Brains are complex, and they engage with complex (social, biological, physical, technological) environments. Susan Fitzpatrick’s essay is a necessary call to action, stressing the importance of embracing this reality if we hope to make significant progress in understanding aging brain function and its breakdown in age-related disease. Central to her discussion is a consideration of the individual.

With the introduction of new methods and tools for measuring and studying the complex organization of the brain and its interacting components, efforts to understand brain function through the lens of networks have been reenergized. Descriptions of Alzheimer’s disease, and brain aging more generally, have frequently invoked network-related concepts to explain patterns of brain structure and function. However, it is only recently that this research has been able to apply a formal science of networks to characterize the observations.

As a cognitive neuroscientist who studies aging brain networks, I am a part of this effort, and I share Fitzpatrick’s enthusiasm about studying the brain as a complex and adaptive system. It’s important to emphasize how a network-based approach has particular appeal when considering the person-to-person variability that accompanies aging. It’s easy to recognize that some individuals maintain good cognitive health well into their later adult years, while others are more vulnerable to rapidly declining cognitive ability and disease, evident even from middle age. However, although there are multiple risk factors for Alzheimer’s disease and other forms of dementia, there are rarely any determinants. The individual variability has often been described with hand-wavy explanations, but an absence of a neural substrate that adequately explains this variability has prohibited significant progress in our understanding of the causes and consequences of cognitive decline and disease. Framing the problem and observations in the context of changes in functional and anatomical brain networks that are defined and measured using formal methods provides an opportunity to understand the individual differences in resilience and vulnerability that accompany aging.
This approach has benefited other domains of science to reveal how variability in both vulnerability to network degradation and consequences of this damage is evident across many real-world networks, and can account for different observed outcomes. For example, understanding differences in citywide public transportation networks has led to a deeper appreciation of why certain cities exhibit greater fault tolerance to short- and long-term interruptions in metro or bus service, and what is needed to support and revitalize preexisting infrastructures given changing transit demands. The application of this type of framework toward understanding brain network variability across individuals is clear.

A second central idea in Fitzpatrick’s essay considers the complexity of an individual’s environment as he or she ages. In neuroscience research, features of an individual’s environment are rarely measured. When they are, they are often coarse summaries, and are primarily treated as sources of group sampling “noise” that must be statistically accounted for. However, even broad characterization of environments reveals robust associations with age-related illness. For example, economic disadvantage is related to greater incidence of dementia and age-related decline. If certain environmental factors promote brain resilience or expose brain vulnerability, it is important to know what they are and how they operate. The determinants of successful brain aging can’t be limited solely to substrates of the brain but must also include the environment with which the brain engages.

Research in cancer is quickly revealing that an effective path toward successful detection, treatment, and prediction of disease progression involves understanding not only cancerous cells but also the local ecosystems in which they flourish or fail—both the “seed” and the “soil” (as first described by the twentieth-century surgeon Stephen Paget). Progress in research on Alzheimer’s disease and other age-related diseases will benefit when we embrace a similar perspective. It’s time to study brain complexity, both in terms of brain networks themselves and also the environments in which individual brain networks develop and mature.

Gagan S. Wig

Assistant Professor of Behavioral and Brain Sciences
Center for Vital Longevity
The University of Texas at Dallas