

9-2008

# Complexity and Limitations of Stress-Endocrine Research in Mental Health

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## Citation of this paper:

Srivastava, Amresh, "Complexity and Limitations of Stress-Endocrine Research in Mental Health" (2008). *Psychiatry Presentations*. 10.  
<https://ir.lib.uwo.ca/psychiatrypres/10>

# **COMPLEXITY AND LIMITATIONS OF STRESS-ENDOCRINE RESEARCH IN MENTAL HEALTH**

**AMRESH SHRIVASTAVA**

# Social Exclusion

*People living on the streets suffer the Highest rates of premature death*



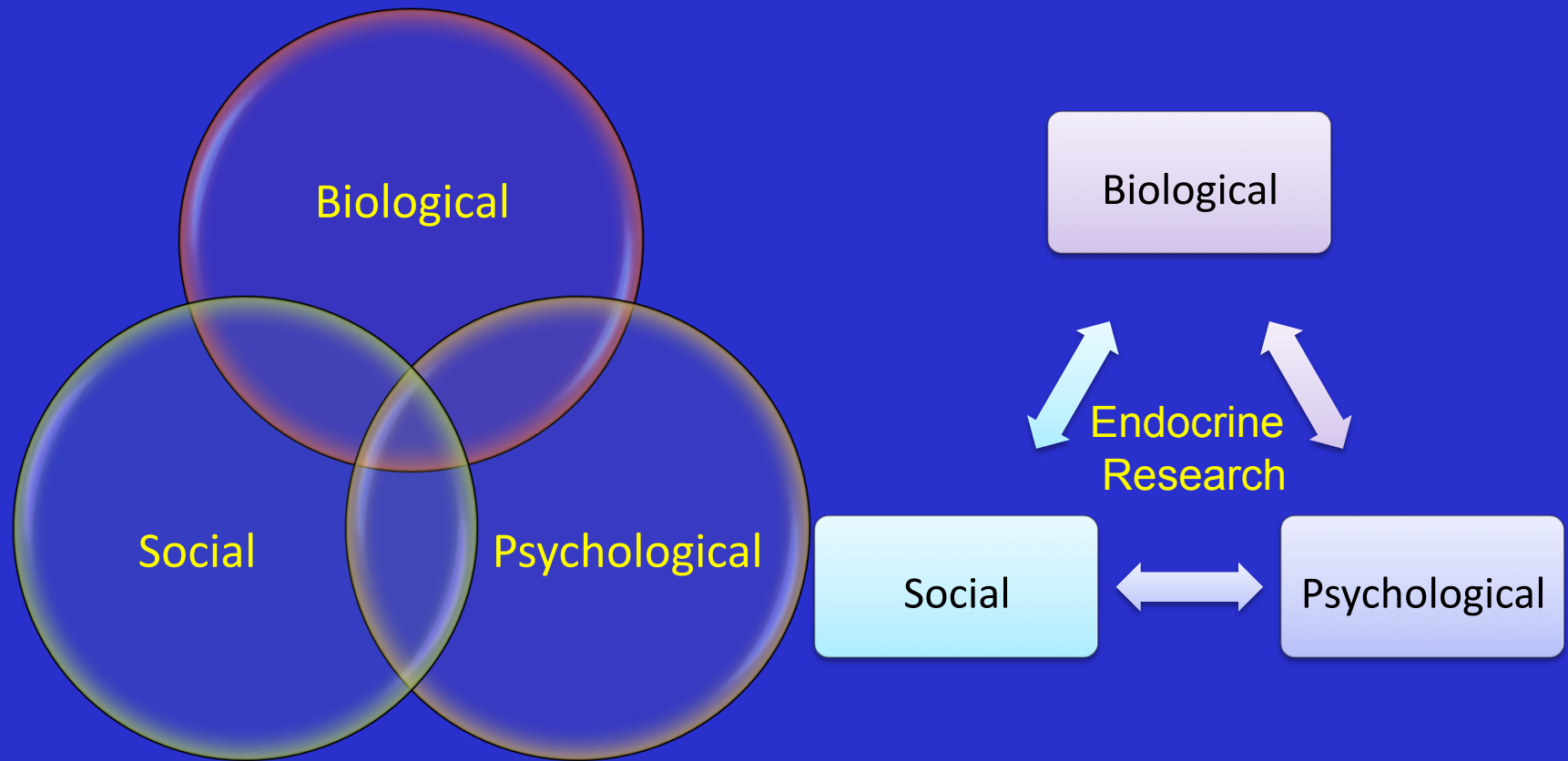
Q1: Concept of illness causation?

Q 2: Are these changes reversed by  
available therapeutic  
Interventions?

Q 3: Does the reversibility affect  
the outcome of therapeutic  
Interventions?



# Exploring Bio-Psycho-social Model



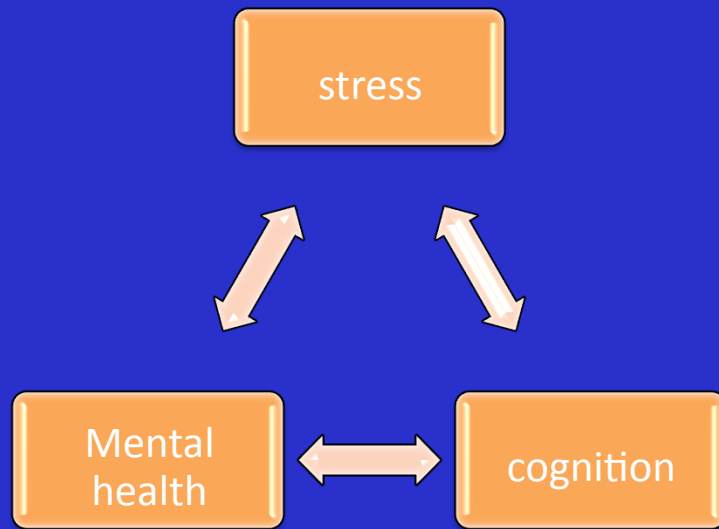
# Psychoendocrine & Mental Health

- Mental health research is very much in need for a simpler understanding of the way biological responses arise in face of psychological and social challenges.
- Though it appears very simple to state that mind and body are integrated, on continuum and even dimensional, however the fact is that very little is known for this complex relationship.

# Research achievements

- Epidemiological
- Clinical
- Behavioral
- Experimental

- HPA Axis
- Pituitary
- Thyroid
- CRH/CRF
- Neurotransmitters ( DA, 5 HT)
- Transporters
- Neuromodulators
- Genetics gene expression & gene material



# Complexity in Research

- Response variability
  - Accurate probe
  - Applying animal research
  - Quantification of response or measurements
  - Synthesis of model
- 
- Understanding the process of psychopathology
  - Exploring environmental influence of brain mechanisms
  - Newer targets for therapeutic interventions



# Limitations

- Laboratory studies allow standardization of the stressor
- Commonly used stressors are mental arithmetic's, speech tasks, the Stroop test, videogame playing, films or videotapes and interviews.
- generalizability of laboratory results, : Caution
- Another strategy is studying the psychoendocrine reaction to real-life stressors, such as bereavement or anticipated loss, academic examinations, everyday work and parachute jumping.

# Limitations

- The subjective perception of the situation is probably a main determinant
- marked variability in individual responses
- Evidently, the 'objective' characteristics : are not the only determinants
- it is mandatory to overcome a rigid dichotomy between psychological and biological processes.

# Unexplained Link: Social Changes affecting Mental health

Early Childhood experiences

Lifestyle research

Trauma & Disaster

Specific stress

# Cross-Cultural & Regional Differences

The probability of a man dying

between the ages of 15 and 60 is 8.2% in Sweden, 48.5% in the Russian Federation, and 84.5% in Lesotho.



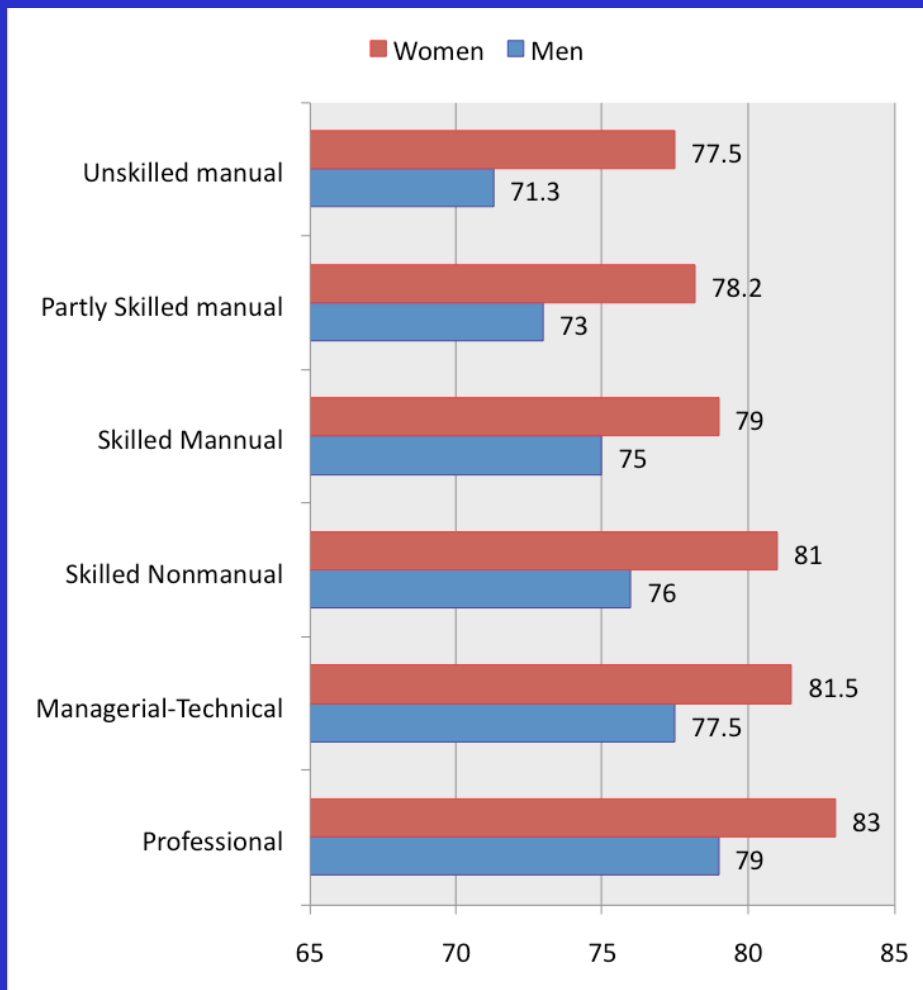
Differences in the quality of life within and

between countries affect how long people live. A child born in Japan has a chance of living 43 years longer than a child born in Sierra Leone.





## Occupational class difference in life expectancy, England, 1997-1999



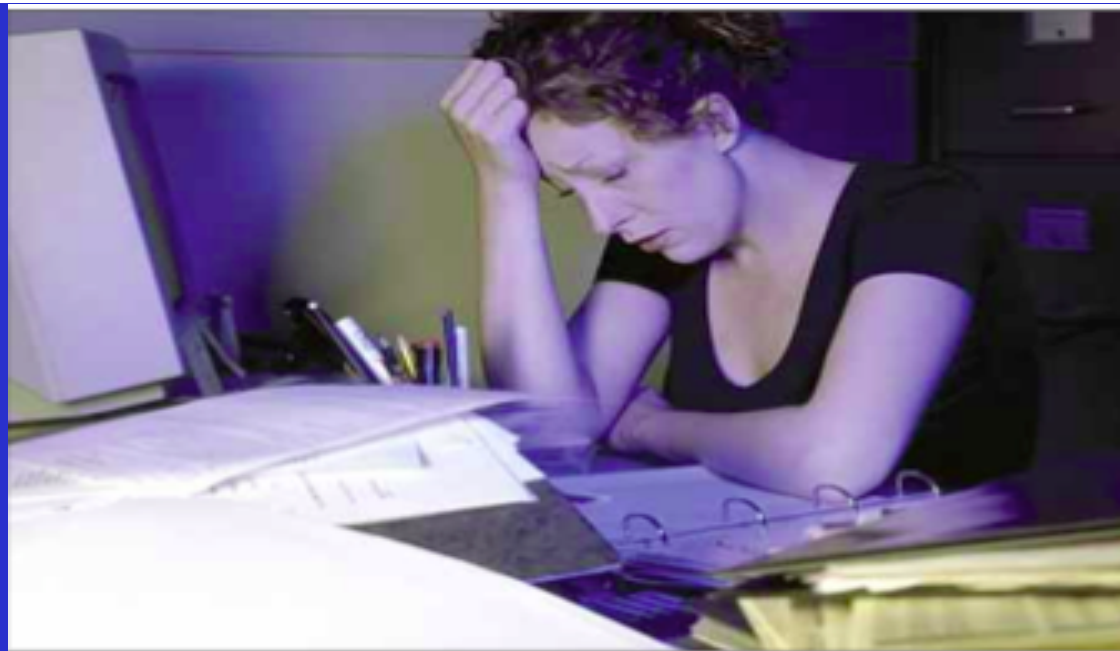
# Stress



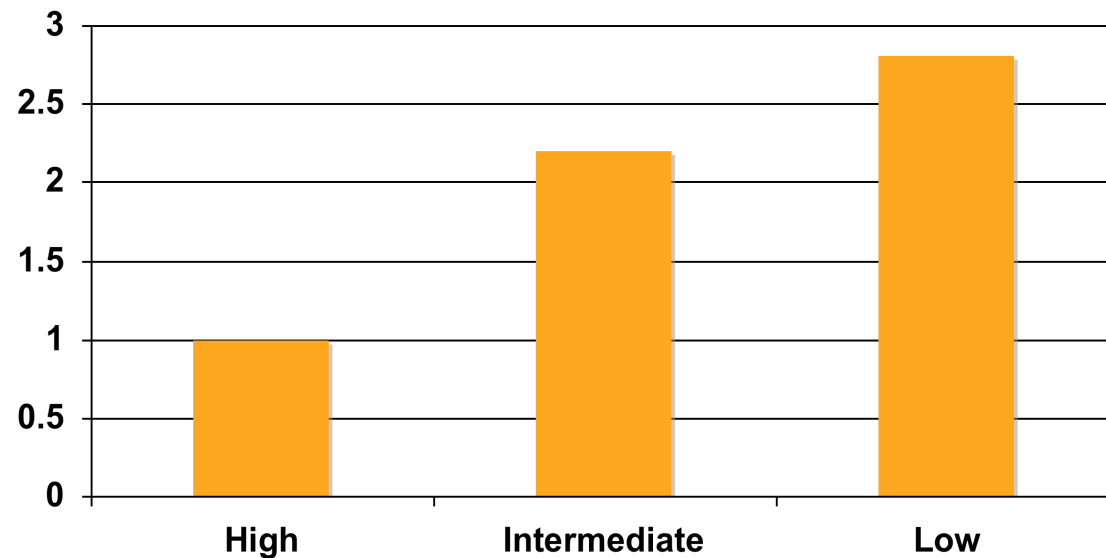
Lack of control over work and home can have powerful effects on health.

# Work

Self-reported level of  
Job control and  
Incidence  
of coronary heart  
disease in men and  
women



Risk of CHD with high job control at 1.0



Poor Control

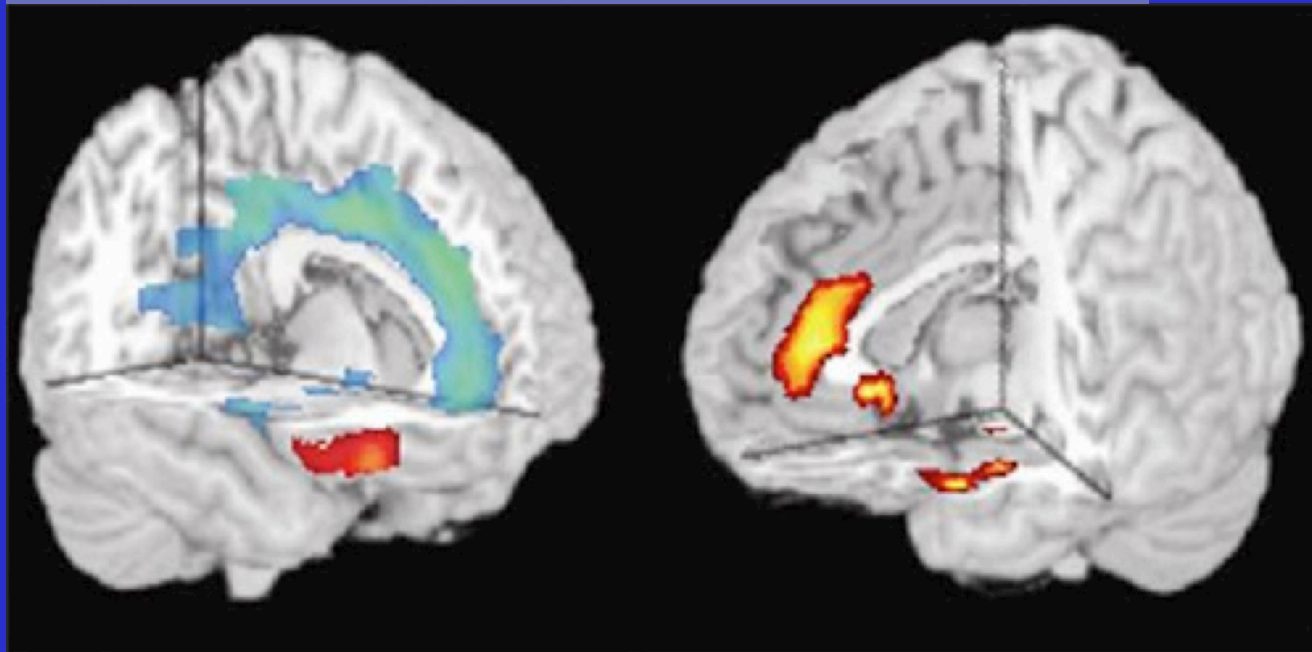
- Inability to use their skills
- Low decision -making authority
- ( European Study)

**Jobs with high demand and control carry special risk**



National Institute of Mental Health

Reducing the burden of mental illness and behavioral disorders through research on mind, brain, and behavior



## Aggression-Related Gene Weakens Brain's Impulse Control Circuits

"By itself, this gene is likely to contribute only a small amount of risk in interaction with other genetic and psychosocial influences; it won't make people violent," explained Meyer-Lindenberg. "But by studying its effects in a large sample of normal people, we were able to see how this gene variant biases the brain toward impulsive, aggressive behavior."

The gene is one of two common versions that code for the enzyme monoamine oxidase-A (MAO-A), which breaks down key mood-regulating chemical messengers, most notably serotonin. The previously identified violence-related, or L, version, contains a different number of repeating sequences in its genetic code than the other version (H), likely resulting in lower enzyme activity and hence higher levels of serotonin. These, in turn, influence how the brain gets wired during development. The variations may have more impact on males because they have only one copy of this X-chromosomal gene, while females have two copies, one of which will be of the H variant in most cases.

# Can More Touching Lead to Less Violence in Our Society?

It probably can if Developmental Neuropsychologist James W. Prescott's Pleasure/Violence Reciprocity Theory is correct.



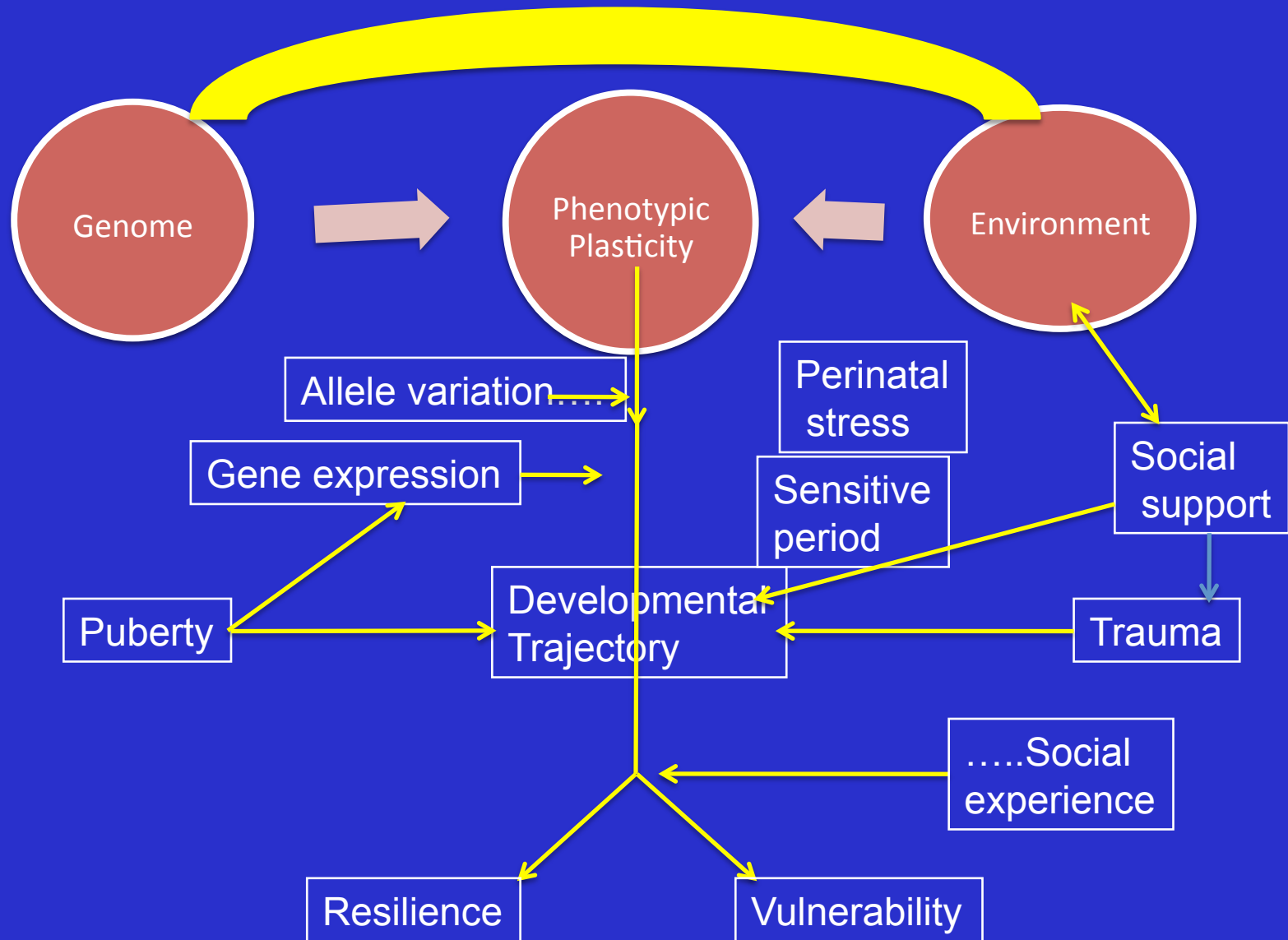




- It is more clearly understood now the genetic mechanism play important role in providing the fertile or infertile background for behavioral characteristics which causes and modulates individual 'vulnerability'

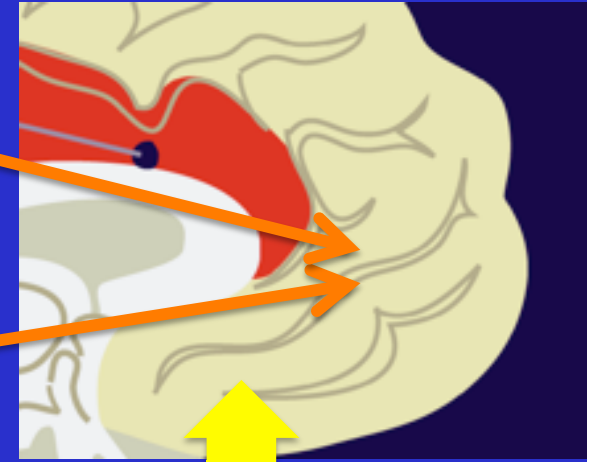
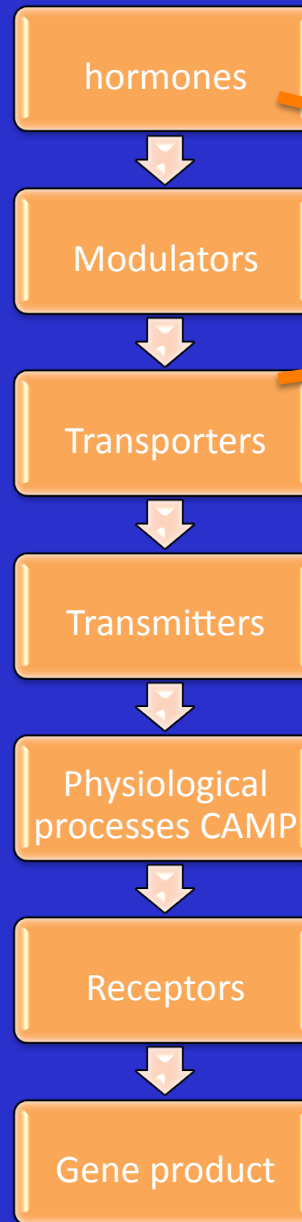
# Developmental determinants of sensitivity & resilience to Stress,

Psychoendocrinology, (2005) 30



## Development of PFC

- Adrenals
- Thyroid
- CRH
- Estrogen
- Prolactin



Molecular genetic approach to investigate individual variations in behavioral & neuroendocrine stress responses.  
Psychoneuroendocrinology (2002)

Molecular Biology as a tool allows systemic screening of significant genes for search of molecular variants

## Psychoendocrinological evaluation of interventions & outcome...Limited evidence

### Social Relationship & Management of Stress

- Stress response can be ameliorated by the presence of members of same species, called social support,
- Bonding partner reduces the activity HPA
- N.Sachser et al , 1998

## Dopamine, aggression and ACE

# Therapeutic advantage?

- Long before it was observed that social changes can induce brain volume changes, There is some more light from current research in the field of imaging.
- However will the stress-endocrine response be able to reach a point of providing specific therapeutic probes remains only a matter of speculations, so far, We hope that the complexity and limitations will be minimized in future.

# Summary

- Complex research
- Hope from molecular genetics
- Synthesis of a model of stress influence is a challenge