

1. Background

Depression and dementia frequently co-occur, but their biological relationship remains difficult to interpret. This review maps convergence across circuits, neurotransmitters, mechanisms and clinical timing.

2. Aim

To identify reproducible points of convergence between depression and dementia and integrate them into a comparative network model of shared neural vulnerability.

3. What is new?

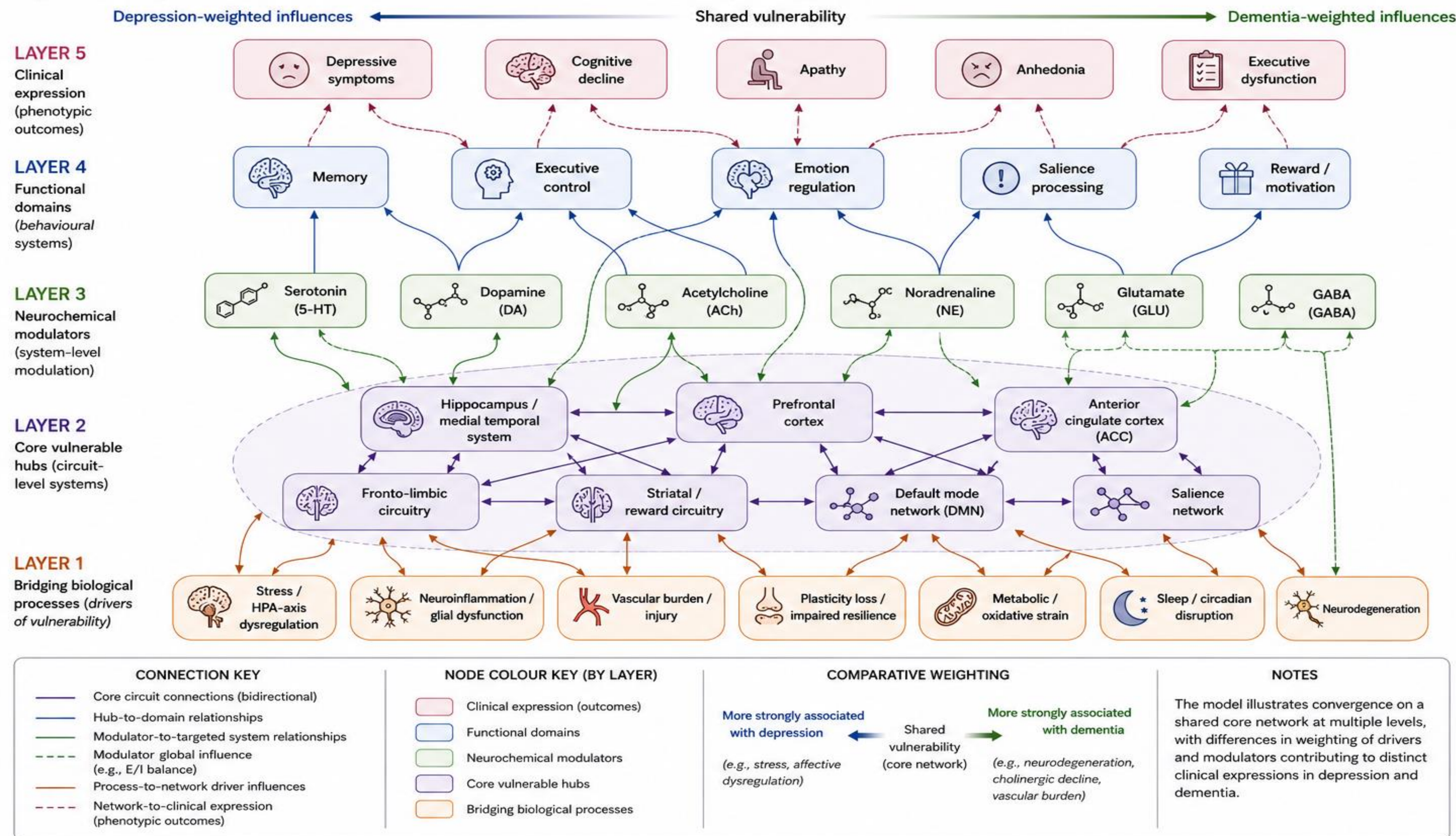
This review integrates neural circuits, neurotransmitter systems, biological mechanisms and clinical timing into a unified comparative model of depression-dementia overlap.

4. Methods

Scoping review of peer-reviewed literature from 2019 onwards. PubMed and Web of Science were searched. 45 sources included: 15 dementia, 15 depression, and 15 comorbid/overlap.

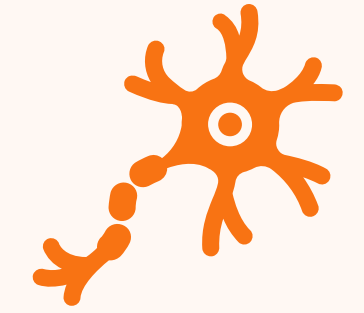
5. Comparative Network Model

Figure 1. Comparative network model of shared neural vulnerability in depression and dementia



6. Bridging Mechanisms

- Stress / HPA-axis dysregulation
- Neuroinflammation / glial
- Vascular burden
- Plasticity loss
- Metabolic strain
- Sleep disruption
- Neurodegeneration



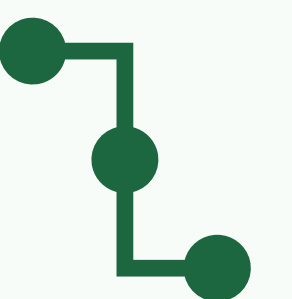
7. Circuit Convergence



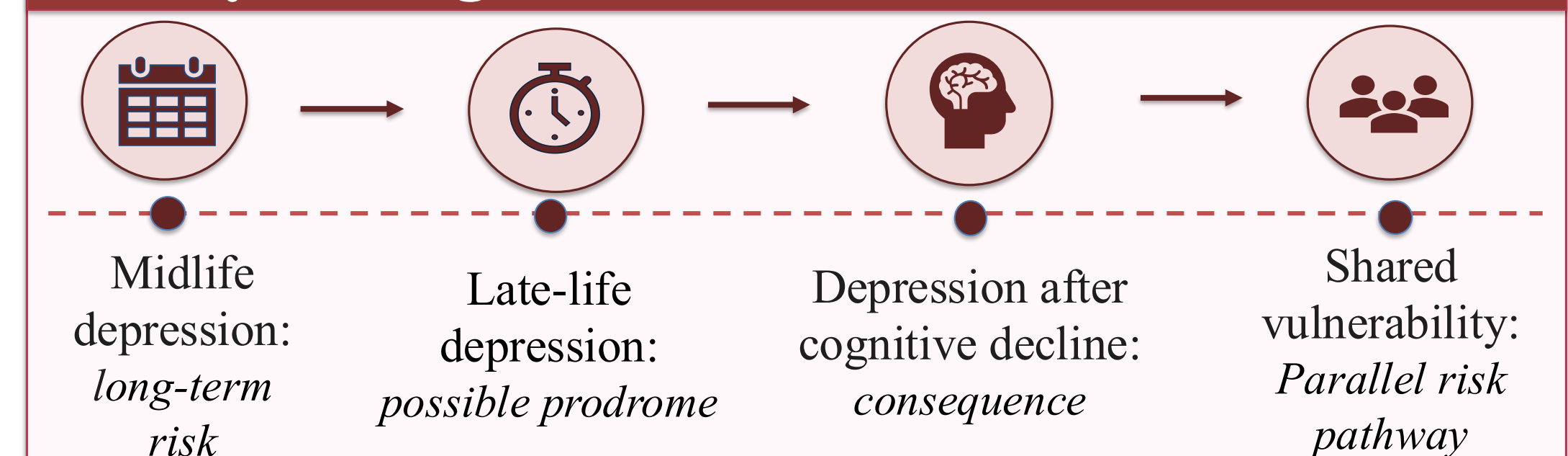
- Hippocampus / medial temporal system
- PFC / ACC
- Fronto-limbic circuitry
- Striatal / reward-motivation circuitry
- Default mode and salience networks

8. Neurotransmitter Convergence

- 5-HT (serotonin)
- DA (dopamine)
- ACh (acetylcholine)
- NE (noradrenaline)
- GLU (glutamate)
- GABA



9. Why Timing Matters



10. Evidence Map: Convergence Across 45 Sources

Convergence point	Evidence base	Functional relevance	Strength
Hippocampus / medial temporal system	D + Dep + O	Memory / stress vulnerability	●●●●○
PFC / ACC	D + Dep + O	Executive control / regulation	●●●●○
Fronto-limbic circuitry	D + Dep + O	Emotion regulation	●●●●●
DMN / salience networks	D + Dep + O	Self-referential / salience processing	●●●●○
Striatal / reward circuitry	D + Dep + O	Reward / motivation	●●●●○
Glutamate / GABA systems	D + Dep + O	E/I balance / plasticity	●●●●●
Cholinergic system	D + O, weaker Dep	Memory / cognitive-affective overlap	●●●●○

Key: D = dementia-focused studies Dep = depression-focused studies O = overlap/comorbid studies ● = stronger evidence ○ = lower strength

11. Clinical Relevance



Mapping shared vulnerability may support earlier identification of dementia risk in people with depression, especially when late-life symptoms co-occur with cognitive, executive, motivational or behavioural change.

This framework may also guide future biomarker and intervention studies targeting stress, inflammation, vascular burden, sleep and neurochemical imbalance.

12. Conclusion / Implications

- Shared vulnerability does not equal shared disease identity.
- The strongest overlap occurs across hippocampal, prefrontal-cingulate, fronto-limbic, salience, reward and neurochemical systems.
- Future longitudinal, multimodal studies should separate midlife from late-life depression to clarify risk, prodrome and intervention pathways.