

Perspective

A general neurologist's perspective on the urgent need to apply resilience thinking to the prevention and treatment of Alzheimer's disease

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Abstract

The goal of this article was to look at the problem of Alzheimer's disease (AD) through the lens of a socioecological resilience-thinking framework to help expand our view of the prevention and treatment of AD. This serious and complex public health problem requires a holistic systems approach. We present the view that resilience thinking, a theoretical framework that offers multidisciplinary approaches in ecology and natural resource management to solve environmental problems, can be applied to the prevention and treatment of AD. Resilience thinking explains a natural process that occurs in all complex systems in response to stressful challenges. The brain is a complex system, much like an ecosystem, and AD is a disturbance (allostatic overload) within the ecosystem of the brain. Resilience thinking gives us guidance, direction, and ideas about how to comprehensively prevent and treat AD and tackle the AD epidemic.

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Keywords:

Complex system; Panarchy; Resilience thinking; Resilience; Adaptability; Transformability; Allostatic load; Allostatic overload

1. Introduction

1.1. There is an urgent need to address the increasing prevalence of Alzheimer's disease

As the prevalence of Alzheimer's disease (AD) is rapidly increasing, it is necessary and urgent to develop effective strategies for diagnosis, prevention, and treatment [1]. The cumulative effects over a patient's lifetime and complex interactions of genetic, lifestyle, and environmental factors determine an individual's risk for AD [2]. Buildup of amyloid-beta (A β) and hyperphosphorylated tau as well as neuronal degeneration, blood-brain barrier pathology, neuroinflammation, oxidative stress, and microvascular, cytoskeleton, and mitochondrial changes are responsible for AD development [3]. Given the multifactorial etiology of AD, it is important to consider use of comprehensive, life course approaches to pre-

vent and treat this disease, and pay more attention to the multiple risk factors of AD such as coronary artery disease, diabetes, hypertension, obesity, cancer [2,4], environmental pollution [5,6], cigarette smoking, and chronic stress [7–9]. As chronic diseases (e.g., insulin resistance and diabetes) are on the rise, the prevalence of AD is expected to increase. There is evidence that neuroinflammation and oxidative stress, linked to environmental pollution, unhealthy diet, disturbance in gut-microbiota [10], and stress, are all common denominators for the aforementioned chronic conditions and dementia. Thus, it makes sense that reducing chronic inflammatory responses and oxidative stress [11,12] by lifestyle changes (e.g., promoting healthy nutrition, exercise, stress management) should become a focus of prevention and treatment of AD. Given the multifactorial nature of AD, collaboration and teamwork between neurologists, geriatricians, primary care providers, social workers, nutritionists, and psychologists need to take place to understand and treat the whole patient rather than each condition separately.

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Another problem that we face in the AD epidemic is the declining number of neurologists [13] due to the decreased interest of medical students in this specialty and increased burnout of neurologists who subsequently cut down on their number of working hours or leave their specialty altogether. Given this, the number of neurological patients (including those with AD) who are underdiagnosed and undertreated is going to increase. Addressing burnout among neurologists and all physicians is an urgent problem to be solved in the era of a worsening epidemic of chronic diseases. Caregiver burnout also is on the rise, leading to an increase in stress-related chronic conditions among caregivers, another challenging and important problem that requires urgent solutions.

Focusing research on elimination of amyloid plaques and neurofibrillary tangles is not enough to tackle the epidemic of AD without enhancing our population's vitality, resilience, social connectivity, and addressing environmental and social issues. AD is a complex problem that needs to be viewed on many different levels and scales, such as the individual patient, health care, family, and society. Biological, psychological, sociological, and technological contexts also need to be taken under consideration.

This perspective is written from the point of view of a general neurologist and proposes merging a holistic approach to a patient with AD with the approach of a clinician specializing in dementia research. The authors (the second author is a psychologist who is very familiar with the socioecological model) feel that both approaches are equally necessary: in the holistic approach, the patient is treated as a unique and interconnected system, embedded within its context; in the clinical specialists' approach that is based on research of the disease, important generalizations and conclusions about AD pathophysiology and natural history are uncovered. In this perspective, the authors address merging a practical approach with theoretical research because of the growing epidemic of the disease, lack of effective treatments, urgency, and angst to find solutions. The authors are part of interconnected systems forming the health care system that include specialists, psychologists, geriatricians, primary care providers, nutritionists, nurses, and staff, whose goal is to address not only a disease but also problems related to it. Because AD is a complex disease affecting all aspects of a person's life, it is essential for the health care system and its parts to communicate, act in unison, recognize, and address those challenges.

2. Method: Review of literature on resilience concepts and resilience thinking

2.1. Resilience research and resilience thinking in health sciences

Resilience thinking originated in ecology [14] and includes the concepts of resilience, adaptability, and transformability [15]. These emerging phenomena characterize

the nature of a complex system and its behavior. Resilience is the capacity of socioecological systems to continually change and adapt while remaining within critical thresholds [16,17]. Adaptability is the capacity of the system to learn, use experience and knowledge, adjust to a changing environment, and continue to develop within critical thresholds. Transformability is the capacity to cross thresholds into new developmental trajectories to create a fundamentally new system when ecological, economic, or social structures make the existing system untenable [15]. Resilience thinking describes a natural, self-evolving, and self-emerging process in all complex systems. It represents a theoretical framework that emerged out of the observations that an ecosystem can thrive while undergoing transformations in response to stress [17].

2.2. Complex systems in resilience thinking

Research in socioecology reveals that we live in multiple complex systems and that complex systems interact with each other and form subsystems of larger systems, a concept known as panarchy [18]. Panarchy takes into consideration the cross-scale, cross-disciplinary, dynamic, and unpredictable nature of complex systems [14]. A complex system consists of agents that interact with each other in a random way (e.g., organisms, neurons) and out of that interaction patterns arise that send feedback to the agents, modulating their behavior [19]. The boundaries of complex systems are arbitrary because the system interacts and often merges with other systems and the environment. The choice of complex system boundaries will determine which agents (components or species) and interactions are analyzed [3]. Examples of complex systems are numerous and include the universe, climate, ecosystem, social organization, community, family, health care system, patient, doctor, brain, or individual cell.

Over time, a complex system changes shape, transforms, and self-evolves in response to the environment, so it must be studied within its context and other interconnected systems. It is never in perfect equilibrium but rather fluctuates between critical thresholds. It may even pass a threshold and become a new system. The driving force is the resilience of the system that moves it forward. The system absorbs the stress, adapts, and changes its shape in response to a constantly changing environment with which the complex system coevolves [17]. Any complex system goes through adaptive cycles and fluctuates between states of growth and collapse [14,16].

2.3. Allostasis: Mechanisms of adaptation in response to stress

Resilience thinking is not only about bringing the system back to balance but also about moving beyond thresholds and developing a new balance (regime shift) in response to challenges. Stress and resilience are tightly linked and influence each other [20]. Resilience incorporates stress or

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