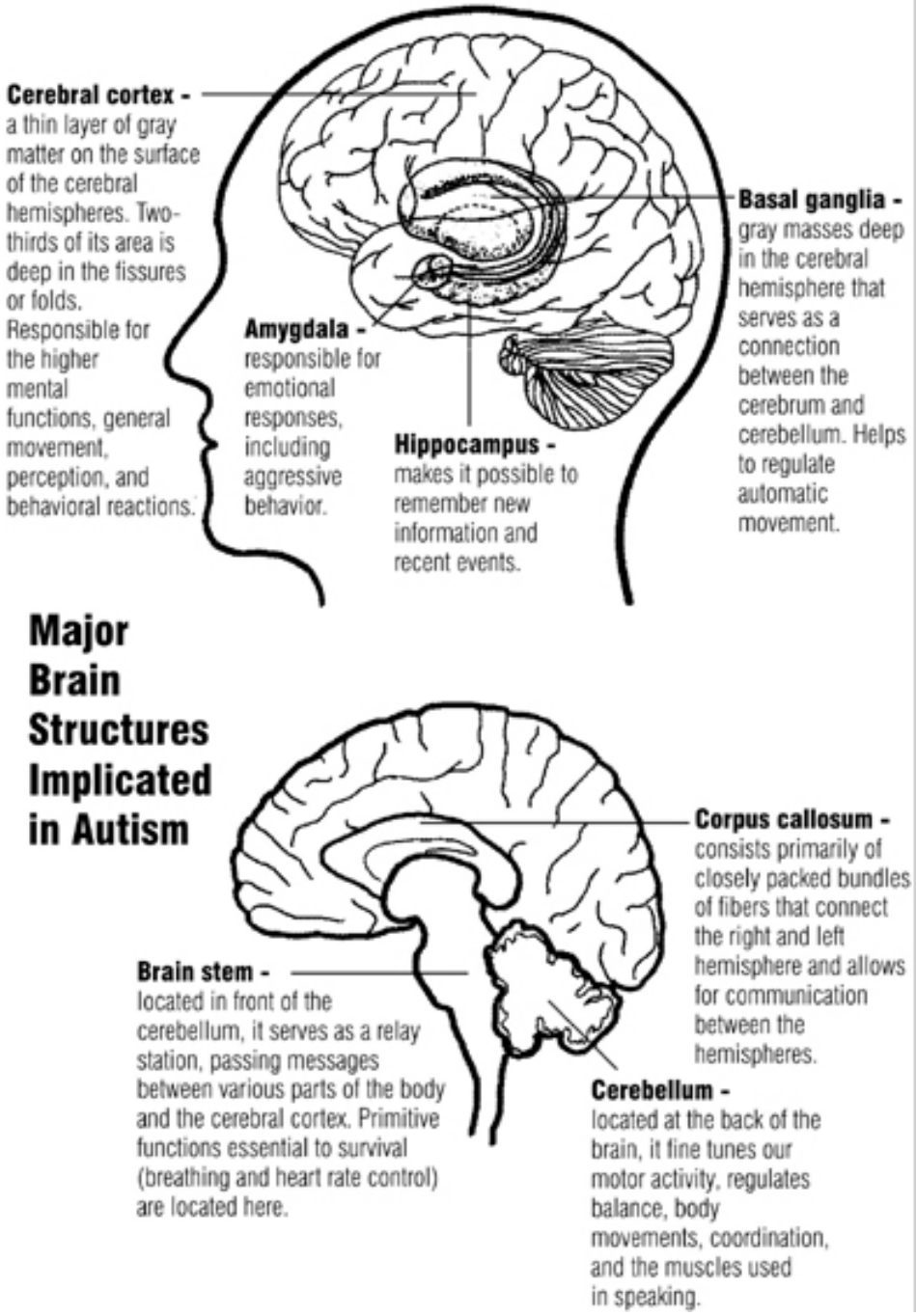

ASD etiology

- Multiple brain regions have been implicated
- Multiple genes / gene variants have been implicated
- Diathesis—stressor explanatory models abound, from relative simple to terrifically complex, multi-factorial ones

http://www.nimh.nih.gov/health/publications/autism/complete-index.shtml

What causes autism?

- Parenting?
- Genes?
- Vaccines?

- Genetic diatheses challenged by generic and/or specific environmental stressors?
- Non-genetic diatheses challenged by generic and/or specific environmental stressors?

“Autism’s puzzle”

“Autism's Puzzle” by Pamela Weintraub

Experience Life

October 2011

http://experiencelifemag.com/issues/october-2011/wellness/autisms-puzzle.php

The heterogeneous biologies of autism

"The heterogeneous biologies underlying autism may conceivably converge onto the autism profile via multiple mechanisms that all somehow perturb brain connectivity. Studying the interplay between the biology of intermediary mechanisms on the one hand and processing and connectivity abnormalities on the other may illuminate relevant final common pathways and contribute to focusing the search for treatment targets in this biologically and etiologically heterogeneous behavioral syndrome."

Herbert, M. 2005. Autism: A brain disorder, or a disorder that affects the brain? *Clinical Neuropsychiatry* 2: 354-379.

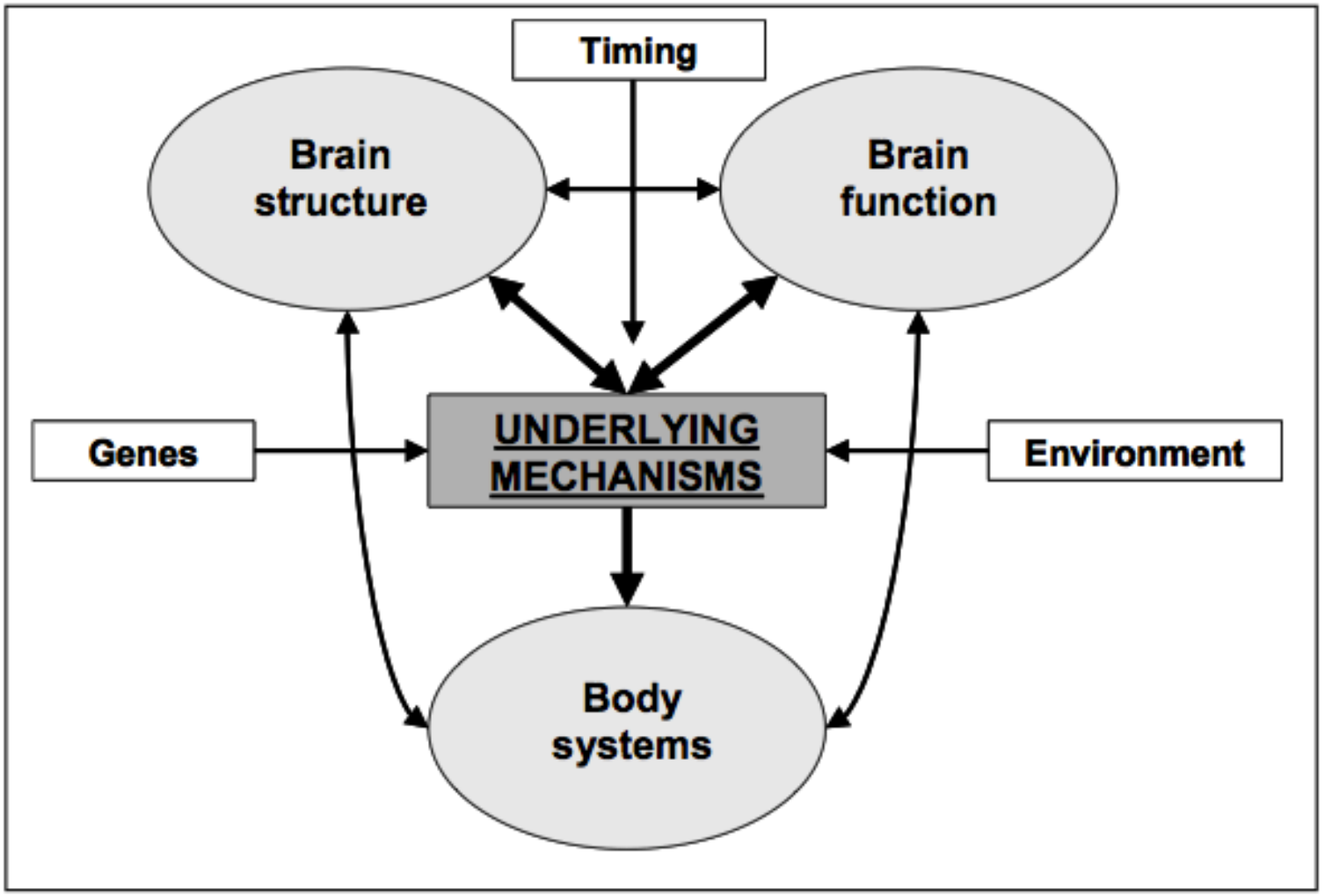

Figure 2. *Common underlying mechanisms, influenced by genes and environments in specific developmental windows, may underlie phenotypic features at multiple levels of the organism.*

Herbert, M. 2005. Autism: A brain disorder, or a disorder that affects the brain? *Clinical Neuropsychiatry* 2: 354-379.

A systems approach to autism

"If we can elucidate the genomic, proteomic [proteins expressed by specific genes] and metabolic differences associated with subtypes of ASD, then we can develop therapies targeted at correcting these imbalances. The ultimate goal is not just treating visible symptoms but actually rebalancing biochemistry — in fact, altering genetic expression — to prevent autism from developing at all," says [Lawrence] Rosen [MD, currently Director of the Whole Child Center in Oradell NJ].

As cited in: Weintraub, P. 2011. Autism's puzzle. *Experience Life* (October), online at http://experiencelifemag.com/issues/october-2011/wellness/autisms-puzzle.php.

Outstanding challenges

- The research agenda
  - Legacy of blame and mistrust
  - Etiological mayhem and phenotypic heterogeneity
- The research enterprise
  - Recruitment, especially given phenotypic heterogeneity
  - Observation of natural history of gXe interactions *vs*. intervention to prevent (further) harm
- The results of research
  - Operationalizing results to make a difference for kids, families
  - Toxic torts on the horizon (genetic susceptibility to specific environmental insults + specific environmental insult = tort claim, even if the environmental insult is not usually causally involved in the phenotype)

Starting at the very beginning: Toward "science with impact"

- Credibility – science produced with integrity: good technical data, sound methods, reasonable analysis, responsible argument, and acknowledgement of limitations of any given study
- Legitimacy/transparency – sensitivity to divergent values among stakeholders, unbiased and fair analysis (especially of opposing views); applies to research agenda setting and knowledge production
- Salience – usefulness to a range of stakeholders, achieved through asking and answering meaningful questions in a way that may inform eventual application in clinical, policy, or other contexts

D.W. Cash *et al*. *PNAS* (2003)