Social Disadvantage, Gene Expression and Depressive Symptoms in a Sample of African American from the Minority Health – GRID

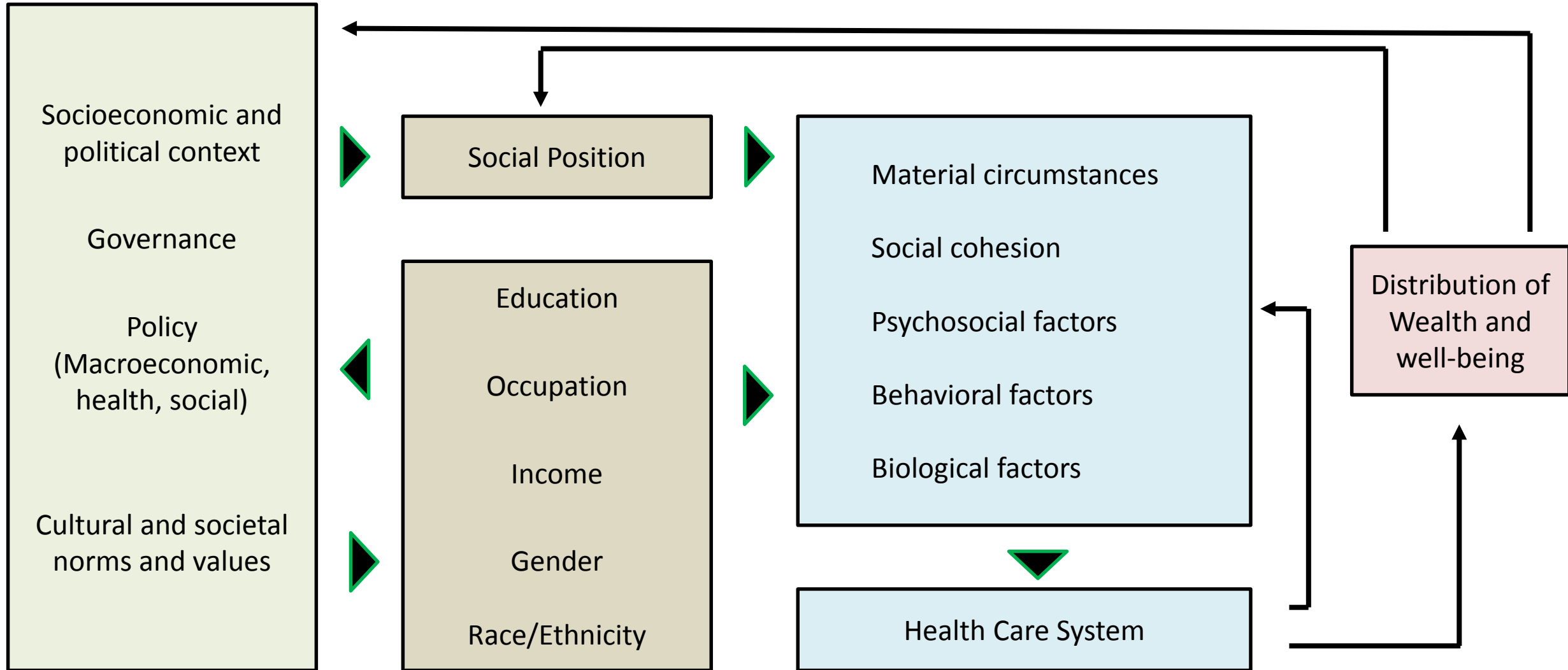**Amadou Gaye[1], Gabriel Goodney[1], Malak Abbas[1], Rakale Quarells[2], Lisa DeRoo[1], Gary H. Gibbons[1§], Sharon K. Davis[1§]**

[1]National Institutes of Health (Bethesda, MD),
[2]Morehouse School of Medicine (Atlanta, GA),
[§]Authors contributed equally

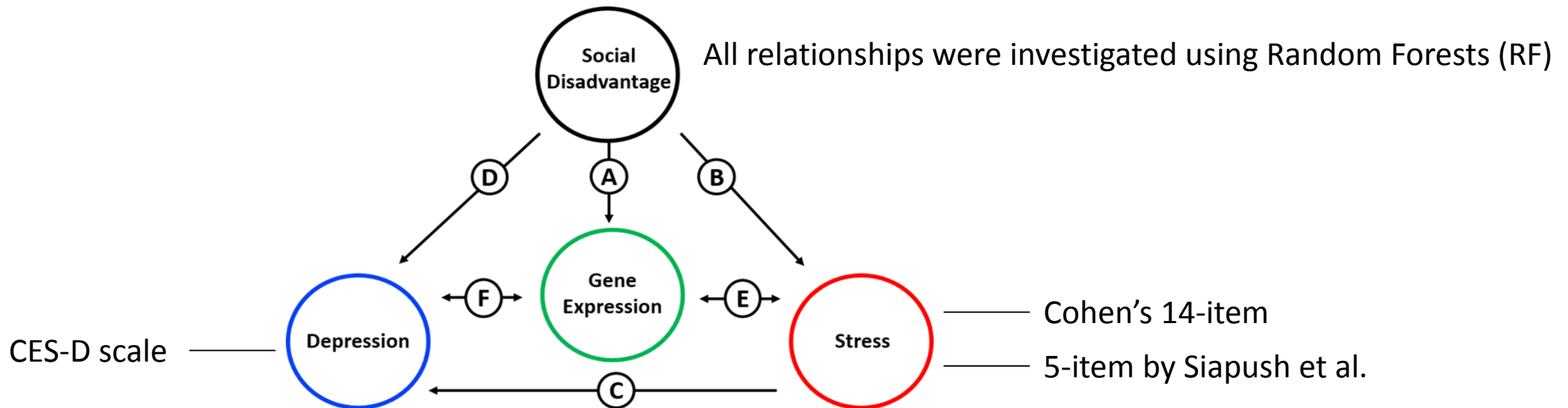❖ **Sustained exposure to unfavorable socioeconomic and environmental conditions leads to disease.**

Simplified WHO conceptual framework on social determinants of health

❖ How stressors caused by adverse socio-economic conditions are internalized?

❖ How are they subsequently manifested as perturbations in biological systems?

❖ Therefore the aim of this work is two fold:

   ❖ **Better understand how social disadvantage is manifested in patterns of gene expression (RNA-seq) in blood.**

   ❖ **Identify potential psychosocial factors that mediate its effect in a sample of 170 African Americans.**

All relationships were investigated using Random Forests (RF)

CES-D scale

Cohen's 14-item

5-item by Siapush et al.

A. Gaye, September 20th 2019, Gibbons Lab Meeting

About 'Social Disadvantage' in this project

Neighborhood Perception

1. Top tertile
2. Middle tertile
3. Bottom tertile

Level of Education

1. High School or Less
2. Technical school, some college or associate degree
3. College degree or more

Social Disadvantage

Per Capita Family Income

1. Top tertile
2. Middle tertile
3. Bottom tertile

## Home Ownership (Wealth)

1. Owns a house
2. Does not own a house

Results

❖ A transcriptome wide signature of social disadvantage involving 191 genes was identified.

❖ 44 of the genes have been reported as differentially expressed in a study of human Major Depressive Disorder by Labonte et al.

❖ Tissue-specific (blood) network, in the *HumanBase* platform, showing interactions between 20 genes in the RF lists of genes related to social disadvantage and depression scale.

Biological Insights

Social Disadvantage

Brain Development Neuroplasticity
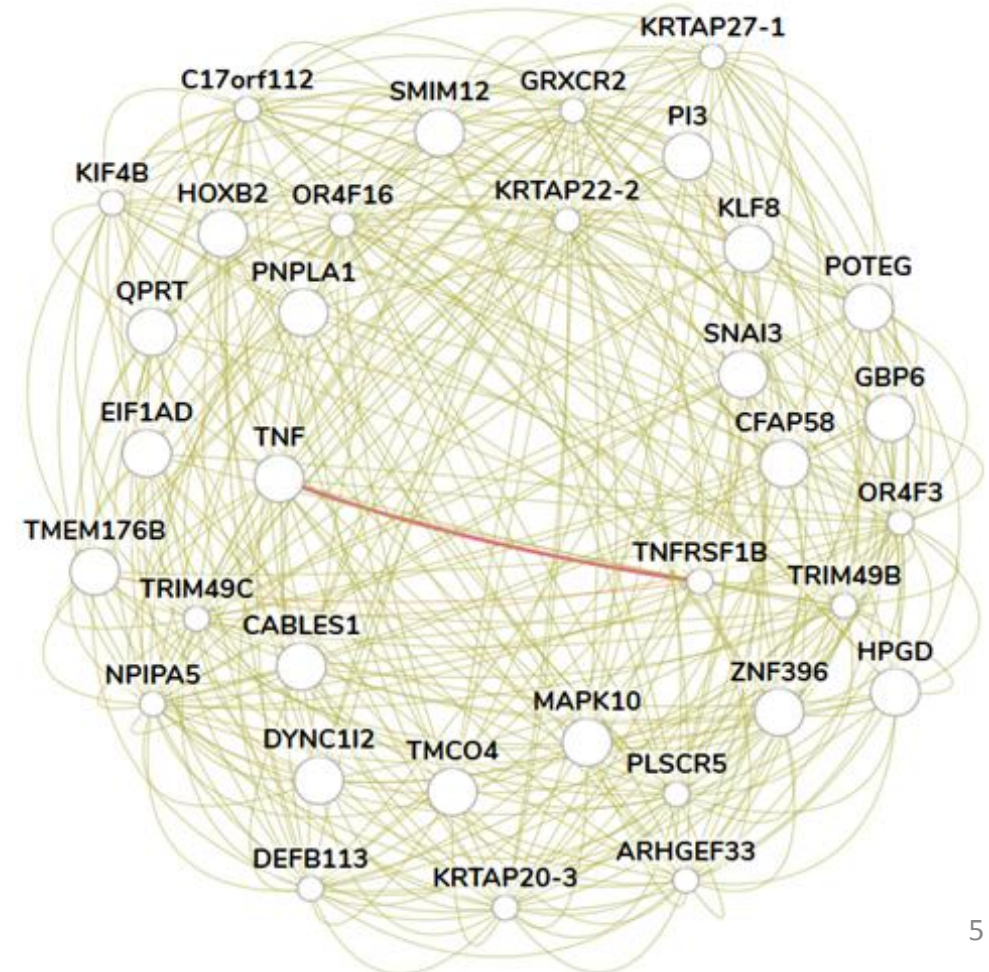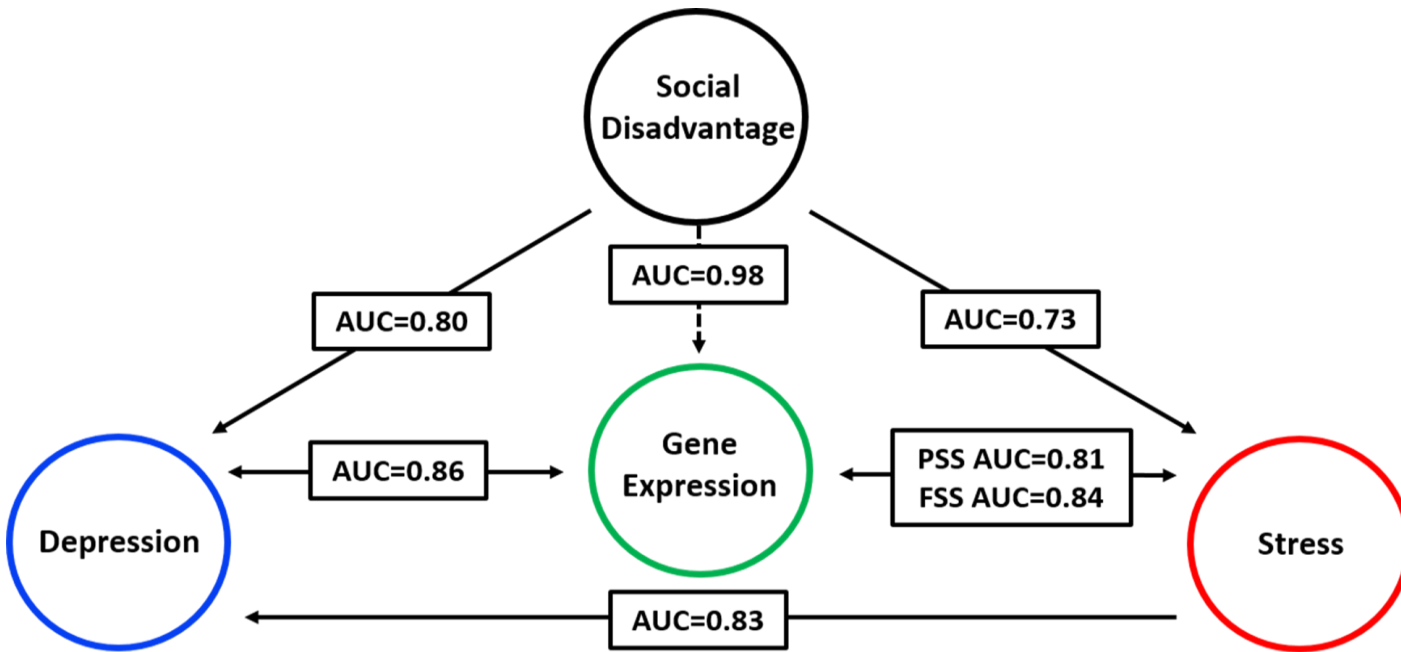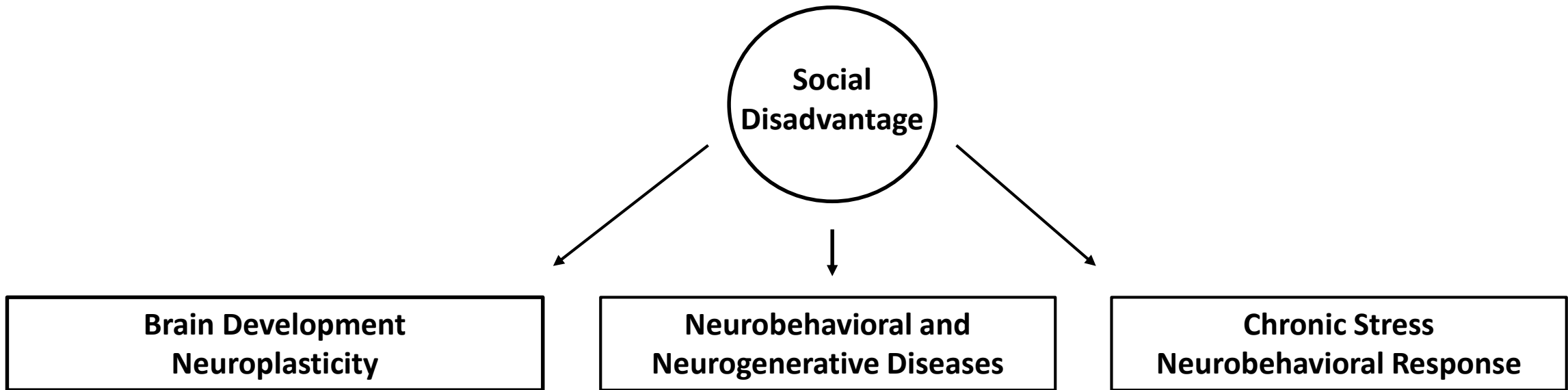
HOXB2
Important role in the formation and morphology of neurons.

CABLES1
Key role of CABLES1 for neural differentiation during embryogenesis.

DYNC1I2
From gene family modulates motors of microtubule function important for axonal transport.

Neurobehavioral and Neurogenerative Diseases

NR4A3
NR4A genes are neuroprotective agent with anti-inflammatory role in microglia and astrocytes.

Analysis of the expression of NR4As, in PBMCs), showed its involvement in Parkinson Disease.

Alteration of these genes has been associated with midbrain dopaminergic (mDA) neuron degeneration , in mice.

Chronic Stress Neurobehavioral Response

TNF
Pro-inflammatory factors like TNF-α cause neuroplastic deficits as opposed to anti-inflammatory cytokines which improve neuroplasticity and provide regenerative effects.

NR4A3
Animal model study revealed a significant reduction of NR4A3 expression under noise stress which resulted in increased blood pressure and vascular dysfunction.