

# Examining the Systemic Complexity of Unipolar Depression

Andrea Wittenborn, PhD  
Michigan State University

Jennifer Rick, MS  
Virginia Tech

Niyousha Hosseinichimeh, PhD, MPA  
Virginia Tech

Hazhir Rahmandad, PhD  
Massachusetts Institute of Technology

# Depression is Remarkably Destructive

- Depression is the world's second leading cause of medical disability (WHO, 2010)
- 1 in 6 U.S. adults will be affected (Kessler et al., 2005)
  - 40-60% of those affected will have more than 1 episode
- The age of onset is decreasing (Kessler et al., 2003)
- Economic burden exceeds \$210 billion/year in the U.S. (Greenberg et al., 2015)

# Depression is Resistant to Change

- Despite decades of widespread public awareness campaigns, research, and intervention, rates remain stable (Ferrari et al., 2013)
- Intervention findings
  - Antidepressants have not shown a consistent advantage over placebo pills (Kirsch et al., 2008)
  - Only half of psychotherapy patients recover after their first course of treatment (e.g., Barber et al., 2012)

# Depression is Heterogeneous

- Diagnosed when 5 or more of the 9 symptoms are present for 2 weeks
  - Symptoms: depressed mood, diminished pleasure, change in appetite, sleep problems, psychomotor changes, fatigue, worthlessness, inability to concentrate, recurrent thoughts of death
- This equates to 1,497 different symptom combinations (Østergaard, Jensen, & Bech, 2011)

# Depression Research is Often Narrowly Focused

- Theories of depressive pathogenesis range from
  - Cognitive theories
  - Hypothalamic-pituitary-adrenal axis dysfunction theory
  - Inflammation theory
  - Neurodegenerative theory
  - Marital discord theory
- Studies are designed to examine one cause of depression

Table 1. Results of PubMed search for articles on major depressive disorder 1980-2014

Terms	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Cognitive bias	331													
2. Rumination	11	263												
3. Memory	3	8	296											
4. Social isolation	4	4	1	363										
5. Financial stress	0	0	2	9	280									
6. Immune response	0	0	1	5	0	816								
7. Cortisol	2	3	12	27	2	56	1884							
8. Hippocampus	0	0	3	4	1	2	15	151						
9. Sleep	3	6	4	7	11	43	127	0	2820					
10. Gene	2	5	5	8	2	58	38	10	37	1552				
11. Personality disorder	9	5	3	6	0	3	17	1	19	7	1225			
12. Diet	2	0	0	0	0	24	5	0	11	15	3	294		
13. Exercise	1	0	3	7	2	16	15	0	47	5	0	15	547	
14. Early adverse experiences	6	4	0	2	0	10	21	8	1	40	16	0	1	347

# Issues in Depression Research

- **Classification Systems**
  - View an underlying “essence” as directly responsible for depression; may benefit from a shift to defining the complex causal mechanisms that underlie and sustain depression
- **Psychometrics**
  - Approaches often assume a linear and latent variable model and fail to estimate intra-individual effects
- **Treatment Approaches**
  - Typically use a trial and error approach instead of one that is personalized

# Qualitative Model of Depression Dynamics

- We created the first conceptual model of depression dynamics using a structured mapping approach (Hu et al., 2011)
  - Broad scope of causal mechanisms and the interactions among them
  - Continuous definition of depression (Aggen et al., 2005; Hankin et al., 2005)
  - Mapped findings from human models (Seok et al., 2013; Lacro et al., 2014)
  - Mapped reinforcing feedbacks only due to breadth of model
  - Genes, personality, gender, SES, diet, exercise, and other random life events are exogenous variables



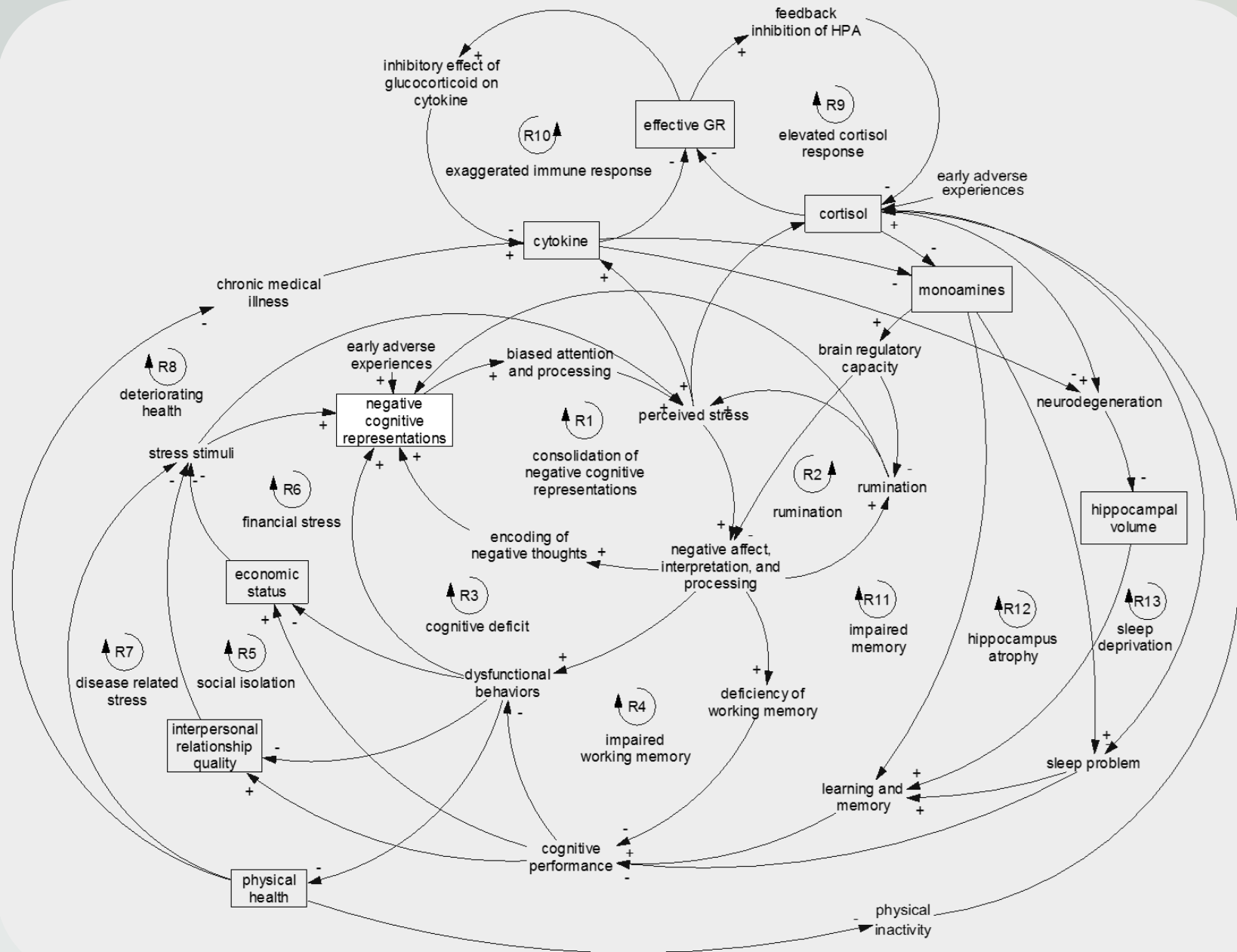


Figure 1. Qualitative model of adult depression dynamics

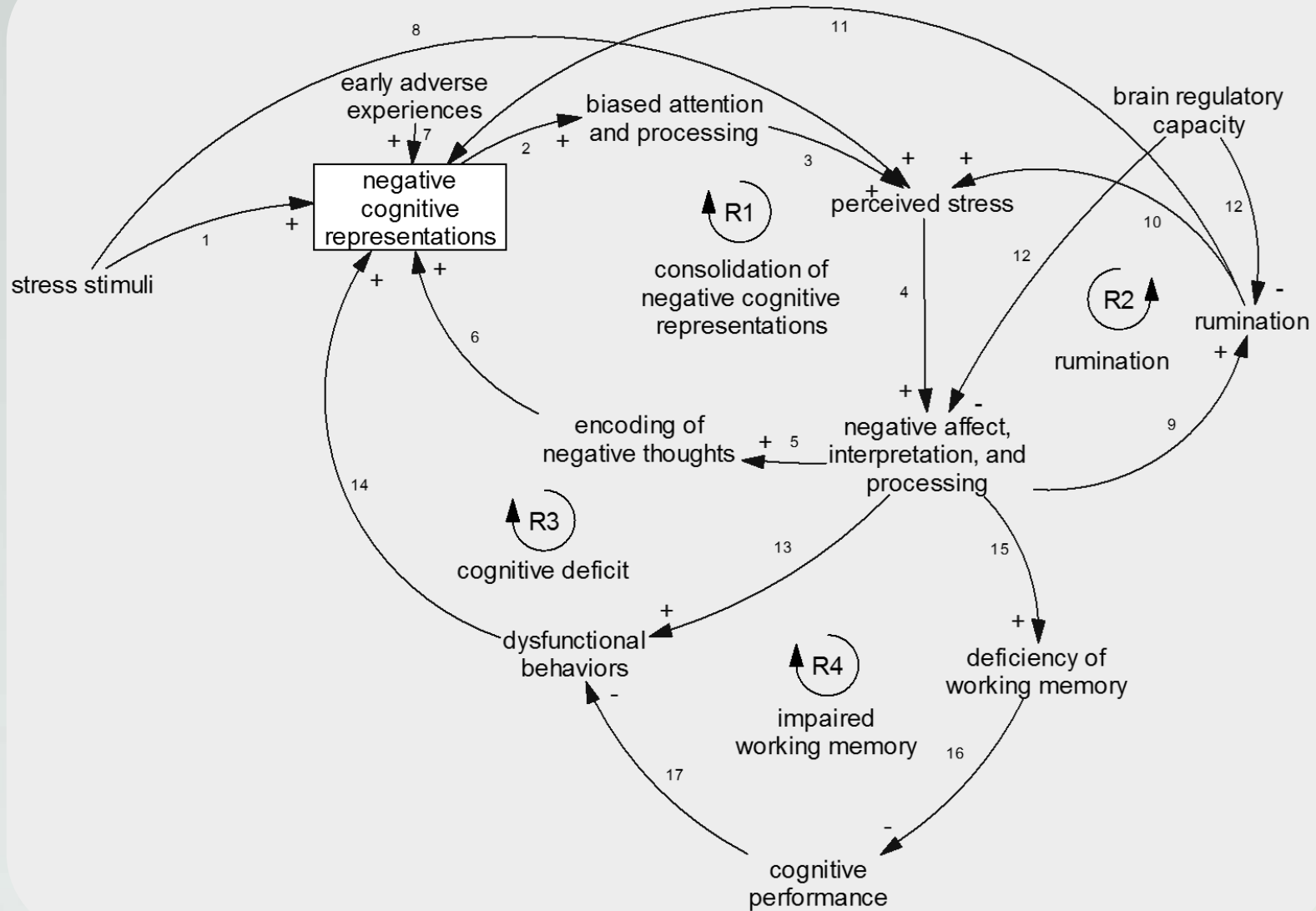


Figure 2. Cognitive dimensions

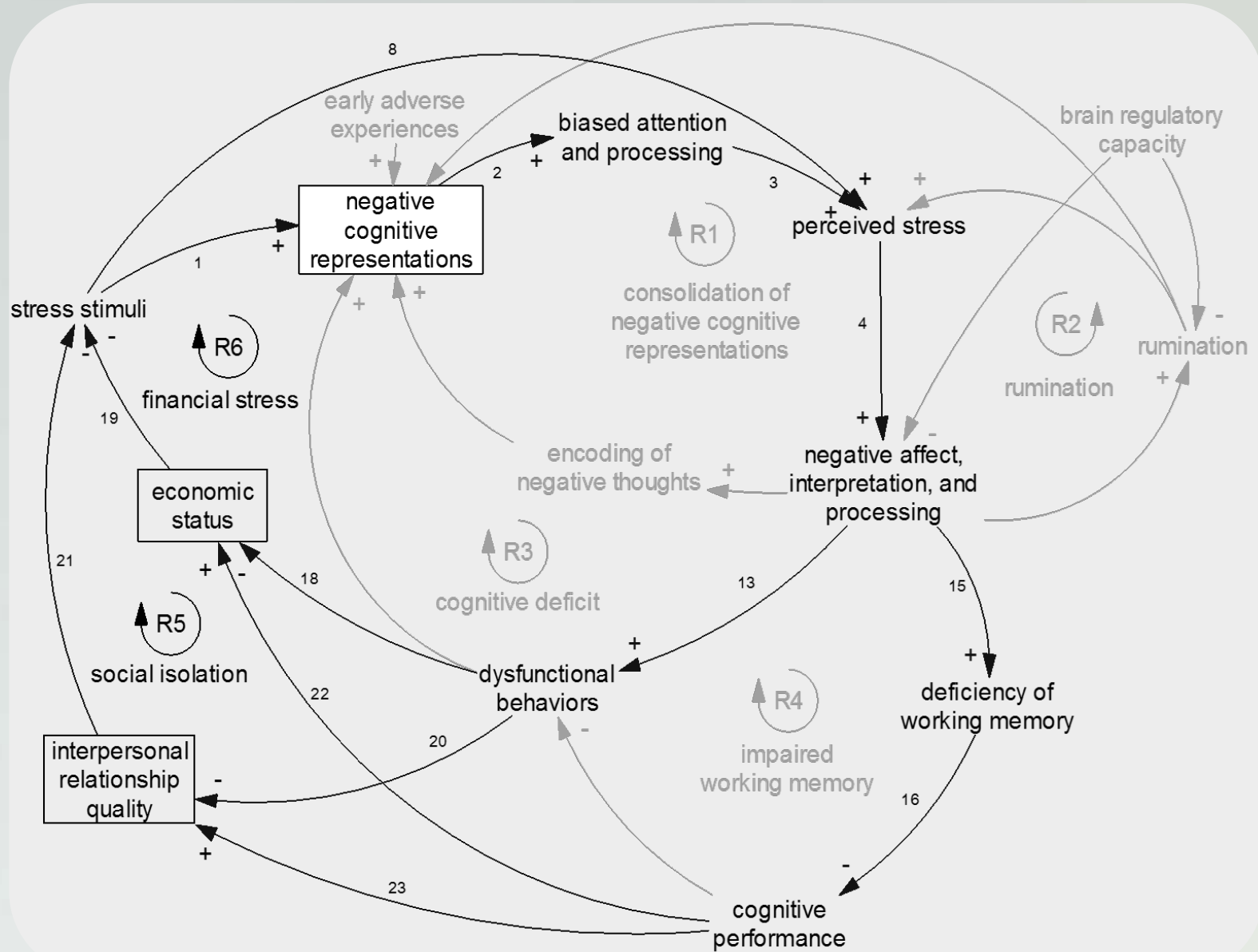


Figure 3. Cognitive, social, and environmental dimensions

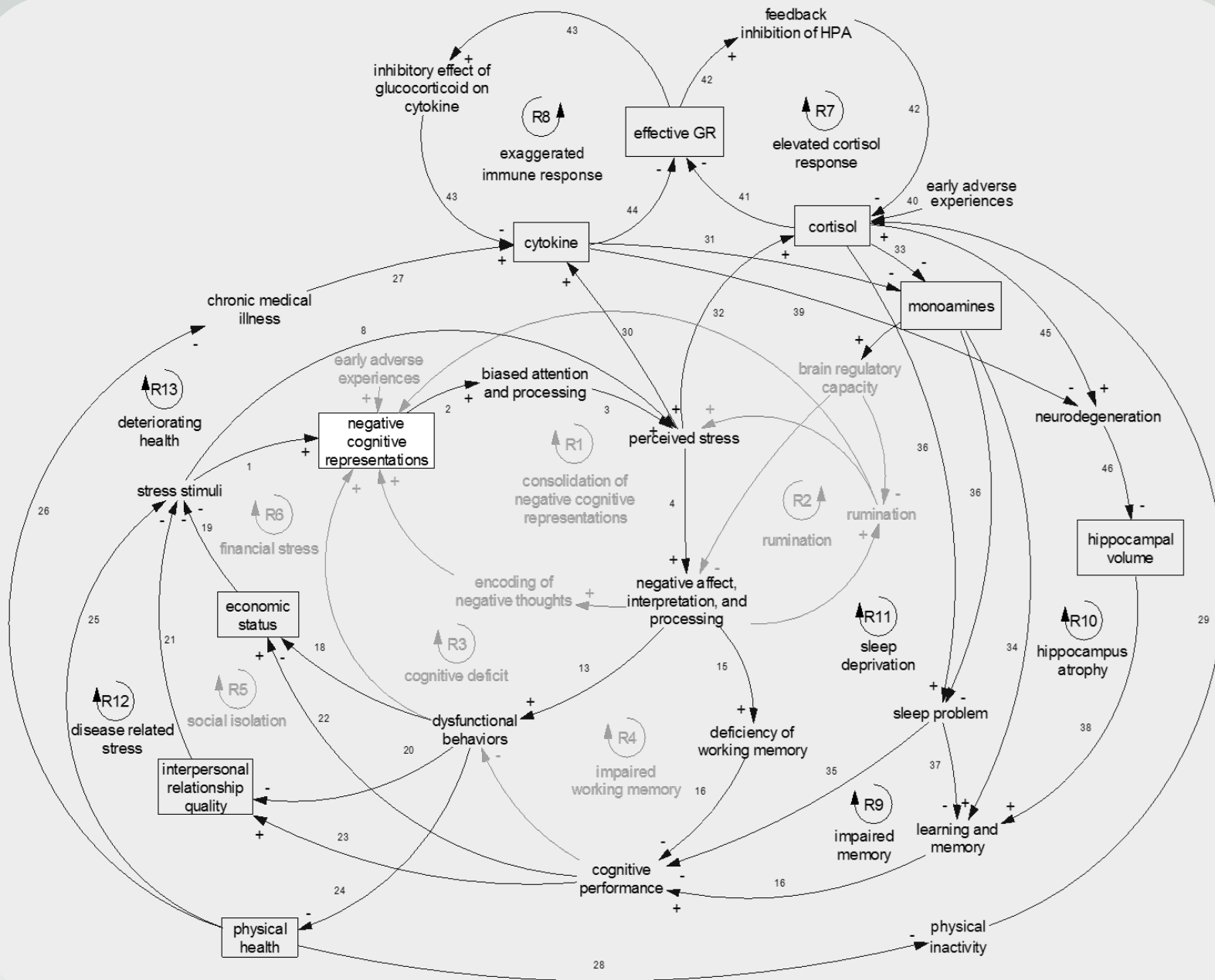


Figure 4. Cognitive, social, environmental, and biological dimensions

## Conceptual insights produced by the model (so far)

- Depression is mapped as a partially endogenous condition
- Stock variables, their speed of change, and interactions among them were identified
- Our model illustrates how feedback loops can reinforce small differences and take patients to distinct equilibria

# Future Directions

- Expansion of qualitative and quantitative modeling of depression dynamics to
  - Identify leverages and priorities at an individual level
  - Map major stock variables and treatment modalities to test for the optimal treatment approach for a given patient
  - Identify vulnerabilities or tipping points of illness to inform prevention strategies

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